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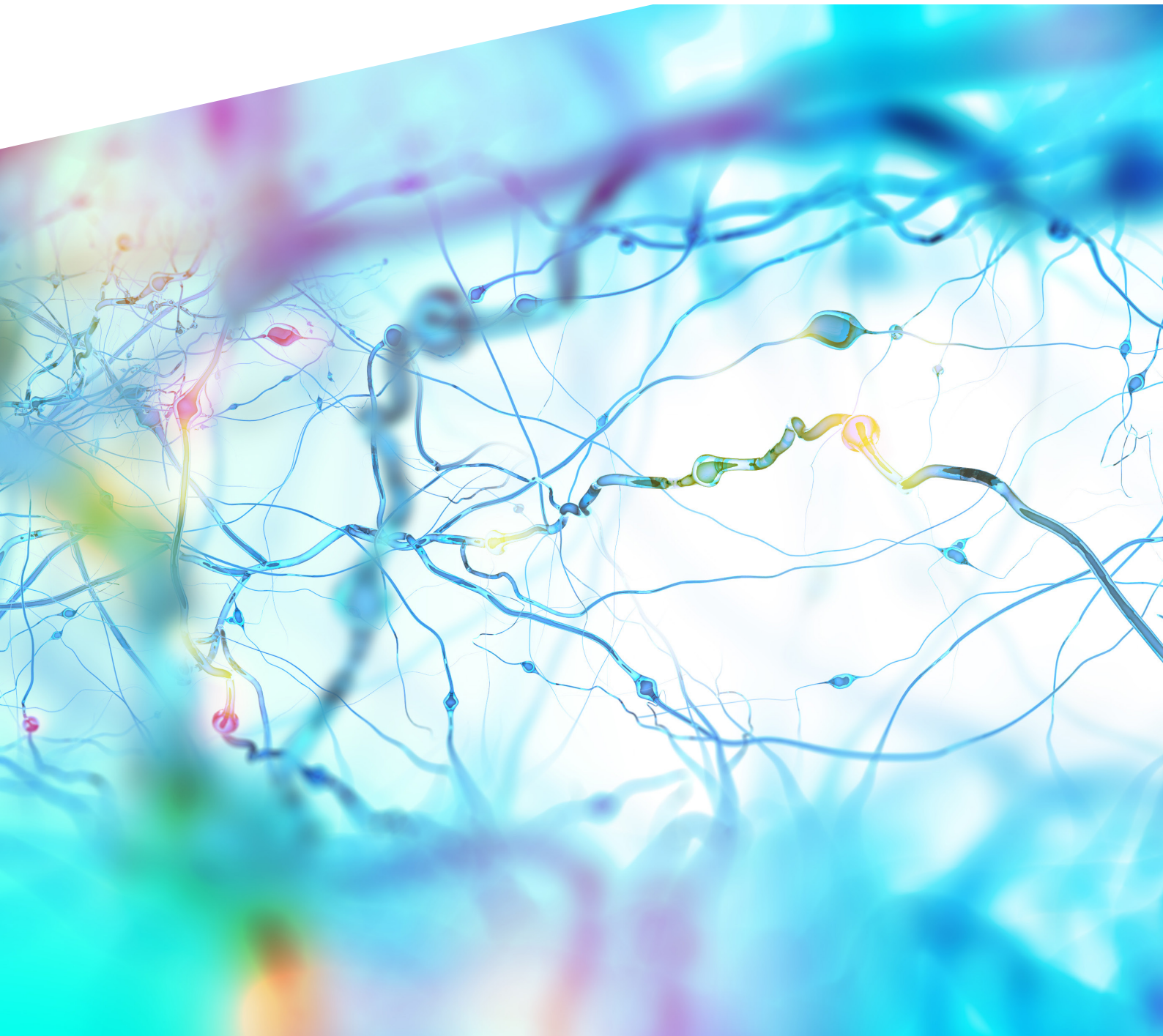

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Aims & Scope

The Ewha Medical Journal (Ewha Med J, http://www.e-emj.org), the official publication of Ewha Womans University College of Medicine and Ewha Medical Research Institute, is published quarterly a year, last day of January, April, July, and October. The first volume was published in March, 1978. It covers all fields of medical science including clinical research and basic medical science. The Journal aims to communicate new medical information between medical personnel and to help development of medicine and propagation of medical knowledges. All manuscripts should be creative, informative and helpful for diagnosis and treatment of the medical diseases and for communication of valuable information about all fields of medicine. Subscripted manuscripts should be written out according to the instructions for the Journal. Topics include original article, case report, images and solution, letter to the editor, invited review article and special issue in the respective field of medicine. The Ewha Medical Journal is indexed/tracked/covered by KoreaMed, KoMCI, KoreaMed Synapse, WPRIM, DOI/CrossRef, EMBASE and Google Scholar.

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Editorial Board

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이화의대지의 새로운 시작을 준비하며

이령아

이화의대지 편집인
이화여자대학교 의과대학 외과학교실

On the Way to New Continuum of The Ewha Medical Journal

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이화여자대학교 의과대학의 역사는 1886년 설립된 보구녀관으로부터 시작한다. 여성교육을 기치로 한 보구녀관의 교육은 이화학당과 이화여자전문학교로 이어진다. 1945년 해방을 맞으면서 1946년 이화여자전문학교는 종합대학교인 이화여자대학교로 승격되었고, 그 아래 한림원, 예림원, 행림원의 3원을 두고, 행림원에 의학과와 약학과를 설치하면서 전문적인 의학교육이 시작되었다. 1947년에는 의학과를 의학부로 승격하고, 그 산하에 4년 과정의 본과와 2년 과정의 예과를 두었다. 1951년 행림원은 의약대학으로 개칭하였다가 1954년 의과대학과 약학대학이 분리되었고, 1971년 의과대학, 간호대학, 부속병원으로 구성된 의료원이 발족하였다. 1970년대에 들어서서 교육과정 개편을 통해 국제적인 기준에 맞춘 의학교육체계를 수립하면서 연구여건의 개선과 연구진작을 위하여 열악한 환경 속에서 1978년 이화의대지를 창간하게 되었다(Fig. 1A, 1B).

당시 학장이었던 김구자 교수의 창간사를 보면 이화여자대학교 창립 92주년, 의과대학 개교 33주년을 맞아 숙원이었던 의화의대지를 발간한다고 하며, 우리의 손으로 만들고 우리의 힘으로 키워나가고자 한다고 하였다(Fig. 1C). 또한 1호 판권란에는 투고규정이 같이 표기되어 있고, 발행인과 편집인을 모두 학장이 겸임하고 있었음을 알수 있다(Fig. 1D). 당시 연 4회 발행하던 이화의대지는 연구환경이 급변하는 2000년을 맞이하면서 원고투고의 감소로 연 3회 발간하다가 2002년부터는 연 2회 발간하게 되었다. 교수들의 업적평가가 국내학술지의 게재논문보다는 국제학술지 데이터베이스인 Science Citation Index(SCI) 게재논문으로 편향되면서 국내학술지인 이화의대지는 논문의 투고가 감소하면서 발행의 어려움을 겪게 되었다. 2008년 web of science를 운영하던 Thomson Reuters 사의 학술지 등재평가방식에서 지역학술지의 우대평가정책이 시행되면서 국내학술지들이 속속 SCI expanded에 등재되는 변화가 시작되었다. 2010년 홍기숙 교수가 이화의대지 편집인으로 취임하면서 국제색인서비스에 등재하는 노력이 필요하다는 결정하에 이화의대지의 표지와 내지를 전면 개편하고(Fig. 2), 논문작성기준을 국제적표준에 맞추는 노력을 하면서 2011년 의학학술지편집인협의회에서 운영하는 KoreaMed와 KoreaMed Synapse에 이화의대지를 등재하게 되었다. 그후 EMBASE와 Google scholar에 등재하면서 국제적인 검색이 가능하게 되었고, 현재는 emerging SCI에 등재되어 그 역량을 인정받고 있다. 2017년부터는 전면 온라인학술지를 표방하면서 실물잡지는 발행하지 않는다.

이화의대지는 의학종합학술지를 표방하고 있으나, 일반학술지와는 달리 의학교육에 중심을 둔 편집정책을 운영하고 있다. 대한의학회 산하 여러 학회에서 발간하는 학술지들이 질적 향상을 도모하면서 전면 영문화하게 되어 현재 주

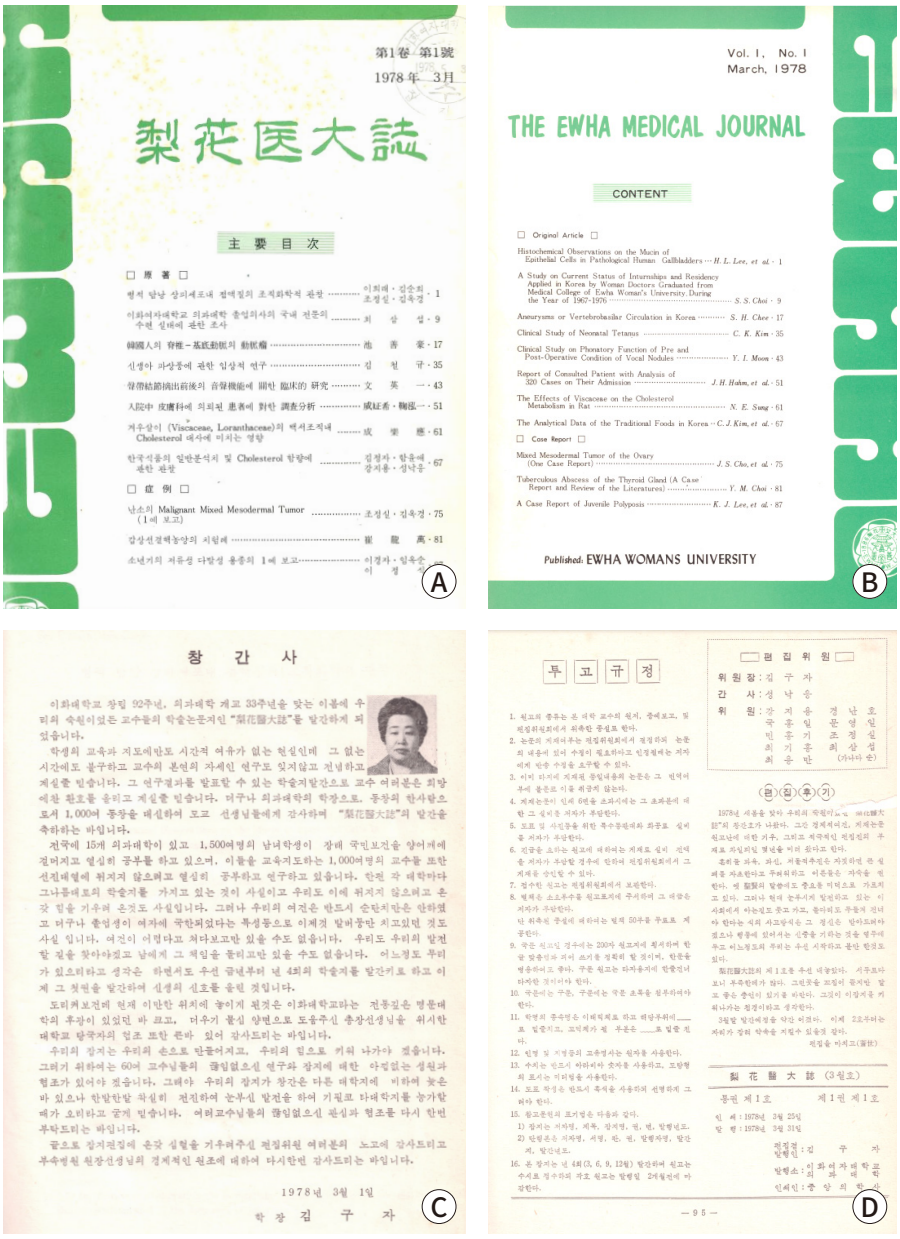

Fig. 1. Cover page of first issue of The Ewha Medical Journal. (A) Front page, (B) back page, (C) opening address of the Dean, Professor Koo-Ja Kim. (D) Copyright page and author instruction.

요 학술단체의 학술지들은 영문으로 발간되고 있다. 일부 국문학술지를 개별 발간하거나 국영문 혼용으로 발간하는 학술지가 있으나, 영문발간정책이 확대되어가는 추세이다. 그러나 이화의대지는 국문 논문을 꾸준하게 발간하면서 종설의 경우 일반인이나 의학의 초보인 학생이나 전공의들이 의학일반에 대한 전문최신지견을 쉽게 접하고 이해할 수 있도록 하고 있으며, 단신증례를 발간하여 실제 임상에서 접할 수 있는, 그러나 진단과 치료가 까다로운 임상의 예를 영상과 함께 제공하여 임상의가 진료에 도움이 될 수 있도록 하고 있다.

3년간의 코로나 판데믹 사태를 겪으면서 교육과 의료 분야도 큰 변화를 앞두고 있다. 무엇보다 인터넷의 기능의 확대가 두드러진다. 이전에도 충분히 가능했으나 보안이나 형평성, 윤리, 개인정보 등 여러가지 문제로 미루어 두었던 다양한 온라인 교육의 확대나 부작용의 우려로 인한 원격진료의 불가피한 시작, 유튜브나 소셜미디어를 통한 정보의 확산 등이 학술지 시장에도 영향을 미치고 있다. 이와 같은 시대적 요구에 발맞추어 이화의대지도 한걸음 나아

Fig. 2. Changed feature at 2011. (A) Cover page, (B) paper inside.

