Successive Diabetic Macroangiopathy for Cerebral, Cardiac and Peripheral Vascular Operation

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Abstract

Current case is 57-year-old male treated by 12-year insulin with type 2 Diabetes (T2D) for 22 years. HbA1c was stable for 6.3-6.8% until 2021. After that, he developed several events of cerebral vascular accident (CVA), ischemic heart disease (IHD) and peripheral artery disease (PAD). He received superficial temporal artery (STA)-middle cerebral artery (MCA) bypass for CVA, percutaneous coronary intervention (PCI) by drug-eluting stent placement for IHD, and treatment of SMART stent at superficial femoral artery (SFA) for PAD. Consequently, he has suffered from macroangiopathy and microangiopathy as neuropathy, retinopathy and nephropathy. Serum creatinine increased 1.03 to 1.67mg/dL for 18 months.

Keywords: Macroangiopathy; Peripheral Artery Disease (PAD); Superficial Femoral Artery (SFA); Percutaneous Coronary Intervention (PCI); STA- MCA bypass.

Introduction

Across the world, type 2 diabetes (T2D) has been crucial problem for medical practice and health care management [1]. T2D is categorized in life style-related disease, where everyone must keep adequate daily activity [2]. In Jan 2023, American Diabetes Association (ADA) announced "Standards of Care in Diabetes" for applicable management [3]. Consequently, the standard diagnosis and therapy for T2D has been continued for clinics and hospitals for years [4].

As regards to T2D, necessary information would be provided for prevention and treatment in various situation [5]. According to the guideline of ADA-2023, several components to be evaluated include in the following. They are macrovascular and microvascular complications, high BP, abnormal lipids, obesity, NAFLD, obstructive sleep apnea (OSA), hypoglycemia, dental visit, dilated eye exam, and so on [6]. For macroangiopathy, cerebral vascular accident (CVA), ischemic heart disease (IHD) and peripheral artery disease (PAD) are main medical problems [7,8]. On the other hand, microangiopathy is also crucial diabetic problems including neuropathy, nephropathy and retinopathy [9,10].

Authors and co-researchers have continued reporting clinical practice and research for years [11,12]. Especially, our diabetic team have tried to provide better glucose variability using insulin and various oral hypoglycemic agents (OHAs) [13,14]. We have recently experienced an impressive T2D patient associated with macroangiopathy, microangiopathy and nephropathy [15]. The case has severe comorbidities receiving for several operations. General clinical progress and some perspective will be described in this report.

Case Presentation

Medical History

The case is 57-year-old male with T2D. The onset of T2D was at the age of 35, and he started insulin therapy at age 45. At 51 years old, he had an episode of slight CVA in the right brain. He has currently slight paresthesia in his left hand and no obvious motor impairment. For his habit perspective, he used to drink alcohol moderately, but he has not drink at all in the last 3 years. However, he could not quit smoking completely, continuing about 5 cigarettes per day.

For recent treatment, he had received insulin and oral medical administration. Regarding diabetic control, he has shown stable situation with HbA1c 6.3% to 6.8% during 2019-2021 (Figure 1). His insulin treatment includes the following: 1) novorapid injection flextouch 0-7-7 units (morning, noon, evening), 2) Insulin Degludec has been provided for 7 units at 2000h, 3) Miglitol 100mg, 4) Metformin 500 mg and 5) Epalrestat 150mg per day. In

addition to diabetic treatment, he has continued other medical agents. They are Clopidogrel 75mg, Amlodipine 5mg, Valsartan 20mg, Mecobalamin 1500mg, Pitavastatin Calcium Hydrate 4mg, Ezetimibe 10mg per day.
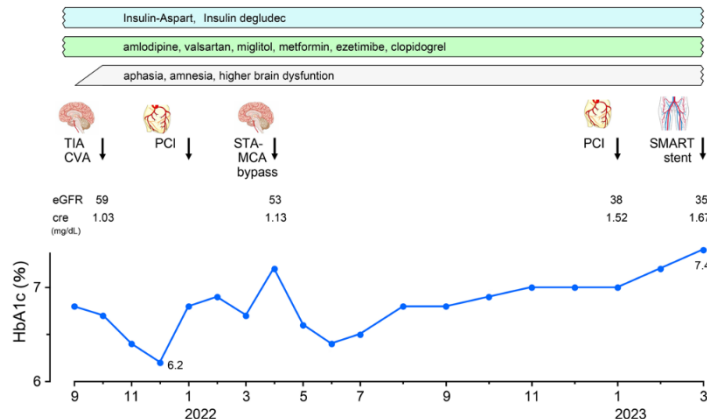

Figure 1: Clinical progress of HbA1c, renal function, events and treatments.

