



A Diabetic Male with Arteriosclerosis and Pericardial Cyst Treated by Imeglimin

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Abstract

The patient is a 70-year-old male who developed back pain in May 2021. He was diagnosed with a ureteral stone and type 2 diabetes (T2D) with an HbA1c of 9.3% in 2021. After a successful operation, he continued treatment for T2D. Pulse wave velocity (PWV) showed an ankle-brachial index (ABI) of 0.78/0.83 (R/L) and a cardio-ankle vascular index (CAVI) of 12.9/13.9, suggesting arteriosclerosis and peripheral artery disease (PAD). Computed tomography (CT) showed a movable lesion adjacent to the right heart, suggesting a pericardial cyst. HbA1c had been stable after that but increased during the summer of 2024; he then started imeglimin (Twymeeeg), which was associated with clinical efficacy and without gastrointestinal adverse effects (GI-AE).

Keywords

Pulse Wave Velocity, Atherosclerotic Cardiovascular Disease, Standard of Care-2025, American Diabetes Association, Imeglimin

Abbreviations

PWV: Pulse Wave Velocity; ASCVD: Atherosclerotic Cardiovascular Disease; SoC-2025: Standard of Care-2025; ADA: American Diabetes Association

Introduction

For some decades, arteriosclerosis has been a crucial medical and health problem in developed countries and also in developing countries. The clinical significance of atherosclerotic cardiovascular disease (ASCVD) has gradually become prevalent, and a paradigm shift in ASCVD prevention has been explored [1]. Although the standard guideline recommends the control of serum levels of low-density lipoprotein cholesterol (LDL-C) in

patients with ASCVD, the rate of successful achievement remains suboptimal [2]. Recently, a large study of health systems for the CardioHealth Alliance was conducted on ASCVD, including vascular disease, coronary heart disease (CHD), heart failure (HF), diabetes (DM), atrial fibrillation (AF), and chronic kidney disease (CKD). As a result, adequate lipid-lowering therapy (LLT) at baseline was not satisfactory.

Case Report

Regarding the relationship between the risk of diabetes and CVD, significant heterogeneity has been present [3]. Several CVD risks of ASCVD, CHD, HF, and stroke were investigated. As a result, DM Risk Scores (DMRS) showed a significant difference in CHD and CVD, but no difference in ASCVD and HF. On January 1, 2025, the American Diabetes Association (ADA) presented the latest Standard of Care (SoC)-2025 for providing adequate diagnosis and treatment for diabetes and ASCVD [4]. This annual edition has been clinically significant for applicable practice and research. The authors have continued daily clinical studies of diabetes and ASCVD for a long time. We recently encountered an impressive case and will describe its outline and related perspectives in this article.

Case Presentation

Medical History:

The patient is a 70-year-old male without any particular diseases until the age of 60. In May 2021, he developed back pain and was diagnosed with a ureteral stone. When he was transferred to the municipal hospital, he was found to have hyperglycemia and an elevated HbA1c of 9.3%. He underwent surgery for the

ureteral stone and was treated with insulin therapy. His glucose variability improved, and he was referred to our clinic for successive adequate treatment of type 2 diabetes (T2D). At the first consultation, his HbA1c was 8.0% in July 2021.

Physical and Laboratory Examinations:

A physical examination in July 2021 showed no abnormalities in consciousness, speech, lungs, heart, abdomen, or neurological findings. Vital signs were as follows: pulse 76/min, regular; blood pressure (BP) 132/80 mmHg, and SpO₂ 98%. The patient's height was 165.3 cm, weight was 67.4 kg, and body mass index (BMI) was 24.7 kg/m².

The biochemical examination data from 2021 to 2024 are summarized in **Table-1**. It shows no significant changes in liver function, kidney function, lipid profile, or complete blood count (CBC). His chest X-ray and electrocardiogram (ECG) were unremarkable. He underwent a pulse wave velocity (PWV) examination, where the ankle-brachial index (ABI) was 0.78/0.83 (right/left), and the cardio-ankle vascular index (CAVI) was 12.9/13.9 (R/L). The findings showed an irregular wave shape, suggesting the presence of arteriosclerosis (**Fig-1A** and **Fig-1B**).

Table-1: Changes in Laboratory Data

	2021	2022		2023		2024	Units
	Dec	Jun	Nov	May	Dec	Jul	
Liver							
AST	19	19	24	24	35	44	(U/L)
ALT	15	18	25	21	35	40	(U/L)
GGT	29	33	31	27	33	45	(U/L)
Renal							
UA	6.7	6.4	6.6	5.8	5.6	5.6	(mg/dL)
BUN	10	10	10	8	9	9	(mg/dL)
Cre	0.83	0.79	0.83	0.76	0.77	0.73	(mg/dL)
Lipids							
HDL	41	43	41	42	44	40	(mg/dL)
LDL	169	99	93	100	91	100	(mg/dL)
TG	209	184	138	124	124	135	(mg/dL)
CBC							
WBC	76	83	82	83	80	85	(x10*2/μL)
RBC	515	530	526	509	509	491	(x10*4/μL)
Hb	16.5	16.9	16.6	16.5	16.2	15.4	(g/dL)
PLT	31.4	27.9]	27.3	24.9	27.6	22.8	(x10*4/μL)
Diabetes							
HbA1c	5.6	6.3	6.7	6.5	7.0	7.3	(%)