Fig. 3. Changed cover page at 2022.

가고자 2022년 7월호를 기점으로 전면 개편하게 되었다. 우선 변화에 순응하는 학술지명의 디자인변경을 시행하게 되었다(Fig. 3). 보다 미래지향적이고 활기차며 국제적인 도약을 지향하는 형태의 최신 트렌드를 고려한 디자인이 채용되었다. 과거 인쇄물로 논문을 접하던 독자보다 컴퓨터나 모바일 디바이스를 통해 논문을 접하는 독자층이 확대되는 것을 감안하여 학술지 내지의 편집형태를 2단 편집에서 1단 편집으로 변경하여 가독성이 좋고 시야의 피로감이 적은 형태로 재개편하였다. 이러한 변화는 새롭게 오픈되는 학술지 홈페이지(https://www.e-emj.org)에서 경험할 수 있다.

이화의대지의 45년의 역사를 감사하는 마음으로 새롭게 시작하고자 한다.

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Not applicable.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Author Contribution

The article is prepared by a single author.

Ethics Approval and Consent to Participate

Not applicable.

Letter to the Editor

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EMJ, A Research Platform for "Future Ready, Ewha Medicine"

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In 1978, the foundation year of The Ewha Medical Journal, Dean Kim Gu-ja first published the academic journal entitled 'The Ewha Medical Journal (EMJ)', which was our long-cherished wish. She emphasized the journal should be published by our hands and we must develop them by our own strength. For this purpose, she also highlighted that professors should constantly conduct research and provide generous support for the journal.

Forty-four years later, we are planning to reorganize the EMJ in 2022. As the Dean of Ewha Womans University College of Medicine (Fig. 1), the first thing I would like to ask is "proactive contribution and participation of all professors and students" to continue the history and tradition of The Ewha Medical Journal.

Through reorganization such as opening to other colleges and providing a reader-friendly environment, the EMJ can quickly share the latest knowledge of medicine and health science to the general public, students, and doctors. And our journal will play the role of a forum where ideas and information can be exchanged and academic discussions will be held among researchers in Ewha Womans University. In addition, various changes such as 'Ewha Medical Education Center (EMEC)' and 'Ewha Medical Award' made under the slogan of "Future Ready, Ewha Medicine" will be significant since they are resulted from medical education research to foster doctors/medical scientists in the era of the 4th Industrial Revolution.

I hope the EMJ will serve as a channel for the professors of our college to present their research results, discuss opinions, and disseminate medical information to the students, scientists and public. I also believe the journal will serve as the foundation for fostering future talents in convergence studies, which is urgently required for medical education.

Marking its 45th anniversary, The Ewha Medical Journal's reorganization can be completed with proactive research and participation by all professors and students of Ewha Womans University. Thus, I would like to ask for your constant interest and support. Last but not least, I sincerely express my gratitude to all the editorial committee members including the editor-in-chief, Lee Ryung-Ah, for their hard work and efforts.

Fig. 1. Eunhee Ha, Dean of Ewha Womans University College of Medicine.

Acknowledgments

Not applicable.

Conflict of Interest
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Review Article

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Diagnostic and Therapeutic Strategies of Type 2 Diabetes Mellitus in Youth

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Key Words
Adolescent; Child; Diabetes mellitus; type 2; Diagnosis; Therapeutics

The incidence of type 2 diabetes mellitus (T2DM) is increasing in youth, largely in correlation with an increase in childhood overweight and obesity. Youth-onset T2DM is a major public health concern worldwide, and tends to show more aggressive features than adult-onset T2DM. Early diagnosis and treatment are important to prevent the occurrence of complications and comorbidities. However, current treatment options are limited and only modestly successful in youth-onset T2DM. Over the last few decades, significant progress has been made in the understanding of youth-onset T2DM. This review summarizes the current understanding of the pathogenesis, diagnosis, and treatment of T2DM in youth. (Ewha Med J 2022;45(3):e3)

Introduction

Type 2 diabetes mellitus (T2DM), previously referred to as *adult-onset diabetes*, is becoming increasingly prevalent in youth worldwide and is largely associated with an increase in childhood obesity [1,2]. According to the Korea School Health Examination Survey, the mean body weight was significantly higher in 2018 than in 2010 for students in most school grades [3]. In the U.S., the incidence of youth-onset T2DM increased by 4.8% per year between 2002 and 2015, with 3,916 youths newly diagnosed with T2DM during that period [4]. Although the prevalence of diabetes in Korean youth is lower than that in the U.S., it almost doubled from 0.2% to 0.4% between 2007 and 2018 [5]. The increase in T2DM in Korean youth started in the early 2000s and was predominant in boys from low-income families [6]. The prevalence of fasting hyperglycemia has also increased from 5.4% to 11.7% in Korean adolescents over the past decade [7]. Deterioration of β-cell function is more rapid in adolescents than in adults [8–10]. Moreover, diabetes-related comorbidities are highly prevalent and rapidly progressing in youth-onset T2DM compared with adult-onset diabetes [11,12]. Although there are limited pharmacologic options for the treatment of T2DM in youth, evidence based on the management of youth-onset T2DM has expanded significantly since 2014 [13]. In this review, we describe the pathogenesis of youth-onset T2DM and discuss the diagnostic and therapeutic strategies for youth with T2DM based on recent consensus guidelines in children and adolescents.

Pathogenesis of T2DM

T2DM is characterized by hyperglycemia caused by insulin resistance and an inadequate compensatory increase in insulin secretion [14]. The etiology of T2DM in youth, similar to that in adults, is multifactorial and includes genetic, environmental, and metabolic factors. Obesity, the main cause of insulin resistance, may partly alter fatty acid metabolism, which interferes with normal glucose metabolism [15]. Adipocyte-secreted factors (such as adiponectin and leptin) and obesity-induced inflammation are likely to be involved in the development of insulin resistance and T2DM [15,16]. In addition to obesity, youth with T2DM often have a family history of T2DM, which is indicative of genetic predisposition. Recent studies have also identified several established genetic risk variants of adult T2DM to be associated with youth-onset T2DM, including *GCK*, *TCF7L2*, *IGF2BP2*, *CDKAL1*, *HHEX*, *HNF1A* [17]. Other clinical risk factors involved in T2DM pathogenesis in youth include maternal diabetes prior to or during pregnancy, low socioeconomic status, sedentary lifestyle, high-risk ethnicity, and female sex [2,14,18]. The onset of T2DM in youth commonly occurs around the onset of puberty, when insulin resistance is normally transiently increased, but an appropriate compensatory increase in insulin secretion is impaired in youth with T2DM, leading to progressive failure of the pancreatic β-cells [17].

Risk-based Screening and Diagnosis of Diabetes

Pediatricians often face challenges in the early diagnosis of diabetes in youth owing to the insidious onset of symptoms, which increases the risk of complications later in life. The American Diabetes Association (ADA) recommends risk-based screening for T2DM or prediabetes in asymptomatic youth with overweight or obesity aged≥10 years (or after the onset of puberty) who have one or more risk factors [19]. These risk factors include maternal or gestational diabetes, family history of T2DM, high-risk ethnicity, signs of insulin resistance, or conditions associated with insulin resistance (such as acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight). Fasting plasma glucose (FPG), 2-hour plasma glucose during a 75-g oral glucose tolerance test (OGTT), and glycated hemoglobin (HbA1c) can be used as screening tests [20]. The diagnosis of diabetes is based on blood glucose levels and the presence of characteristic symptoms such as polydipsia, polyuria, nocturia, and unexplained weight loss [13,19]. The diagnostic criteria for diabetes in youth given by the ADA are the same as those for adults: (1) in youth with classic symptoms of hyperglycemia, diagnosis can be made if random plasma glucose≥200 mg/dL; (2) in the absence of symptoms, hyperglycemia (FPG≥126 mg/dL, 2-hour post-OGTT plasma glucose≥ 200 mg/dL, or HbA1c≥6.5%) should be confirmed by repeat testing on another day [19]. Once the diagnosis of diabetes is established, pancreatic autoantibody testing, especially for glutamic acid decarboxylase 65 autoantibodies and tyrosine phosphatase-related islet antigen 2, is useful in the determination of diabetes type [13,21,22].

Complications and Comorbidities

Youth-onset T2DM is associated with poor glycemic control and early micro- and macrovascular complications [23,24]. Insulin resistance-related comorbidities, such as hypertension, dyslipidemia, and non-alcoholic fatty liver disease, may also be present at the time of T2DM diagnosis, which can accelerate the occurrence of micro- and macrovascular

complications [25–27]. Therefore, screening for and management of complications and comorbidities is recommended at the time of T2DM diagnosis in youth and regularly thereafter [13,19]. Blood pressure measurement, assessment of random urine albumin-to-creatinine ratio, foot examination, dilated eye examination, liver transaminases, and lipid screening (preferably after optimizing glycemia) should be performed at diagnosis. Other comorbidities associated with pediatric obesity, such as obstructive sleep apnea, polycystic ovary disease, and psychosocial concerns, also should be screened on a regular basis [13,19].

Current Management of Youth-onset T2DM

The management of youth-onset T2DM should include lifestyle changes, education for diabetes self-management, and pharmacological treatment [19]. Lifestyle changes, including a healthy diet and increased physical activity, are the cornerstone of treatment and should be initiated at the time of T2DM diagnosis [28]. Healthy eating recommendations include reduced high-carbohydrate and high-fat intake, increased fiber intake, and decreased consumption of calorie-dense foods, especially sugar-containing drinks [19,29]. The recommended distribution of macronutrients is carbohydrates 45%–50% of energy, fat<35% of energy (saturated fat<10%), and protein 15%–20% of energy [30]. Additionally, aerobic and/or resistance exercises are considered to have a positive effect on insulin sensitivity [31]. Youth with T2DM should be encouraged to engage in at least 1 hr of moderate-to-vigorous physical activity daily and to reduce sedentary time [13,19]. For pharmacologic treatment, only three drug classes have currently been approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of youth-onset T2DM: metformin, insulin, and glucagon-like peptide (GLP)-1 analogues. According to the Consensus Guidelines of the ADA and International Society for Pediatric and Adolescent Diabetes (ISPAD), the initial treatment of T2DM in youth should include metformin and insulin, either alone or in combination: (1) in asymptomatic patients with HbA1C<8.5%, metformin is the treatment of choice; (2) in patients with HbA1C≥8.5% together with related symptoms without acidosis, combination therapy with metformin and basal insulin is suggested; (3) in patients with acidosis, including diabetic ketoacidosis or hyperglycemic hyperosmolar nonketotic syndrome, intravenous insulin alone should be initiated without metformin, and metformin should be added after acidosis is resolved in combination with continued subcutaneous insulin therapy [13,19]. Many youths with T2DM can successfully discontinue insulin treatment and switch to metformin monotherapy after a 2–6 weeks transition period by decreasing the insulin dose while metformin is increased [32] (Fig. 1).

For most youth with T2DM, the goal of initial treatment is to attain an HbA1c of <7.0%, and <6.5% may be appropriate for patients who have had diabetes for a short period of time, lesser degrees of β-cell dysfunction, and those who achieved significant weight improvement [19]. A higher target of HbA1C (e.g., <7.5%) can be considered in patients with an increased risk of hypoglycemia [19]. Glycemic status should be measured every three months. If patients fail to achieve adequate glycemic control with metformin at the maximally tolerated dose (up to 2,000 mg/day), basal insulin can be added, with subcutaneous liraglutide, a GLP-1 analog, as an acceptable alternative [33]. For patients who fail to meet glycemic targets despite combination therapy with metformin and basal insulin, either liraglutide or prandial insulin can be added. Bariatric surgery may be considered in young patients with T2DM who have severe obesity (body mass index>35 kg/m^2) and those who have uncontrolled hyperglycemia and/or serious comorbidities despite intense lifestyle interventions together with combination therapy with

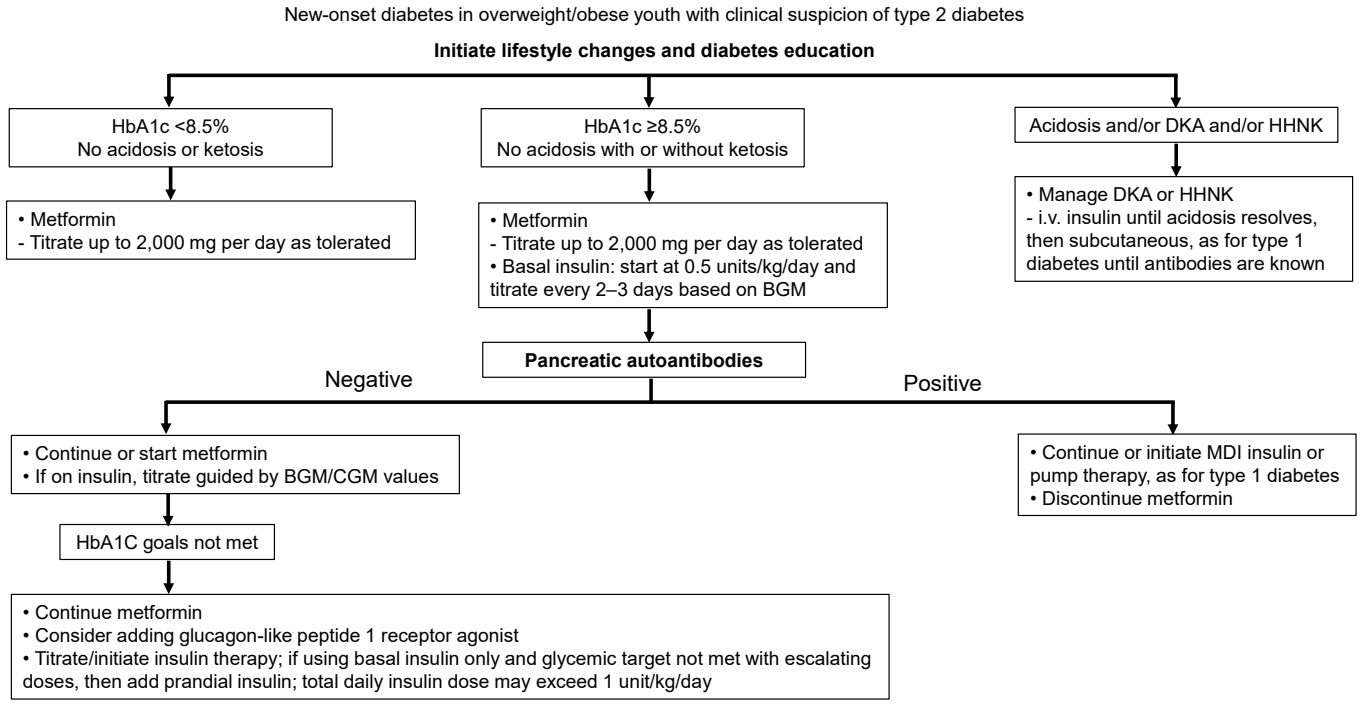

Fig. 1. Management of overweight or obese youth with new-onset diabetes. Adapted from the American Diabetes Association (ADA) position statement in 2022 with License for Non-Commercial Reuse [19]. HbA1c, glycated hemoglobin; DKA, diabetic ketoacidosis; HHNK, hyperosmolar hyperglycemic nonketotic syndrome; BGM, blood glucose monitoring; CGM, continuous glucose monitoring; MDI, multiple daily injections.

metformin, insulin, and liraglutide at maximal doses [19].

Ongoing Clinical Trials in Youth with T2DM

Clinical trials of various categories of anti-hyperglycemic agents used in adults, are underway in pediatric populations (Table 1). For example, phase III studies using GLP-1 analogs designed for once-weekly subcutaneous injections (NCT 05260021) and oral preparations (NCT 04596631) are recruiting young people with T2DM. Phase III studies of sodium-glucose cotransporters-2 (SGLT2) inhibitors are also ongoing in patients with T2DM aged 10–17 years: ertugliflozin (NCT 04029480) and canagliflozin (NCT 03170518). Furthermore, there are ongoing phase III studies using dipeptidyl peptidase-4 (DPP-4) inhibitors, including dapagliflozin and saxagliptin (NCT 03199053) and linagliptin and empagliflozin (NCT 03429543) in youth with T2DM.

Conclusion

Youth-onset T2DM is a relatively recent public health problem resulting from the obesity epidemic in many countries. While sharing a similar pathophysiology with adult-onset diabetes, T2DM in youth has the unique characteristics of rapid progression and rapid development of complications. Early detection and treatment are crucial to prevent serious comorbidities and complications. As current treatment options are not as effective in youth as they are in adults, various pathophysiology-based treatments, including GLP-1 analogs, SGLT2, and DPP-4 inhibitors, are being investigated. Further research regarding the pathogenesis of youth-onset

Table 1. Ongoing clinical trials in youth with type 2 diabetes

NCT	Phase	Drug (route)	Categories	Age of participants
05260021	III	Tirzepatide (weekly SC)	GLP-1 analog	10–18 years (child, adult)
04596631	III	Semaglutide (oral)	GLP-1 analog	10–17 years (child)
04029480	III	Ertugliflozin (oral)	SGLT2 inhibitors	10–17 years (child)
03170518	III	Canagliflozin (oral)	SGLT2 inhibitors	10–17 years (child)
03199053	III	Dapagliflozin, Saxagliptin (oral)	DPP-4 inhibitors	10–18 years (child, adult)
03429543	III	Linagliptin, Empagliflozin (oral)	DPP-4 inhibitors	10–17 years (child)

The National Clinical Trial (NCT) numbers denote ClinicalTrial.gov identifiers.
SC, subcutaneous; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose transporter-2; DPP-4, dipeptidyl peptidase-4.

T2DM is warranted to provide a basis for the development of new therapeutic and preventive strategies.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Review Article

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Screening and Management for Dyslipidemia in Korean Children and Adolescents

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Dyslipidemias; Children; Adolescent; Diagnosis

Cardiovascular disease (CVD) is the most common cause of death worldwide, and dyslipidemia is a major risk factor. Atherosclerosis can begin in childhood and continue into adulthood, thereby contributing to CVD development. Obesity is the most common cause of dyslipidemia, and the prevalence of childhood obesity and dyslipidemia is increasing worldwide, making it a public health concern. As clinical evidence has accumulated, guidelines for dyslipidemia in children have been continuously revised since 1992. The limitations of screening tests for individuals with a family history of dyslipidemia emphasize the necessity of universal screening, and non-HDL cholesterol assessment is recommended as a screening test for dyslipidemia in children. The guidelines for dyslipidemia in Korean children and adolescents published in 2017 recommend that non-HDL cholesterol screening tests be performed in non-fasting conditions at 9–11 years and 17–21 years of age. The main purpose of this article is to describe the history and rationale of lipid screening recommendations in children and adolescents and to review the currently recommended screening methods and treatments for dyslipidemia. (Ewha Med J 2022;45(3):e4)

Introduction

Dyslipidemia is a risk factor for cardiovascular disease (CVD), a major cause of morbidity and mortality worldwide. CVD is becoming more prevalent worldwide, and the CVD-associated mortality rate in Korea has steadily increased, similar to that in the United States (U.S.) [1,2]. Dyslipidemia is closely related to other CVD risk factors, such as obesity, diabetes mellitus (DM), hypertension, smoking, and metabolic syndrome (MetS) in children and young adults [3]. In Korea, as the smoking rate no longer increases and hypertension is well controlled, the incidence of cerebral hemorrhage has decreased. In contrast, the incidence of coronary artery disease and cerebral infarction has increased with an increase in the obese population [4]. Obesity is associated with an increased risk of developing insulin resistance [5]. An increase in the incidence of obesity is accompanied by an increase in MetS and DM, diseases associated with insulin resistance and dyslipidemia [6–9]. The prevalence of pediatric obesity in Korea increased from 8.6% in 2001 to 9.8% in 2017 [10]. The tendency of dyslipidemia to worsen in Korean children is also increasing. Based on the data of the Korea National Health and Nutrition Examination Survey (KNHANES) IV (2007–2009), the prevalence of total pediatric dyslipidemia was 19.7%, and according to KNHANES VII (2016–2018) data analysis, the proportion of

dyslipidemia among the pediatric population showed a tendency to worsen to 39.5% in boys and 29.7% in girls [11,12]. Approximately 20% of Korean children and adolescents aged 10–19 years have at least one type of dyslipidemia, and 56.1% of Korean obese adolescents have dyslipidemia [13]. Dyslipidemia in children and adolescents is closely related to atherosclerosis in childhood, as well as dyslipidemia, atherosclerosis, and CVD in adulthood. In addition, the first stage of CVD is atherosclerosis, which can begin in childhood, and its progression is associated with dyslipidemia [14]. Therefore, dyslipidemia is considered the most important risk factor for atherosclerosis compared to other risk factors, and aggressive diagnosis and treatment are important to lower the incidence and mortality associated with CVD [15]. Through early detection and intervention of dyslipidemia in childhood, pediatricians play a role in preventing the progression of dyslipidemia, which is very important for public health. This review focuses on the development process of pediatric lipid disorder screening guidelines, rationale for universal screening methods, and treatment for dyslipidemia in children and adolescents.

Definition of Dyslipidemia in Children and Adolescents

According to the type of increased lipid, dyslipidemia is classified into hypertriglyceridemia, hypercholesterolemia, combined hyperlipidemia (increased cholesterol and triglycerides [TG]), and hypo-HDL cholesterolemia [16]. The cutoff point for dyslipidemia in children and adolescents differs according to age, sex, and ethnicity. In 1992, the National Cholesterol Education Program (NCEP) and the American Academy of Pediatrics (AAP) suggested reference values corresponding to the 90–95th percentile for hypercholesterolemia (≥200 mg/dL) and hyper- LDL cholesterolemia (≥130 mg/dL) based on the distribution of serum lipid concentrations in children aged 6–19 years [17]. The criteria for using NCEP Panel III modified for children define hypertriglyceridemia as TG level≥110 mg/dL and hypo-HDL cholesterolemia as HDL cholesterol<40 mg/dL [18]. In 2011, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel revised the cutoff points initially developed by the NCEP and the AAP based on the population distribution [19]. The cutoff points of total cholesterol and LDL cholesterol suggested by the NHLBI, the AAP, and the NCEP were similar, but there was a difference in the cutoff points of TG and HDL cholesterol depending on the dyslipidemia research organization. The American Heart Association (AHA) recommends that TG≥150 mg/dL and HDL cholesterol<35 mg/dL be considered abnormal in children and adolescents [20]. The International Diabetes Federal (IDF) classified hypertriglyceridemia as a TG≥150 mg/dL and hypo-HDL cholesterolemia according to sex and age, with HDL cholesterol<40 mg/dL in children aged 10–15 years and HDL cholesterol<40 mg/dL (boys) and <50 mg/dL (girls) in children aged 16 years and older as standard values [21]. According to the AAP, based on the revision by the NHLBI, serum total cholesterol≥200 mg/dL, LDL cholesterol≥130 mg/dL, non-HDL cholesterol≥145 mg/dL, TG≥130 mg/dL (≥100 mg/dL in children under 10 years of age), and HDL cholesterol<40 mg/dL were defined as dyslipidemia in children and adolescents [19].

According to the KNHNES, the 95th percentiles for total cholesterol, TG, LDL cholesterol, and non-HDL cholesterol were 203, 185, 129, and 145 mg/dL, respectively, and the 10th percentile for HDL cholesterol was 38 mg/dL in Korean children and adolescents [13,22]. The distribution of lipid levels in Korean children and adolescents was reported to be similar to that in American children and adolescents [23]. Based on this, the 2011 U.S. NHLBI guidelines were adopted to produce the guidelines for dyslipidemia in children and adolescents in Korea [19,24].

The diagnostic criteria for dyslipidemia in children and adolescents in Korea were based on

the NHLBI definition. The cutoff points for defining total cholesterol, LDL cholesterol, non-HDL cholesterol, TG, and HDL cholesterol levels in children and adolescents from the guidelines are presented in Table 1. According to the Korean Society of Pediatric Endocrinology (KSPE) Clinical Practice Guidelines Committee, total cholesterol 200 mg/dL, LDL cholesterol≥130 mg/dL, non-HDL cholesterol≥145 mg/dL, TG≥130 mg/dL (≥100 mg/dL in children under 10 years of age), and HDL cholesterol<40 mg/dL were defined as dyslipidemia in children and adolescents. Recommended cutoff points for diagnosing dyslipidemia in young adults are total cholesterol≥225 mg/dL, LDL cholesterol≥160 mg/dL, non-HDL cholesterol≥190 mg/dL, TG≥150 mg/dL, and HDL cholesterol<40 mg/dL, as described in Table 2 [19].

Causes of Dyslipidemia in Children and Adolescents

The etiology of dyslipidemia can be classified into primary and secondary types [16]. Table 3 summarizes primary and secondary pediatric dyslipidemias [25]. Primary dyslipidemia is an inherited lipoprotein disorder that is often present in youth at a high risk of future CVD. Primary dyslipidemia is related to the production and degradation of specific proteins involved in the production, transport, and metabolism of lipoproteins, and abnormalities in specific genes have been identified. Secondary dyslipidemia is caused by a variety of diseases and conditions, including endocrine (hypothyroidism, DM, and pregnancy), exogenous (drugs, obesity, and alcohol), renal (nephrotic syndrome and chronic renal failure), hepatic (cholestasis, biliary atresia, hepatitis, and biliary cirrhosis), and immunological (human immunodeficiency virus infection/acquired immunodeficiency syndrome) conditions [25]. Obesity is a common cause of secondary dyslipidemia in children and adolescents. Various factors are involved in the pathophysiology of dyslipidemia in obese patients. In obese patients, increased fatty acid

Table 1. Definition of dyslipidemia for lipid cutoff levels in children and adolescents

Variable	Acceptable	Borderline	Abnormal
Total cholesterol (mg/dL)	<170	170–199	≥200
LDL cholesterol (mg/dL)	<110	110–129	≥130
Non-HDL cholesterol (mg/dL)	<120	120–144	≥145
Triglycerides (mg/dL)			
0–9 yr	<75	75–99	≥100
10–19 yr	<90	90–129	≥130
HDL cholesterol (mg/dL)	>45	40–45	<40

Table 2. Cutoff levels for lipids in the diagnosis of dyslipidemia in young adults

Variable	Acceptable	Borderline	Abnormal
Total cholesterol (mg/dL)	<190	190–224	≥225
LDL cholesterol (mg/dL)	<120	120–159	≥160
Non-HDL cholesterol (mg/dL)	<150	150–189	≥190
Triglycerides (mg/dL)	<115	115–149	≥150
HDL cholesterol (mg/dL)	>45	40–44	<40

Table 3. Differential diagnosis of pediatric dyslipidemia

Primary disorders	Secondary disorders
Familial hypercholesterolemia	Hypothyroidism
Autosomal recessive	Diabetes
Hypercholesterolemia	Pregnancy
Autosomal dominant	Drugs
Hypercholesterolemia	Obesity
Familial ligand-defective apoB-100	Alcohol
Sitosterolemia	Nephrotic syndrome
Familial combined hyperlipidemia	Chronic renal failure
Familial hypertriglyceridemia	Cholestasis
Familial chylomicronemia syndrome	Biliary atresia
Hypoalphalipoproteinemia	Hepatitis
Dysbetalipoproteinemia	Biliary cirrhosis
	Human immunodeficiency virus infection/acquired immunodeficiency syndrome

flow from adipose tissue to the liver and hepatic *de novo* fatty acid synthesis are important contributors to elevated serum TG levels. Abundant TG prevent intrahepatic degradation of Apo B-100 and increase very-LDL formation and secretion, which is an important contributor to elevated serum TG levels. The pro-inflammatory state is a characteristic observed in obesity, and cytokines produced in macrophages and adipokines produced in adipocytes affect lipid metabolism [26]. Before considering primary dyslipidemia, the cause of the secondary dyslipidemia must be excluded. If dyslipidemia persists even after the cause of secondary dyslipidemia has been treated, the patient may need dietary therapy and may need to consider medication [27].