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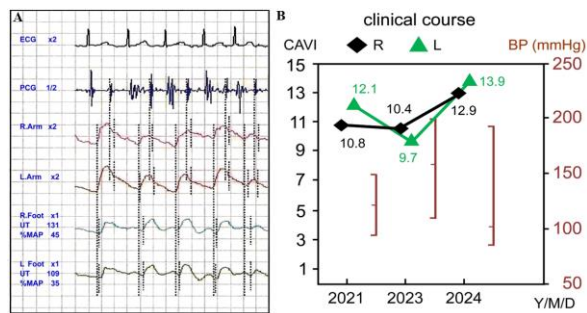


Fig-1: Pulse Wave Velocity (PWV) Exam

- PWV showed decreased values of ABI
- CAVI showed elevated values indicating arteriosclerosis

A CT scan of the chest and abdomen was conducted in June 2021, with the following findings (**Fig-2A** and **Fig-2B**). A cystic mass with slightly low absorption was observed along the visceral pleura on the right edge of the heart. A pericardial cyst was suspected, but the patient's medical history must also be considered. A decrease in the density of the liver parenchyma was observed, raising the possibility of severe fatty liver. No space-occupying lesion (SOL) was detected. The right kidney was slightly swollen, with noticeable fuzziness on the edge. There was dilation of the renal pelvis and a stone in the upper ureter. Cysts were observed in both kidneys. A small amount of ascites was noted. No significant changes were observed in the bladder. A stone in the right ureter and dilation of the renal pelvis were observed, raising the possibility of inflammatory complications.

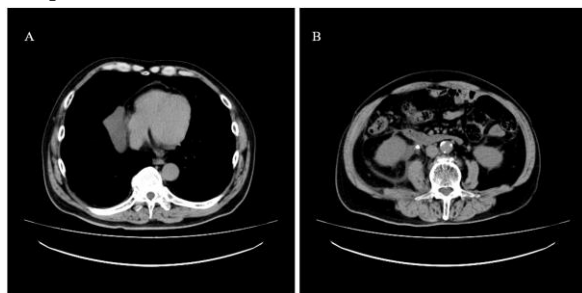


Fig-2: Image of Abdominal Computed Tomography in 2021

- cystic mass exists on the right edge of the heart
- dilated renal pelvis and stone in the upper ureter

As part of the follow-up, a CT scan was conducted in February 2023 (**Fig-3A** and **Fig-3B**). Both lungs were relatively well-filled, with mild thickening near the pleural attachment of the right interlobar fissure. These findings were similar to those in the previous

examination. The cystic mass that was previously observed on the right edge of the heart and above the diaphragm had now moved upward and slightly outward and was now in contact with the pericardium and bronchi. Based on these findings, the lesion appeared to be a pericardial or bronchial cyst. Its shape had changed from the previous examination, and it was mobile. The cyst in the right kidney remained unchanged from the previous exam. There was also no significant difference in the decreased density of the liver parenchyma compared to the previous examination.

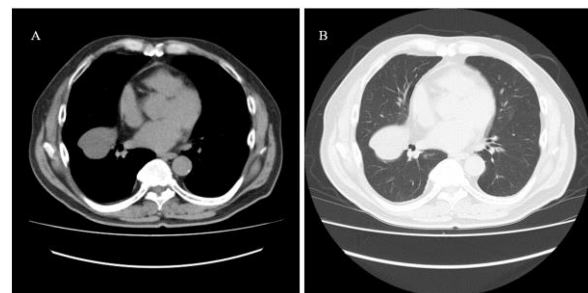


Fig-3: Image of chest computed tomography in 2023

- cystic mass moved upward and outward
- mass in contact with pericardium and bronchi

Clinical Progress

After undergoing surgery for urinary stones, the patient underwent a detailed examination and treatment for diabetes. In May, postprandial blood glucose was over 400 mg/dL, the HbA1c level was high at 9.3%, and the serum creatinine level was 1.26 mg/dL. Blood glucose was controlled with insulin before and after the operation, and voglibose, dapagliflozin, silodosin, and Quercus salicina were started as OHAs. Successively, linagliptin, metformin, aspirin, and rosuvastatin were then added. This diabetic case was controlled at our hospital from July, and the HbA1c level steadily decreased each month to 8.0%, 6.7%, 6.3%, and 5.6% (**Fig-4**). Until the year 2023, the HbA1c level remained below 7% with good control. However, since 2024, the HbA1c level has gradually increased, so the patient started taking imeglimin (Twymee) at 2000 mg/day in October. Since then, HbA1c has been decreasing by 0.3% each month. No side effects, particularly gastrointestinal adverse effects (GI-AE), have been observed until now, and the patient's condition has progressed smoothly.