Lipid Screening in Pediatric Populations

Pediatric lipid testing is based on evidence that the early identification and management of dyslipidemia in children can reduce the risk and severity of CVD in adulthood [28]. To date, a unified diagnostic criterion for dyslipidemia in children and adolescents has not yet been established worldwide. Guidelines for dyslipidemia in children were first developed by the NCEP of the NHLBI in 1992 [29]. They were created based on expert opinion and extrapolation of data collected from adults, and the composition did not include a complete formal review of evidence to grade evidence. Three categories were presented for lipid screening in the pediatric population: acceptable, borderline-high, and high. Population-based approaches focus on the identification and treatment of dietary and lifestyle problems in the entire population and the identification and treatment of high-risk children and adolescents. Individual approaches rely on family history. Children with first- and second-degree relatives with early onset coronary artery disease or stroke should be screened. The committee considered universal screening but decided that a selective screening approach would be more efficient, recognizing the effects of genes and the environment.

However, it is difficult to determine whether screening for dyslipidemia reduces the incidence

of myocardial infarction or stroke in adulthood in asymptomatic children and adolescents. Therefore, the US Preventive Services Task Force reported a grade I recommendation in its review of the evidence for cholesterol testing in children and adolescents [30]. This indicates that there is insufficient evidence for lipid testing in children and adolescents.

In 2011, the NHLBI published the results of a complete review and grading of evidence for the screening and treatment of CVD risk factors, including dyslipidemia, in children and adolescents [19]. In contrast to the previous guidelines, universal screening for lipid disorders was recommended. This is because studies have shown that using only a selective screening approach based on family history can potentially miss children and adolescents with significantly high cholesterol levels.

In 2017, the KSPE published guidelines for dyslipidemia in Korean children and adolescents [24]. These guidelines were determined in consideration of the country and existence of evidence by referring to the NHLBI recommendation level standards.

Screening in children and adolescents is aimed at reducing the incidence of CVD in adults by the early detection and management of dyslipidemia. Long-term follow-up studies have demonstrated that dyslipidemia in children and adolescents is an important predictor of dyslipidemia in adults [31]. Therefore, the purpose of the screening test is to identify children and adolescents with a very high risk of early CVD due to dyslipidemia.

Although family history of CVD is important in predicting future CVD, using a family history of dyslipidemia or early CVD to determine the need for dyslipidemia screening misses up to 60% of children with dyslipidemia. Therefore, the accuracy or reliability of information on family history is low, and the absence of a family history does not mean that there is no dyslipidemia in children and adolescents [19]. The Coronary Artery Risk Detection in Appalachian Communities Project found that using family history to determine the need for cholesterol testing in children missed many individuals with moderate dyslipidemia and failed to detect a significant number of potential genetic dyslipidemias requiring pharmacological treatment. Project HeartBeat! investigated the sensitivity, specificity, and positive predictive value of lipid tests in children using factors such as positive family history alone, body mass index (BMI) above the 85th percentile alone, and positive family history and BMI above the 85th percentile. The authors concluded that using one of the three screening criteria could miss a significant number of children with dyslipidemia [32]. Therefore, it is emphasized that universal cholesterol testing to prevent future atherosclerosis can be used to identify all children with severe dyslipidemia, allowing appropriate intervention and follow-up [33]. The pattern of normal cholesterol concentration does not change much after 2 years of age, but the lipid level decreases by 10%–20% during puberty and increases again in the 20s. Therefore, considering these normal change patterns, screening tests are required at the ages of 9–11 and 17–21 years for all children and adolescents, even if there is no clinical marker or family history.

The KSPE recommends non-HDL cholesterol assessment as a screening test. It is recommended that all children and adolescents be screened for non-HDL cholesterol under non-fasting conditions at the ages of 9–11 and 17–21 years. Screening for dyslipidemia is not recommended from birth to 2 years of age. Non-HDL cholesterol level is obtained by subtracting HDL cholesterol from total cholesterol [24]. It is less affected by fasting than LDL cholesterol and is a useful method for measuring lipoproteins that cause atherosclerosis. In children, non-HDL cholesterol appears to be a better predictor of CVD than LDL cholesterol [34]. According to a recent study using KNHNES data, the universal screening method using non-HDL cholesterol in obese adolescents above the 95th percentile of BMI, the current Korean screening test for lipid

disorders, was more effective in detecting familial hypercholesterolemia (FH) than the method of measuring total cholesterol [35].

In the initial stage, a fasting test is not required; if there are abnormal findings as a result of the primary test, a fasting test is recommended. It is also recommended that fasting lipid testing be performed at ages 2–8 and 12–16 years for individuals with risk factors for dyslipidemia [24].

After fasting for at least 9 h, total cholesterol, TG, HDL cholesterol, and LDL cholesterol levels are measured to diagnose dyslipidemia. Two or more fasting tests are performed at intervals of 2 weeks or more within 3 months, and the average value is used to diagnose dyslipidemia [19,36]. The risk factors for dyslipidemia are shown in Table 4 and are categorized into family history, high-risk factors, and moderate risk factors [24].

Treatment

Interventions for dyslipidemia include lifestyle modifications, such as healthy diet and regular physical exercise, and drug therapies. The increase in dyslipidemia among Korean children and adolescents has been greatly influenced by Western lifestyle [37]. Lifestyle modification is recommended for the treatment of dyslipidemia in children, and drug treatment is considered a secondary treatment when dyslipidemia cannot be corrected with lifestyle modifications [19,24].

1. Lifestyle modifications

Factors associated with dyslipidemia include alcohol consumption, smoking, diet, and obesity [19]. Obesity is one of the risk factors for dyslipidemia, and lifestyle modification to improve obesity is the priority in dyslipidemia treatment. Through lifestyle modifications, all children and adolescents should aim to reach their ideal body weight (BMI≤85th percentile for age and sex). The KSPE guidelines recommend that children and adolescents increase their activity by engaging in moderate or more physical activity for at least one hour each day. They also mention reducing sedentary lifestyles as much as possible, including watching television and playing video games. Smoking and alcohol drinking should also be strongly discouraged [24,36].

For children with dyslipidemia, the Cardiovascular Health Integrated Lifestyle Diet 1 (CHILD 1)

Table 4. Risk factors for dyslipidemia

Classification	Explanation
Family history	·Parent, grandparent, aunt, or uncle has a history of myocardial infarction, angina pectoris, coronary artery bypass surgery/stent/angioplasty, sudden death in male<55 years of age or female<65 years of age
High level risk factors	·Hypertension requiring medication ·Smoking ·BMI≥97th percentile ·High risk conditions: type 1 and type 2 diabetes mellitus, chronic kidney disease/end-stage renal failure/kidney transplantation, heart transplantation, Kawasaki disease with aneurysm
Moderate level risk factors	·Hypertension that does not require medication ·95th percentile≤BMI<97th percentile ·HDL cholesterol<40 mg/dL ·Moderate risk conditions: Kawasaki disease with improved coronary aneurysm, chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis), human immunodeficiency virus infection, nephrotic syndrome

BMI, body mass index.

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is recommended for 3–6 months, as suggested by the 2010 Dietary Guidelines for Americans to reduce the risk of CVD and provide the nutrition necessary for growth in children and adolescents [38]. CHILD 1 recommends exclusively breastfeeding up to 6 months of age and, if not possible, using iron-fortified formula. Breastfeeding should continue until at least 12 months of age, and juice should be limited to 120 mL/day. After 12 months, low-fat milk is recommended, the consumption of carbonated drinks should be limited, and drinking water is encouraged. The total fat content should be maintained at 30% of the total calories, saturated fatty acids at 8%–10%, and monounsaturated and polyunsaturated fatty acids at up to 20%. Individuals with a family history of obesity, heart disease, or hypercholesterolemia should consult their healthcare provider regarding low-fat milk intake after 12 months of age. After 2 years of age, daily fat intake should be limited to 25%–30% of the total daily caloric requirement, saturated fat to 8%–10%, and unsaturated fat to 20%. The cholesterol intake should be limited to 300 mg/day. The recommended amount of dietary fiber is 14 g/1,000 kcal, and salt intake should be limited [24].

If dyslipidemia is not controlled by CHILD 1 within 3 months, CHILD 2-LDL and CHILD 2-TG are performed. Compared to CHILD 1, CHILD 2 reduces cholesterol from 300 mg to 200 mg and saturated fatty acids from 8%–10% to 7%. CHILD 2-LDL is performed in children with high LDL cholesterol levels. If TG levels are high, CHILD 2-TG is performed, reducing the intake of simple carbohydrates, replacing simple carbohydrates with complex carbohydrates, and increasing the intake of omega-3 fatty acids. CHILD 2 reduces cholesterol from 300 mg to 200 mg and saturated fatty acids from 8%–10% to 7% compared to CHILD 1. CHILD 2-TG involves reducing sugar intake and increasing the intake of omega-3 fatty acids in the CHILD 2-LDL diet [3].

2. Drug therapy

Drug treatment is recommended for children and adolescents aged≥10 years when lifestyle and dietary changes for 6–12 months are not effective [19,24,36]. Decisions on drug treatment should be based on the average fasting blood lipid concentration measured twice, at least 2 weeks apart, within the last 3 months. Drug treatment for dyslipidemia according to age is summarized in Table 5.

Children younger than 10 years do not usually start statin therapy. However, some experts recommend starting statins at 8 or 10 years of age. Its use is limited to cases of homozygous familial

Table 5. Drug treatment for dyslipidemia in children and adolescents

Ages	Treatments
Newborn – 9 years old	·Lipid lowering therapy is limited to cases of homozygous familial hypercholesterolemia, LDL cholesterol≥400 mg/dL, primary hypertriglyceridemia (≥500 mg/dL), cardiovascular disease, and heart transplantation.
10–21 years old	·Immediately refer to an expert - LDL cholesterol≥250 mg/dL or triglycerides≥500 mg/dL ·Statin treatment 1) LDL cholesterol≥190 mg/dL 2) LDL cholesterol between 160–189 mg/dL with a family history of premature CVD or one or more high-level risk factors, or at least two moderate-level risk factors 3) LDL cholesterol between 130–159 mg/dL with two or more high-level risk factors, or at least one high-level risk factor and two moderate-level risk factors · Omega-3 fatty acids (fish oil) - Triglycerides≥200–499 mg/dL, non-HDL cholesterol≥145 mg/dL · Consider treatment with statins, fibrates, or niacin - If non-HDL cholesterol≥145 mg/dL even after LDL cholesterol has reached target

CVD, cardiovascular disease.

hypercholesteraemia (HoFH), LDL cholesterol≥400 mg/dL, and primary hypertriglyceridemia (TG≥ 500 mg/dL) [24]. Initiation of statin therapy from childhood in patients with FH resulted in a slower progression of carotid intima-media thickness and a reduced risk of CVD in adulthood [39]. The use of statin preparations may be considered when LDL cholesterol does not improve after 6 months of lifestyle modifications and dietary changes in children aged≥10 years [19]. If LDL cholesterol is <250 mg/dL or TG level is 500 mg/dL in children aged 10 years or older, CHILD 1 or CHILD 2 is performed for 3–6 months, and BMI is at or above the 85th percentile, then increasing physical activity and reducing sedentary lifestyle are recommended. If the lipid concentration does not reach the target level despite these lifestyle modifications and dietary changes, drug treatment is considered [29].

The goal of hyper-LDL cholesterolemia treatment in children and adolescents is to maintain it below the 95th percentile (≤130 mg/dL) [19]. In children at a high risk of atherosclerosis, such as individuals with chronic kidney disease, type 1 and type 2 DM, Kawasaki disease with coronary aneurysm, and heart transplantation, drug therapy to reduce LDL cholesterol should be considered [40]. Children with HoFH and LDL cholesterol>500 mg/dL should undergo LDL separation every 2 weeks [29].

For patients aged 10 years or older, statins, fibrates, or niacin may be considered if non-HDL cholesterol is ≥145 mg/dL, even if LDL cholesterol is within the target range [24]. For hypertriglyceridemia, when the TG is 200–499 mg/dL and non-HDL cholesterol is ≥145 mg/dL, intake of omega-3 fatty acids can be increased along with lifestyle control, but there are still concerns about safety due to insufficient studies in children [41]. The main effects of current dyslipidemia treatments are summarized in Table 6 [24,36]. Statins and acid-binding resins are currently the main drugs used for the treatment of dyslipidemia in children.

Statins are approved for use in children over 10 years of age by the U.S. Food and Drug Administration (FDA) and are the initial treatment of choice for children with elevated LDL cholesterol or non-HDL cholesterol levels. Statins reduce intracellular cholesterol levels by inhibiting hydroxylmethylglutaryl coenzyme A reductase, the rate-limiting enzyme in the synthesis of cholesterol, and decrease LDL cholesterol levels by upregulating LDL receptors [42]. Statins should be started at the lowest dose administered once daily. The target level of LDL cholesterol is <130 mg/dL, and it is ideally maintained below 110 mg/dL [43]. If the LDL

Table 6. Major effects of current medications for dyslipidemia

Type of medication	Major effects	Adverse effects	Medications	FDA approval in pediatrics
HMG-CoA reductase inhibitors	↓LDL-C, TG, VLDL synthesis ↑Hepatic LDL receptors, HDL-C	Increased liver enzyme and creatine kinase, myopathy, rhabdomyolysis	Lovastatin 20–80 mg/day Simvastatin 20–80 mg/day Pravastatin 20–80 mg/day Atorvastatin 5–80 mg/day	Approved
Bile acid sequestrants	↓LDL-C, bile excretion ↑TG	Trouble of gastrointestinal tract; gas, bloating, constipation, cramps	Cholestyramine 8–16 g/day Colestipol 2.5–20 g/day Colesevelam 1.25–4.375 g	Evidence-based studies in children are lacking but used in clinical practice
Cholesterol absorption inhibitors	↓LDL-C ↑HDL-C	Trouble of gastrointestinal tract, myopathy, headache	Ezetimibe 10 mg/day	Not approved
Fibric acid derivatives	↓TG ↑HDL-C	Dyspepsia, constipation, myositis, anemia	Gemfibrozil 1,200 mg/day Fenofibrate 48–145 mg/day	Not approved
Nicotinic acid	↓TG and LDL-C	Flushing, hepatic tocixity	Niacin 1,000–2,250 mg/day	Not approved
Omega-3-fish oil	↓TG, VLDL production	Gastrointestinal trouble	DHA 2–4 g (adults)	Not approved

FDA, Food and Drug Administration; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; VLDL, very-low-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; DHA, docosahexaenoic acid.

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cholesterol level does not reach the target level, the dose of the drug can be increased once, and the blood test is repeated after 4 weeks. If the LDL cholesterol level still does not reach the target concentration, the dose may be increased one more time or a bile acid sequestrant or cholesterol absorption inhibitor may be added [44]. Statins have been reported to be effective in reducing cholesterol levels by 20%–50% compared to baseline, have no effect on growth in children, and rarely cause side effects. The side effects of statins include myopathy and elevated liver enzyme levels. Therefore, it is necessary to monitor the levels of alanine aminotransferase, aspartate aminotransferase, and creatinine kinase every 3–6 months [45]. Hazardous liver enzyme levels are more than three times higher than the upper limit of normal levels. The risk of muscle toxicity is more than 10 times the upper limit of normal creatinine kinase levels, and the effect of physical activity should be considered. If abnormalities are found in blood tests or symptoms are reported, it is observed whether myopathy disappears after discontinuing the drug and follow-up shows a decrease in blood test values after 2 weeks. When abnormal levels are normalized, drug treatment can be started again with close examination [46].

Bile acid sequestrants are drugs that block the reabsorption of cholesterol in enterohepatic circulation. As they are not absorbed systemically, they can be used as a first-line treatment for dyslipidemia in children. However, compliance is poor owing to side effects of the digestive system, such as nausea, diarrhea, and constipation.

Ezetimibe is a cholesterol absorption inhibitor that reduces bile reabsorption and cholesterol absorption in enterohepatic circulation. This drug is approved for use as an adjuvant in children aged≥10 years. In adult studies, ezetimibe has been reported to lower LDL cholesterol levels by 20%; however, studies in children and adolescents are not yet sufficient [47]. There have been no studies on the use of cholesterol absorption inhibitors as monotherapy in children and adolescents. In children aged 10–17 years with FH, the combined administration of simvastatin and ezetimibe resulted in a greater reduction in LDL cholesterol than simvastatin alone [48]. Niacin is a drug that increases HDL cholesterol and reduces LDL cholesterol and TG and is only used as an adjuvant treatment. However, niacin is not FDA-approved for pediatric patients with dyslipidemia and presents serious side effects such as flushing, itching, headache, and elevated aminotransferase levels, making it a limited treatment option for adolescents [49]. Fibric acid derivates lower TG and increase HDL cholesterol. In children, fibrates are used to treat severe hypertriglyceridemia with a risk of acute pancreatitis. Fibrate may increase the therapeutic effect when combined with statins, but may cause rhabdomyolysis and is not approved by the FDA for dyslipidemia in children [41].

Omega-3 fatty acid reduce TG levels and may be considered in treatment of hypertriglyceridemia, but data on their effectiveness in pediatric patients are limited and are not FDA-approved for the treatment of pediatric dyslipidemia [50].

Conclusion

Atherosclerosis can begin in childhood and is associated with CVD onset in adulthood. Therefore, early detection and appropriate management of dyslipidemia in children and adolescents is the optimal way to reduce CV morbidity in adults. Clinical practice guidelines for dyslipidemia in children and adolescents have been developed to help clinicians reduce unnecessary care variability and to improve outcomes when managing dyslipidemia. Non-HDL cholesterol assessment, presented as a universal screening method for dyslipidemia in children, is a screening test that does not require fasting and is inexpensive; therefore, it can be conveniently performed

by pediatricians in the clinic. For these guidelines to be implemented in practice, clinicians should be alert and pay close attention to the risk of dyslipidemia in children and adolescents. Research on dyslipidemia in children and adolescents should be continued, and the development of updated clinical guidelines based on accumulated evidence is necessary.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Not applicable.

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Case Report

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Giant Cardiac Rhabdomyoma with Mixed Atrial Tachycardia and Nonsustained Ventricular Tachycardia in a Newborn with Tuberous Sclerosis

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Key Words
Rhabdomyoma; Tachycardia; Ectopic atrial; Tachycardia; ventricular; Tuberous sclerosis

Cardiac rhabdomyomas are typically presented in the tuberous sclerosis. Although benign and often associated with spontaneous regression, in rare circumstances huge mass size and critical location can lead to heart failure, ventricular outflow tract obstruction and refractory tachyarrhythmias. An 1-day-old girl was diagnosed as cardiac tumor during perinatal period. At birth, transthoracic echocardiography revealed huge cardiac mass located in septal area of both ventricle measuring 34×30 mm. It protruded into the left ventricular (LV) outflow tract, potentially obstructing it. A surface ECG revealed atrial tachycardia with nonsustained ventricular tachycardia with heart rate of 217 beats per min. The tachyarrhythmias were controlled with intravenous amiodarone. Reduction of the giant cardiac mass was treated with mammalian target of rapamycin pathway inhibitor sirolimus. However, she unfortunately died at 10 days-old because of sudden cardiac arrest maybe due to LV outflow tract obstruction during therapy. Gene analysis revealed TSC2 mutation after death. (Ewha Med J 2022;45(3):e5)

Introduction

Rhabdomyomas are the most common cardiac tumor in pediatric patients. In many cases, they are associated with tuberous sclerosis which is an autosomal dominant disorder caused by mutations in the TSC1 or TSC2 genes that are part of mammalian target of rapamycin (m-TOR) pathway [1]. Although benign and often associated with spontaneous regression, in rare circumstances huge mass size and critical location can lead to heart failure, ventricular outflow tract obstruction and refractory tachyarrhythmias [2]. Here we present a fatal case of mixed atrial and ventricular tachycardia (VT) in a newborn with giant cardiac rhabdomyoma and tuberous sclerosis.

Case Presentation

An 1-day-old girl was born by cesarian section at a gestational age of 36 weeks with birth weight of 2,710 g. Cardiac tumor was diagnosed during perinatal period. At birth, transthoracic echocardiography revealed huge cardiac mass located in septal side of both ventricle involving free wall of the ventricle and the outflow tract measuring 34×30 mm in its longest axis. It protruded into the left ventricular (LV) outflow tract, potentially obstructing it (Fig. 1). And other

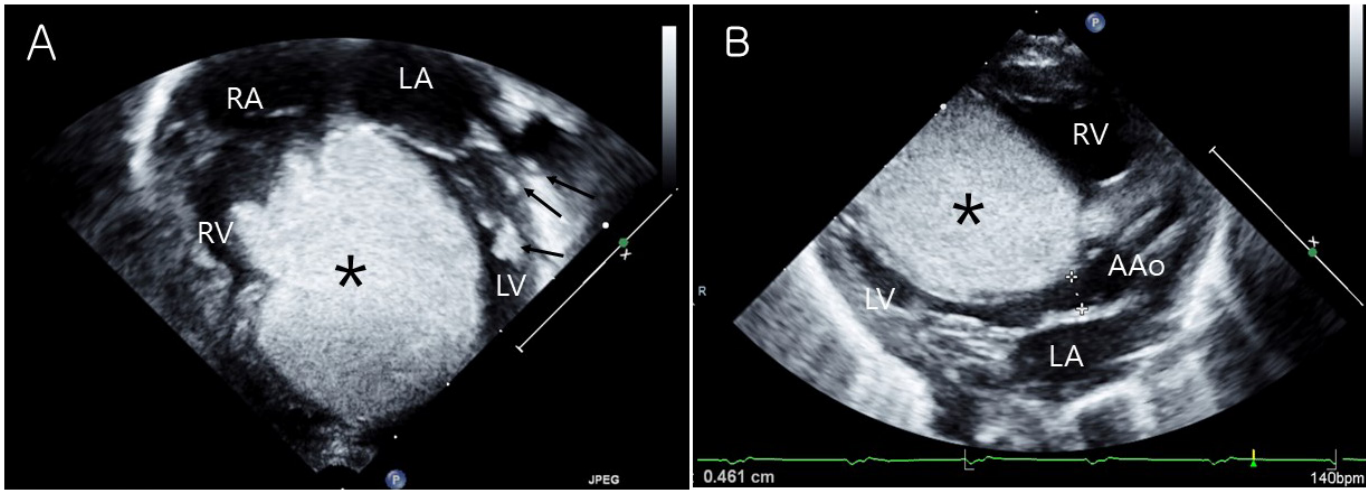

Fig. 1. Transthoracic echocardiography of rhabdomyoma. (A) Huge cardiac mass (asterisks) located in both ventricle measuring 34×30 mm on apical four chamber view. Small multiple cardiac masses (arrows) were located in papillary muscle and chordae tendinae of LV. (B) Cardiac mass (asterisks) protruded into the left ventricular (LV) outflow tract, potentially LV outflow tract obstruction on parasternal long axis view. RV, right ventricle; RA, right atrium; LA, left atrium; LV, left ventricle; AAo, ascending aorta.

small multiple cardiac masses were located in papillary muscle and chordae tendinae of LV. No other visible mass was observed in the atria, and ventricular systolic function was preserved. Brain ultrasound showed multiple cortical and subcortical tubers on both fronto-parieto-occipital area related to the tuberous sclerosis (Fig. 2). A 12-lead surface ECG revealed atrial tachycardia (AT) with nonsustained VT which showed wide QRS tachycardia with heart rate of 217 beats per min (Fig. 3A). To reduction of the giant cardiac mass, m-TOR inhibitor sirolimus was treated. In addition, the tachyarrhythmias were controlled to intravenous amiodarone, which was given 5 mg/kg bolus followed by continuous infusion up to 10 mcg/kg/min. After that, atrial tachyarrhythmias were converted to nonsustained AT and then frequent atrial premature beats with bigeminy (Fig. 3B, Fig. 3C). No VT was observed any more. However, she unfortunately died at 10 days-old because of sudden cardiac arrest maybe due to LV outflow tract obstruction during therapy. Gene analysis revealed TSC2 mutation after death.

Discussion

Rhabdomyomas are the most common cardiac tumours diagnosed in fetuses and neonates.

Cardiac rhabdomyomas in neonates tend to regress spontaneously and are not usually operated upon. However, they may lead to arrhythmias, heart failure, and ventricular inflow/outflow tract obstruction in the neonatal period [2]. If they become obstructive or hemodynamically compromised, causing life threatening complications, surgical resection is indicated. Because removing all cardiac masses from within the myocardium does more damage in neonate, surgeons resect only the obstructing intracavitary portions. In one series 10% cases of cardiac rhabdomyoma required surgical subtotal tumor excision [3].