Case Report

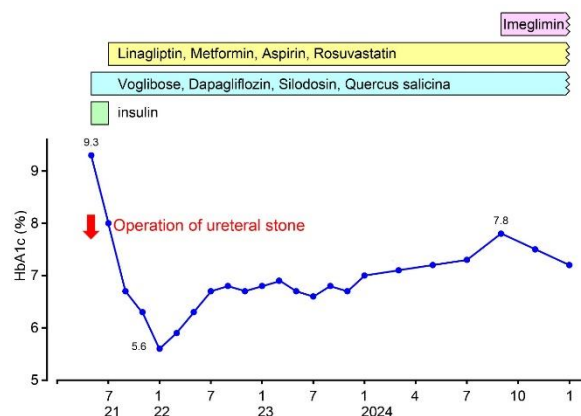


Fig-4: Clinical progress with HbA1c and treatment

Ethical Standards

This article complies with the guidelines of the Declaration of Helsinki [5]. In addition, some comments are presented regarding the regulation of the information. The principle includes ethical regulations for clinical research and practice. The guidelines were applied from the Japanese Ministry, which includes the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor, and Welfare. The current authors established the ethical committee, which is in Sakamoto Hospital, Kagawa, Japan. The main staff members include the hospital president, physicians, nurses, pharmacists, nutritionists, and legal professionals. They discussed the matter in a satisfactory manner and agreed on the protocol. Informed consent was obtained from the patient in written form.

Discussion

The current patient has several medical and health problems. These include: i) T2D, ii) arteriosclerosis, iii) possible peripheral artery disease (PAD), iv) probable pericardial cyst, v) dyslipidemia, vi) post-operation of ureteral stone, vii) benign prostatic hyperplasia (BPH), viii) allergic dermatitis taking Chinese medicine *Quercus salicina*. Among these, some perspectives are discussed below.

In this case, a cystic lesion was observed on the right side of the heart, which is thought to be a pericardial abnormality. Pericardial abnormalities are often encountered in various clinical settings and are becoming more common due to the widespread use of computed tomography (CT) and magnetic resonance

imaging (MRI) [6]. Pericardial abnormalities include pericardial effusion, pericarditis, cardiac tamponade, pericardial stenosis, and pericardial cysts. Pericardial effusion is a common imaging finding of fluid accumulation in the pericardial sac. With the increasing use of CT and MRI, pericardial diseases are being discovered more frequently. Certain developments in the latest pericardial imaging and clinical guidelines have been found in the American Society of Echocardiography (ASE), the European Association of Cardiovascular Imaging (EACVI), and the European Society of Cardiology (ESC) [7].

Pericardial cysts are relatively uncommon and are benign in nature. They sometimes cause clinical symptoms depending on their size and location in the body [8]. If a definitive diagnosis cannot be made, recurrent percutaneous pleural aspiration may be attempted for evaluation and treatment. Differential diagnoses for pericardial cysts include pericardiac cysts, cardiac cysts, bronchogenic cysts, hepatic cysts, pericardial hydatid cysts, and duplication cysts [9-11]. Although pericardial cysts are often asymptomatic and benign, they may sometimes lead to life-threatening complications. Consequently, regular follow-up is recommended, and in certain cases, minimally invasive interventions or surgery may be required [12].

This patient is a 70-year-old male with lifestyle-related diseases, including T2D, dyslipidemia, arteriosclerosis, and possible PAD. The results of the pulse wave velocity (PWV) examination showed elevated cardio-ankle vascular index (CAVI) and decreased ankle-brachial index (ABI), indicating the necessity of follow-up for the progression of arteriosclerosis. Currently, he has been taking aspirin, but in the future, he may be required to take a direct oral anticoagulant (DOAC). From an atherosclerotic cardiovascular disease (ASCVD) perspective, cerebrovascular accident (CVA), coronary heart disease (CHD), and PAD should be monitored to prevent possible cardiovascular events.

ASCVD has been broadly associated with acute coronary syndrome (ACS), myocardial infarction (MI), various revascularization procedures, transient ischemic attack (TIA), stroke, PAD, and aortic aneurysm

[14]. Cardiovascular disease (CVD) ranks first in mortality and morbidity among common diseases. Arteriosclerosis and diabetes play a major role as risk factors for CVDs, influencing each other. For evaluating disease progression, brachial-ankle pulse wave velocity (baPWV) can be useful [15]. A study protocol involving an Asian population (n=59,268, mean age 48.1 years) reported 1,830 cases of developing CVDs. Using multivariate Cox regression analysis, CVD risks were calculated as follows: hazard ratio (HR) 1.88 for diabetes, 1.40 for arteriosclerosis, and 2.12 for comorbidity groups. Furthermore, HR values for CVDs were 1.16 for fasting blood glucose and 1.22 for baPWV.

Some limitations may be present in this case. The current problem of the pericardial cyst has not yet been confirmed by biopsy or histological diagnosis. Consequently, radiological evaluation such as CT will be continued for follow-up.

Conclusion

In summary, a 70-year-old male case was reported here. Several clinical conditions related to ASCVD are present. Careful monitoring will be required in the future. It is expected that this article will serve as a useful reference for research on diabetes and arteriosclerosis.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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