Cardiac rhabdomyomas are typically presented in the tuberous sclerosis in the newborn. Tuberous sclerosis is multisystemic disease caused by gene mutation of TSC1 or TSC2 that are part of m-TOR pathway. Multiple systemic harmatomatous growth is resulted from m-TOR activation. Recent studies have reported successful treatment of life-threatening cardiac

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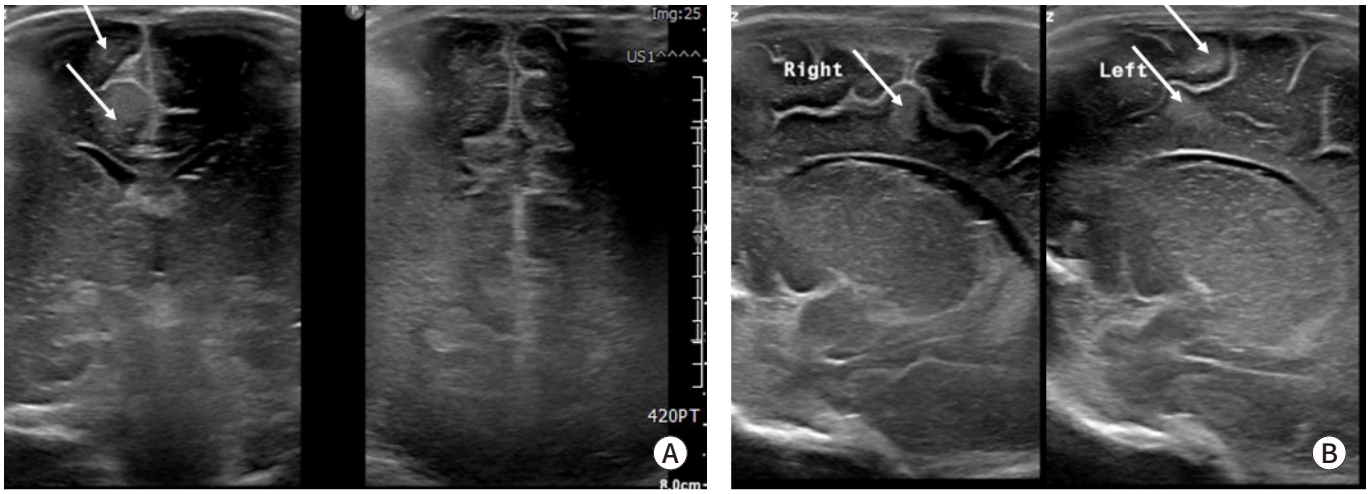

Fig. 2. Brain ultrasound image in neonate with tuberous sclerosis. Multiple cortical and subcortical tuber (arrows) in fronto-parieto-occipital area are showed in (A) coronal view and (B) parasagittal view of right and left brain.

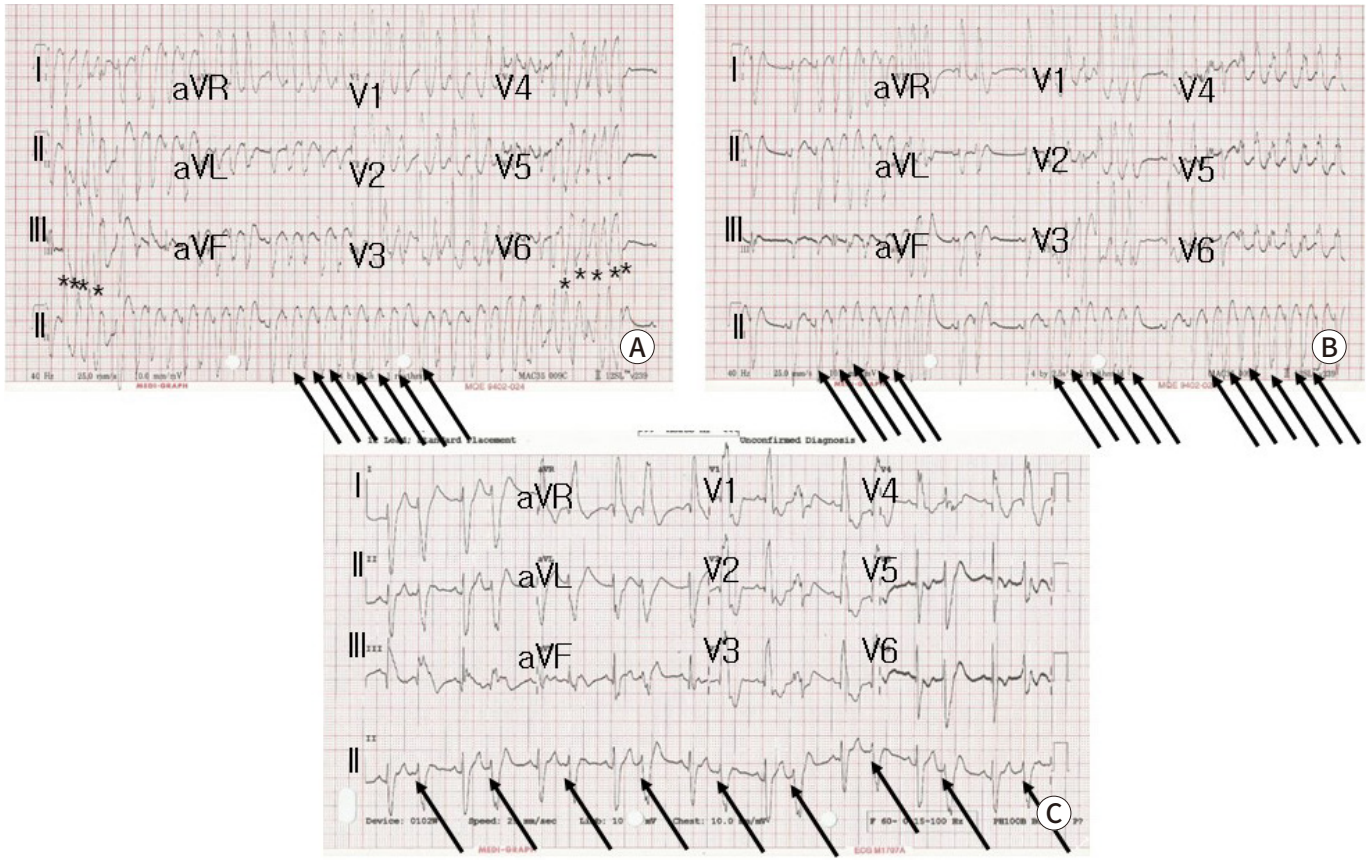

Fig. 3. 12 leads surface ECG showing wide QRS tachycardia. (A) Initial ECG shows atrial tachycardia (arrows) with nonsustained ventriculat tachycardia (asterisks). (B) After amiodarone infusion, nonsustained atrial tachycardia (arrows) and (C) frequent atial premature complex with bigeminy (arrows) are shown.

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rhabdomyoma in a newborn infants with m-TOR inhibitors. Therapy with m-TOR inhibitor has shown decreased the cardiac mass size relieving the ventricular outflow tract obstruction and improving the cardiac function when not eligible for resection or as alternative [1,4–6].

In the case, we initially started m-TOR inhibitor because cardiac mass was inoperable lesion without definite ventricular outflow tract obstruction. During therapy, hemodynamic condition was stable and tachyarrhythmias were relatively well controlled by intravenous amiodarone infusion. However, patient was compromised as blood pressure suddenly dropped in day 10 of hospitalization.

Cardiac rhabdomyomas are frequently multiple, involving the both ventricular septal and free wall and also involve either atrium. A wide spectrum of clinical symptom especially, various cardiac arrhythmias can be associated with rhabdomyoma in pediatric patients [1,2]. Previous study reported that atrial and/or ventricular ectopic beats were seen in 24% of neonates and infants. And other critical arrhythmias, such as pre-excitation syndrome, refractory ectopic AT and incessant VT were demonstrated in cardiac rhabdomyomas [1,7,8]. In the case, nonsustained VT was intermittently observed. So, it was not clearly documented on 12-lead ECG. Although ECG findings were limited, nonsustained VT showed positive QRS vectors in lead I, II, III, and V6. The suspected origin of VT is probably seen as the high septum area which was coincided with cardiac mass location. In fetal cardiac rhabdomayoma, pre-excitation syndrome was present in 80% of the fetuses and more common in fetal life than infants and children [9]. The infantile pre-excitation is known to regress over the first year after birth [10]. Although all types of arrhythmias have been described, ventricular tachyarrhythmias related with cardiac rhabdomyoma are rare than atrial tachyarrhythmias. In the study, multiple cardiac mass were mostly present in the ventricle but the majority of arrhythmias ware manifestated as atrial origin. Even though atrial tumor are not visible, undetected small abnormal atrial tissue with greater automaticity of atrial cells may be contributed to atrial tachyarrhythmias.

The majority of cardiac arrhythmias spontaneously healed or was gradually reduced of arrhythmia burden. In case of critical tachyarrhythmias, antiarrhythmic agents have been shown to control successfully. Although there is no clear first-line therapy for neonatal tachyarrhythmias, intravenous amiodarone is known to effective for neonatal supraventricular and ventricular dysarrhythmias for intracavitary occupying structural heart disease. Use of propranolol or digoxin for neonatal supraventricular tachyarrhythmias can be considered as maintenance therapy. Lidocaine is first-line therapy for wide QRS tachycardia of unknown mechanism [11]. However, there are several reports of m-TOR inhibitor therapy about successful management of intractable rhabdomyoma-related tachyarrhythmias unresponsive to antiarrhythmic drugs [7,10]. Although atrial and ventricular arrhythmias were responsive to amiodarone and m-TOR inhibitor, tumor regression was unsatisfactory for 10 days in the case. The cause of death is presumed that ventricular outflow tract obstruction contributed to the hemodynamic instability but adverse effect of the drugs may be considered as other factor.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Case Report

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Embarrassed Radiofrequency Catheter Ablation of Supraventricular Tachycardia in Pectus Excavatum

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Key Words
Tachycardia; Atrioventricular nodal reentry; Catheter ablation; Pectus excavatum; Nuss operation

A 16-year-old patient with pectus excavatum visited our hospital because of palpitation. He underwent first Nuss operations at the age of 3. When he was 13 years old, the slow-fast type atrioventricular nodal reentrant tachycardia was documented during electrophysiology study. However, the catheter ablation was not conducted because of recurrent atrial fibrillation during procedure. At that time, second Nuss operation was performed due to progressive chest wall deformity. And then, atrioventricular nodal reentrant tachycardia was successfully treated by radiofrequency catheter ablation at the higher position than usual slow pathway zone under the modified fluoroscopic view with the cranial angle although distorted right atrial geometry and radiographic obstacle of Nuss operation bar. The concern about abnormal cardiac and electrical anatomy, and the accurate and modified procedure technique are essential in patients with pectus excavatum. (Ewha Med J 2022;45(3):e6)

Introduction

Chest wall deformity such as pectus excavatum is associated with different types of cardiac arrhythmias. Supraventricular and ventricular arrhythmia often occur regardless of chest repair operation (Nuss operation), which is caused by compression of the anterior sternal wall [1–4]. In addition, repair operation of pectus excavatum can change thoracic cavity dimension and geometry [5]. It might cause several challenges of catheter ablation for supraventricular tachyarrhythmias. Here, we report atrioventricular nodal reentrant tachycardia (AVNRT) with successful catheter ablation, in spite of distorted cardiac geometry and radiographic obstacle of Nuss operation bar.

Case Report

A 16-year-old patient with pectus excavatum visited our hospital because of palpitation. He had history of Nuss operations at the age of 3. With progressively worsening chest wall deformity for several years after Nuss operation, he felt frequent palpitation. The 12-leads surface ECG revealed wide QRS tachycardia with heart rate of 180 bpm, that is supraventricular tachycardia with incomplete right bundle branch block pattern (Fig. 1A, 1B). He had taken propranolol and flecainide. When he was 13 years old, electrophysiology study was performed at other hospital. The slow-fast type AVNRT was documented during electrophysiology study. However, the

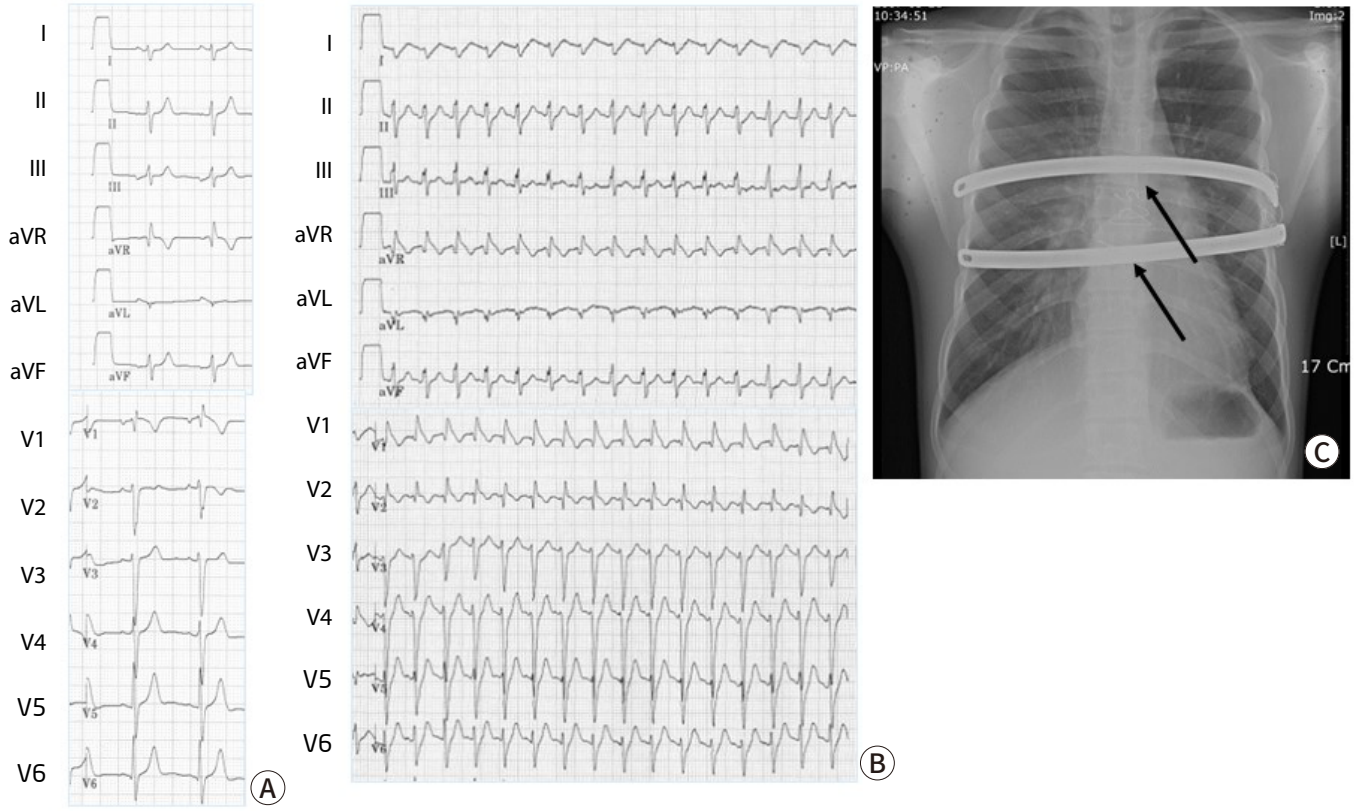

Fig. 1. 12-lead surface electrocardiogram and Chest X-ray. (A) The baseline surface electrocardiogram showing incomplete right bundle branch block. (B) A wide QRS tachycardia with heart rate of 180 bpm suggesting supraventricular tachycardia with incomplete right bundle branch block pattern. (C) Chest X-ray showing Nuss operation bar (arrows).

catheter ablation was not conducted because atrial fibrillation (AF) was frequently induced by programmed electrical stimulation during procedure. At that time, combined severe chest wall deformity was corrected by the second Nuss operation at other hospital. In spite of antiarrhythmic medications, palpitation was not controlled well. He was referred to our hospital for radiofrequency catheter ablation.

Chest X-rays revealed an enlarged cardio-thoracic ratio with two radiopaque Nuss bar (Fig. 1C), and transthoracic echocardiography revealed severely right atrial compression against the sternum (Fig. 2).

After obtaining written informed consent, the electrophysiology study was performed under local anesthesia. Multielectrode duodecapolar, decapolar and quadripolar catheters were placed in the right atrium (RA), right ventricular (RV) apex, His bundle region and coronary sinus (CS) via the right or left femoral vein and right internal jugular vein, respectively. During catheter manipulation, sustained AF was induced. Then, we terminated AF by internal cardioversion of 10 joule. Nonsustained AF was frequently induced during procedure. However, most of AF occurrence was spontaneously terminated. After confirming slow-fast type AVNRT which was reproducibly induced during electrophysiology study (Fig. 3A), we first targeted the slow pathway zone between CS ostium and tricuspid annulus at the level of CS ostial roof. However, slow pathway was not ablated adequately because of distorted RA geometry and radiographic obstacle of Nuss operation bar. So, we repositioned the His catheter to find the location where

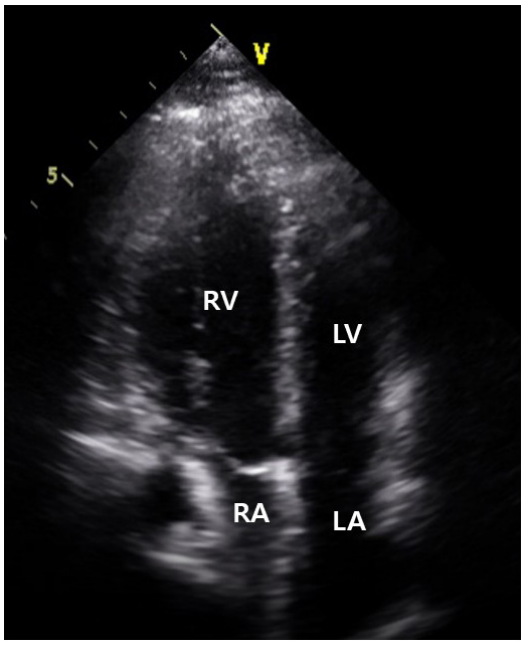

Fig. 2. Transthoracic echocardiography showing the compression of right atrium on apical four chamber view. RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium.

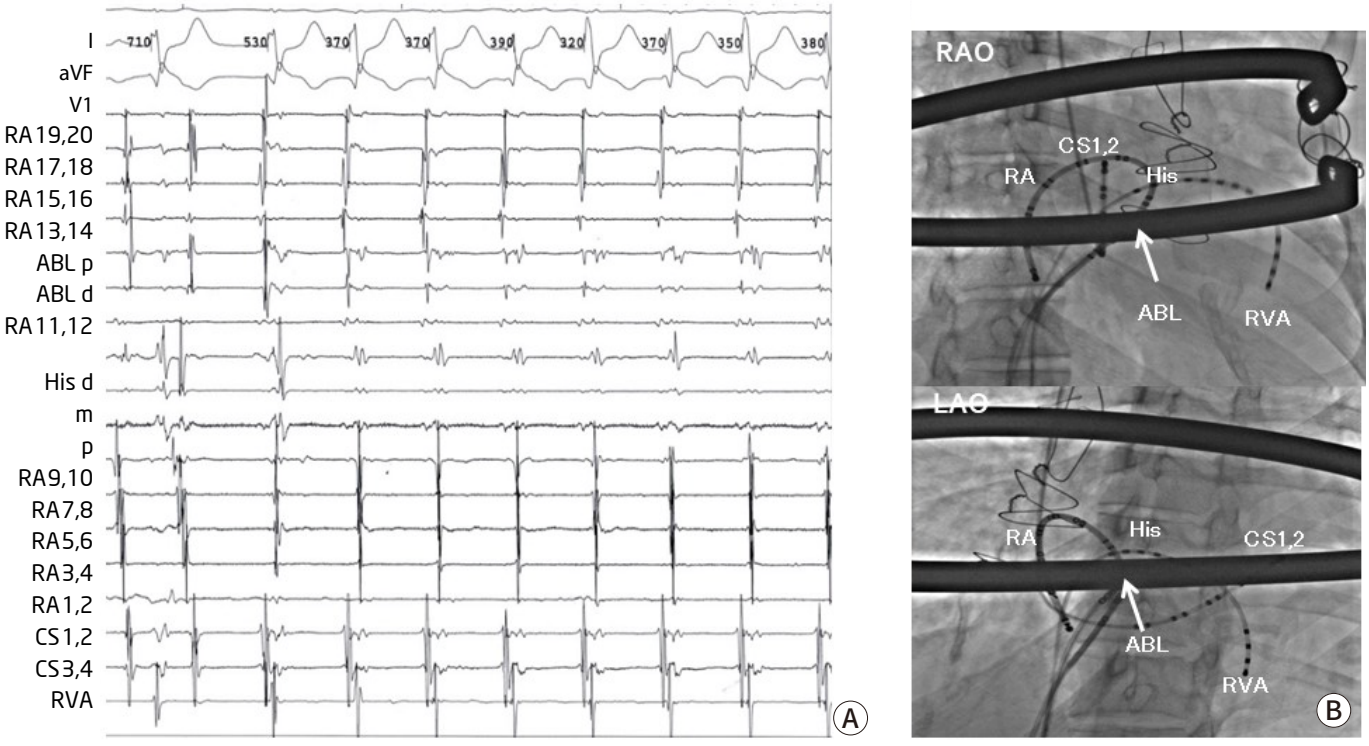

Fig. 3. Successful ablation site of atrioventricular nodal reentrant tachycardia. (A) Intra-cardiac electrogram showing the atrioventricular nodal reentrant tachycardia with earliest atral activation site of His area at a cycle length of 380 ms. (B) Fluoroscopic images in the left anterior oblique (LAO) and right anterior oblique (RAO) projection showing the masablation catheter positioned at the higher site than usual slow pathway zone. RA, right atrium; CS, coronary sinus; ABL, ablation catheter; RV, right ventricular catheter; His, His potential.

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the His signal was greatest and set the fluoroscopic view as the cranial angle to accurately see the movement of the ablation catheter. We finally gave radiofrequency energy at the higher position than usual slow pathway zone (Fig. 3B), producing junctional rhythm with 1:1 retrograde conduction during radiofrequency delivery. After ablation, the patient remained free from the tachycardia during 3 year of follow-up.

Discussion

Pectus excavatum is the most common congenital chest wall deformity. It causes cardiac compression and distorsion, resulting in cardiac dysfunction and arrhythmias. In patients with pectus excavatum, chest wall compression-induced arrhythmias often occur regardless of chest repair operation. Cardiac arrhythmias are caused by compression of RA and RV against the sternum, left atrium (LA) compression against the spinal column, and lateral displacement of the heart to the left. The observed arrhythmias are supraventricular tachycardia, AF, premature ventricular complex, and VT [1–4]. AF was documented in two thirds of the patients with mild form pectus excavatum. The possible explanation of the development of AF in pectus excavatum is that direct RA compression and LA mechanical compression could trigger the development of AF in a mechanism similar to that proposed for swallowing AF, which is thought to potentially result from the mechanical stimulation of the LA and/or the activation of vagal reflexes during swallowing [1]. Monomorphic or polymorphic VT were caused by mechanical compression and abnormal rotation of the RV [2,6]. Previous studies demonstrated preoperative arrhythmia showed marked improvement after surgical repair of pectus excavatum [6,7]. In addition, difficult surgical and catheter ablation were demonstrated in several reports [8,9].

The Nuss procedure has been used as a minimally invasive repair for pectus excavatum. A convex steel bar is usually inserted under the sternum through bilateral thoracic incisions. When the steel bar is in position, the bar is turned over to the anterior chest, thereby correcting the chest wall deformity [10]. After correction of anterior depression of the sternum, compensatory narrowing of chest width was observed. Changes in thoracic dimensions following the Nuss procedure were distinct in patients aged above 13 years [5]. In the present case, the patient underwent Nuss operation at the age of 3. The surgery performed at that time may not have been sufficiently corrected. Furthermore, as the chest wall gradually deformed, the tachyarrhythmia seemed to be getting worse. Initially catheter ablation for AVNRT was failed because repetitive occurrence of AF during procedure. After second Nuss operation of severe chest wall deformity, nonsustained AF was frequently induced during catheter ablation. However, most of AF was spontaneously terminated. Internal cardioversion was performed only once because of sustained AF. Regarding the mechanism of AF in pectus excavatum, decreased mechanical stimulation may reduce the sustained AF after operation for pectus deformity.

In the previous report, symptomatic pediatric patients much improved 2 years postoperatively, while the bar was in place [11]. In case of sustained tachycardia, the ablation procedure can be considered at least 2 years after surgery.

The slow pathway was unusually located owing to cardiac distorsion. So, we repositioned the His catheter to find the location where the His signal was greatest. And the location of ablation catheter was not clear due to Nuss operation bar on the fluoroscopic views. Therefore, we set the fluoroscopic views to the cranial angle of the right and left anterior oblique view to accurately confirm the movement of the ablation catheter. The 3-dimensional electroanatomic mapping system may help locate catheter position in this condition.

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The cardiac and electrical geometry is influenced not only by the chest wall deformity itself but also Nuss operation. Therefore, the concern about distorted cardiac and electrical anatomy, and the accurate and modified procedure technique are essential in patients with pectus excavatum.

Acknowledgments

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Case Report

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Minute Colon Perforation by a Nonabsorbable Suture Knot after Uterine Myomectomy

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Key Words
Colon; Perforation; Suture; Non-absorbable

We report a rare case of suture material-related colon perforation. A 60-year-old woman visited clinics because of the nonspecific abdominal discomfort for several months. There were no specific medical history except previous laparoscopic myomectomy 15 years ago. Colonoscopy and abdomen-pelvis computed tomography revealed an unknown foreign body penetrating the sigmoid colon wall adjacent to the uterus. We performed laparoscopic exploration with foreign body removal and primary colon wall repair. The foreign body was identified as a non-absorbable suture material suggestive of used in previous myomectomy. With recent trends for minimally invasive procedures in the field of pelvic organ surgery, surgeons, especially those without sufficient training have to pay attention to selecting the proper surgical suture materials. (Ewha Med J 2022;45(3):e7)

Introduction

During the surgical process suture and tie are most widely used basic techniques in spite of development of automatic stapling device. For optimal wound repair and tissue healing, selection of appropriate suture material for each wound would be trained from the first of the surgical residency. The successful wound healing was achieved by proper suture technique with appropriately selected suture materials. In general, suture materials are classified according to their behavior in tissue (absorbable or non-absorbable), their structure (monofilamanent, or multifilament), and their material (synthetic, organic, or metallic) [1]. A suitable suture does not trigger an inappropriate tissue reaction, but also maintains sufficient tensile strength until proper wound healing is achieved [1].

An ideal suture has the property of being absorbed after complete tissue healing so that a foreign body does not continue to exist in the wound [2]. However, the absorptiveness of suture materials is associated with different advantages and disadvantages leading to a variety of preferences among practicing surgeons. Many surgeons believe that non-absorbable suture materials are superior to absorbable suture materials, because they are easier to tie, are unlikely to break early, and induce a weaker inflammatory response [2]. Others favor absorbable suture materials since they disappear spontaneously and cause less pain and discomfort for the patient [3]. There is still no consensus on which suture material to use, and the choice usually depends on the surgeon's preference.

In this report, we present a rare case of minute bowel perforation due to a non-absorbable

suture material after myomectomy, which may be informative for surgeons regarding the choice of proper suture materials.

Case

A 60-year-old woman who had no medical disease history except uterine myoma was referred to the colorectal surgery department after colonoscopy. She underwent colonoscopy because of the nonspecific abdominal discomfort lasted for 6 months. Colonoscopy revealed a polypoid lesion with an unknown foreign body at the sigmoid colon (Fig. 1). There was no abnormal findings in previous several routine colonoscopic evaluation. Abdomen-pelvic computed tomography showed radiopaque foreign body that was probably penetrating the uterus and abutting the sigmoid colon (Fig. 2A, 2B). Because of the possibility of colon perforation and previous laparoscopic myomectomy history 15 years ago, we decided to remove the foreign body by laparoscopic approach. The laboratory examinations revealed normal serum levels of white blood cells (3,950/μL; reference range, 4,000-10,000/μL) and C-reactive protein (0.05 mg/dL; reference range, 0-0.5 mg/dL).

Elective laparoscopic surgery under general anesthesia was done and revealed that two non-absorbable monofilament sutures were laid on the middle and left part of the uterus, forming an adhesion between the nearby omentum and the sigmoid colon (Fig. 3A, 3B). After adhesiolysis, we recognized that one of the knots at the left uterus was penetrating the sigmoid colon. Upon removing the penetrating suture, we observed minute but definite colon wall perforation. Primary repair of the perforated colon wall was performed with continuous synthetic absorbable polyglactin sutures (Vicryl®), and the surgery was then finished. It was clearly evident that the excised suture knot was a nonabsorbable material, but the specific type of the suture material remained unknown – since we did not have access to information about the earlier surgery (Fig. 4).

The patient showed a favorable condition during the hospital course after surgery, and she was discharged on the fourth day postoperatively without any problems. After discharge, we conducted outpatient check-ups and verified that her condition continued to be stable without any gastrointestinal symptoms.

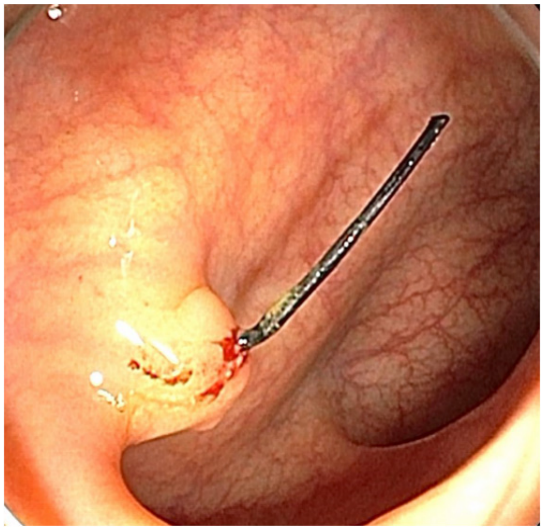

Fig. 1. Colonoscopic findings. A polypoid lesion with an unknown foreign body was found in sigmoid colon.

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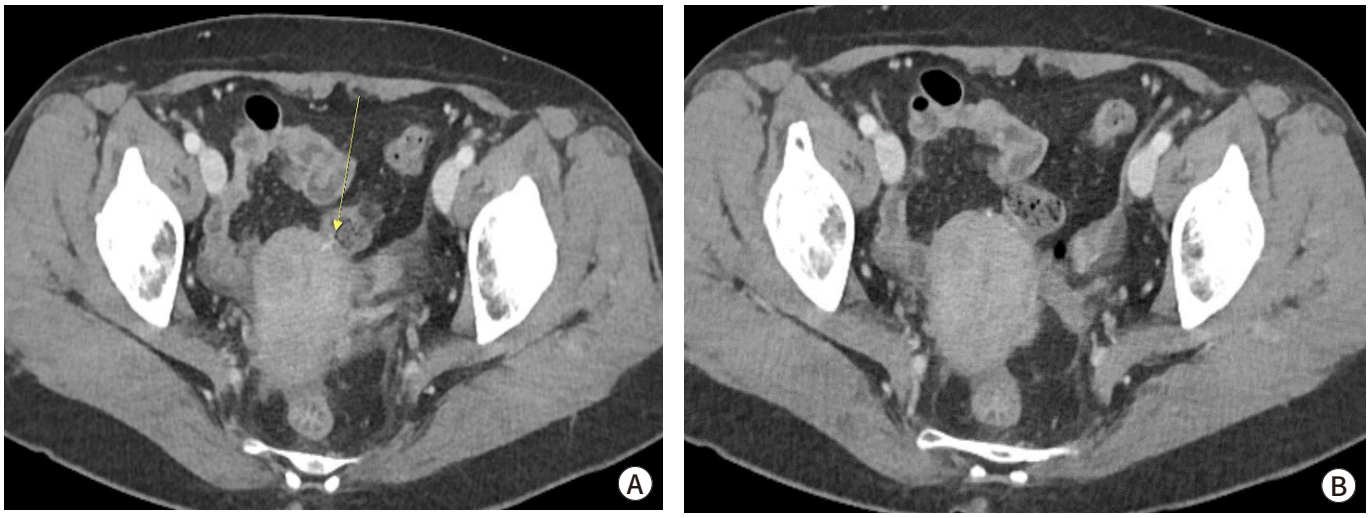

Fig. 2. Pelvic CT findings. (A) A radiopaque foreign body was probably penetrating the uterus and abutting the sigmoid colon (yellow arrow). (B) There was no free air and fluid collection around the penetrated site.

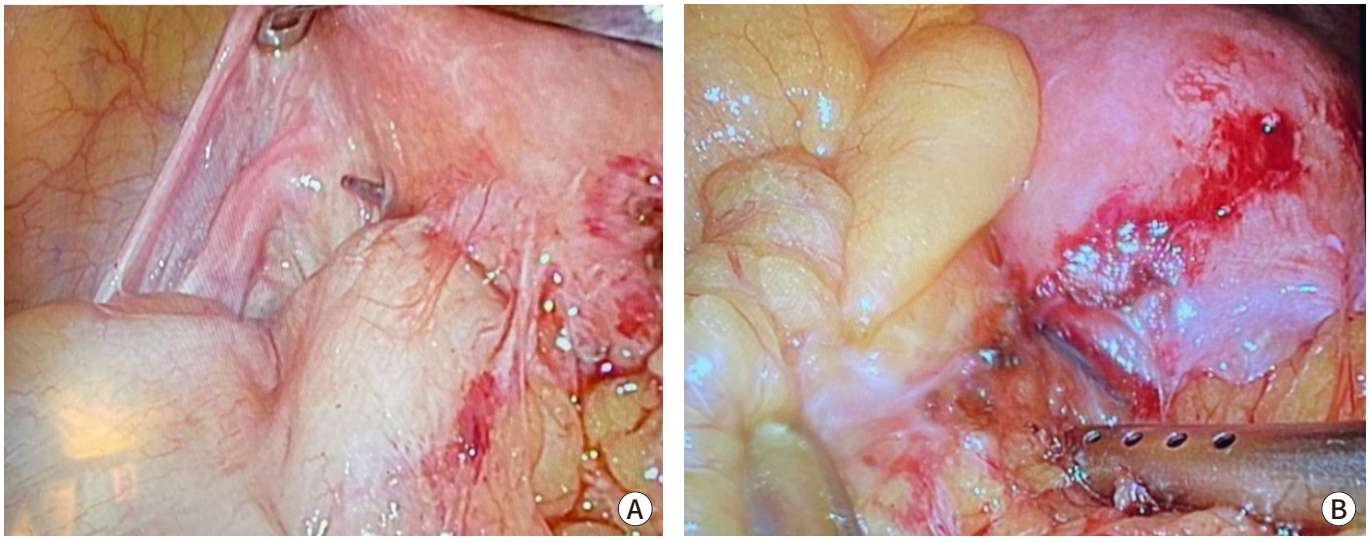

Fig. 3. Operative findings. (A) A suture knot at the left-upper uterus wall formed an adhesion with the sigmoid colon that was predicted to penetrate the abutting colon wall. (B) A suture knot at the mid-upper uterus wall formed adhesion with nearby omentum.

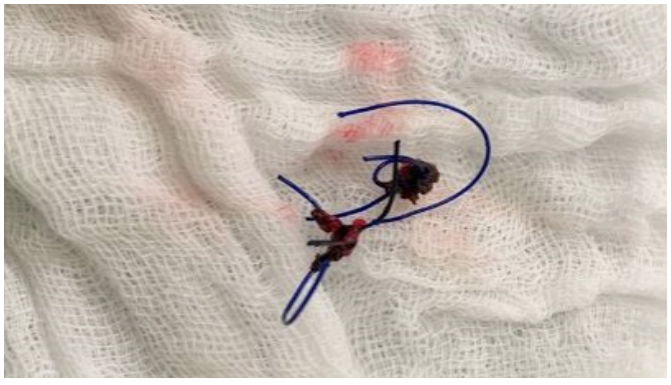

Fig. 4. The removed suture knot that was penentrating the colon wall, and was predicted to be a non-absorbable monofilament suture.

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Discussion

The factors for selecting a proper suture material are the characteristics of the material, the nature of the tissue, and the surgeon's personal preference. The main goal when choosing a suture material is for the suture to maintain the tensile strength of the wound until tissue healing provides sufficient stability. Therefore, this is an important choice for surgeons to make, and there are also fundamental recommendation for each tissue type since various tissues need different times for wound healing. In tissues such as muscles, subcutaneous tissues, and the skin, a few days are enough to heal. In contrast, fascia or tendons require weeks to months to heal; thus, several studies have indicated that absorbable sutures, which lose their tensile strength relatively slow, are superior to non-absorbable sutures. When delayed wound healing is predicted because of patient-specific factors, non–absorbable sutures are also indicated. In parenchymal organs such as the kidney or liver, a synthetic absorbable monofilament is preferable. Synthetic absorbable monofilaments can also be recommended for hollow viscous organs such as intestine or bladder, but exceptions still exist because suture selection is affected by patient characteristics, especially in patients with obesity, neoplasia, malnutrition, infection, steroid treatment, and collagen disorders.

When selecting suture materials, surgeons should keep in mind the complications that each suture could provoke. In fact, the literature contains some relevant cases of complications related to different suture types (Table 1) [4-6]. Khanal et al. [4] reported that a non-absorbable propylene suture that was used in a previous operation acted as a foreign body and led to adhesion formation [4]. The adhesion resulted in complete bowel obstruction with small bowel strangulation by constricting the band around the jejunum. The bowel strangulation was solved by removing the propylene suture and resecting the nonviable small bowel. Wang et al. [5] reported two cases of bowel obstruction and perforation caused by absorbable monofilament barbed sutures used to suture the peritoneal defect site in transabdominal preperitoneal patch surgery [5]. The obstruction was caused by a volvulus that was triggered due to an elongated tail of the barbed suture. Emergency laparoscopic exploration was performed, the embedded suture was excised and then the volvulus was solved. The second case, which involved bowel perforation, suggested that the tail of a barbed suture could penetrate the bowel wall. After the piercing barbed suture was removed, primary closure was performed at the serosal and muscular defect site. In thoracic surgery, Nakano et al. [6] reported bronchial penetration by an absorbable monofilament endoloop suture that was used for pulmonary vein ligation ; for

Table 1. Suture material related complications reported in medical database

Sex	Age	Diagnosis	Operation	Outcome	Country	Reported year
M	75	Penetration of the monofilament across the wall of the bronchus	No treatment	Absorbable monofilament endoloop suture could bring out bronchial penetration.	Japan	Nakano et al., 2017 [6]
M	66	Small bowel obstruction with strangulation	Adhesiolysis and small bowel segmental resection and anastomosis	Non-absorbable propylene suture caused complete bowel obstruction	Nepal	Khanal et al., 2021 [4]
M	45	Small bowel obstruction	Removal of the embedded tail of the barbed suture from the mesentery	Bowel obstruction could be caused by an absorbable monofilament barbed suture.	Japan	Wang et al., 2021 [5]
M	50	Small bowel perforation	Removal of the tail of the barbed suture and closure of the serosal and muscular defect	Bowel obstruction could be caused by an absorbable monofilament barbed suture.	Japan	Wang et al.,2021 [5]

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treatment, the suture was removed [6].

In this case, we found that a non-absorbable monofilament suture caused bowel wall penetration even 15 years after the previous operation. Unlike the absorbable sutures, which are broken down by hydrolysis, non-absorbable sutures can be hidden in nearby tissue by being encapsulated or walled off by fibroblasts. Thus an adhesion could form around the nonabsorbable suture site. These adhesions may not usually lead to any symptoms, but in sporadic cases, they could induce complications such as bowel obstruction or strangulation. However if the encapsulation is not completed, the remaining suture knot could trigger another problem, such as bowel perforation, as we showed in this case report. We have summarized some remarkable cases that resulted from variable types of suture materials, and surgeons should consider a number of factors to select an optimal method for each patients. Along with personal caution, we need more education and efforts to improve awareness of the importance of deciding upon the suture material in surgery, without ignoring the complications happened that can be cause by even a tiny suture. Further research is also needed as to which suture material is better in certain circumstance and how delayed complications could be prevented after using non-absorbable suture materials.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

Not applicable.

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