Physicals Examination

His physical examination in Jan 2023 showed the following status. Consciousness was alert, conversation was normal, vital signs were within normal ranges for pulse 72 /min, BP 130/78 mmHg, SpO2 97%. He showed negative findings of lung, heart and abdomen. Neurological examination showed no apparent motor impairment in upper and lower extremities, and felt slight paresthesia in the left hand. His physique showed height 177cm, weight 75kg, 23.9 kg/m^2 and body surface area (BSA) 1.92 m^2.

Laboratory Examination

The laboratory data in Jan 2023 were as follows: HbA1c 7.0%, post-prandial blood glucose 190 mg/dL, RBC 4.29 x 10^6 /μL, Hb 12.7 g/dL, Ht 39.6 %, MCV 92.3 fL (80-98), MCH 29.6 pg (27-33), MCHC 32.1 g/dL (31-36), WBC 7050/μL, Plt 25.8 x 10^4 /μL, GOT 13 U/L, GPT 14 U/L, GGT 13 U/L, LDH 193 U/L (124-222), CK 154 U/L (59-248), T-Bil 0.3 mg/dL, Uric acid 5.4 mg/dL, BUN 29 mg/dL, Cre 1.52 mg/dL, eGFR 38 mL/min/1.73m^2, Na 139 mmol/L, K 4.9 mmol/L, Cl 107 mmol/L, HDL 42 mg/dL, LDL 65 mg/dL, TG 99 mg/dL, TP 5.8 g/dL, Alb 3.4 g/dL, CRP 0.06 mg/dL. Urinalysis: urobilinogen (+/-), glucose (2+), protein (3+), pH 6.0, ketone bodies (-). Chest X-ray exam showed negative. Electrocardiogram (ECG) showed normal axis, pulse 76/min, ordinary sinus rhythm, and slight ST-T depression in V$_{3-5}$.

CVA Problems

From CVA point of view, he had clinical problems and operation. From August 2021, he gradually developed difficulty to have a smooth conversation. He had no overt neurological symptoms at that time. MRI showed hyperintensity in the left coronary radiata on diffusion weighted imaging (DWI) and evidence of left middle cerebral artery (MCA) obstruction. He was then started on aspirin and clopidogrel. On Nov 24, 2021, the episode of aphasic Transit

Ischemic Attack (TIA) was found, in which his speech was lost for 2-3 hours. For Hasegawa Dementia Scale-Revised (HDS-R), he got the perfect score of 30 points. However, the patient himself is working as a caregiver and is familiar with the HDR-R well.

He was transferred to Neurosurgery (NS) department of University Hospital. Head MRI-MRA shows a new cerebral infarction in the left coronary radiatum, occlusion of the left middle cerebral artery (MCA) proximal to M1, and stenosis of the right MCA proximal to M1. Because of repeated ischemic attacks in a short period of time, it was determined that revascularization was necessary. Due to his work, the procedure was postponed for some time. Due to the obstruction of the left proximal M1, extracranial to intracranial (EC-IC) bypass was planned for powers stage 2. In early April 2022, he received the operation of *STA-MCA* bypass, which was successfully conducted without any problems (Figure 1).

CAD and PAD

For coronary artery, he received the treatment of percutaneous coronary intervention (PCI). The drug-eluting stent placement (Synergy XD 2.5*28mm) was performed for severe stenosis in the right middle coronary artery (MCA) in last Jan 2023 (Figure 2). It was successfully performed with enough expansion.

Figure 2: Successful operation of drug-eluting stent placement.

In the light of peripheral artery disease (PAD), he had further evaluation in March 2023 (Figure 3). Left lower extremity arteriography showed the occlusion of left superficial femoral artery (SFA) more than 20 cm. Peripheral dispersal of plaque was observed after balloon dilatation. Catheter aspiration was performed and a SMART stent (8 cm x 150 cm) was placed in the proximal region of the left SFA. Satisfactory blood flow was maintained after surgery (Figure 3).
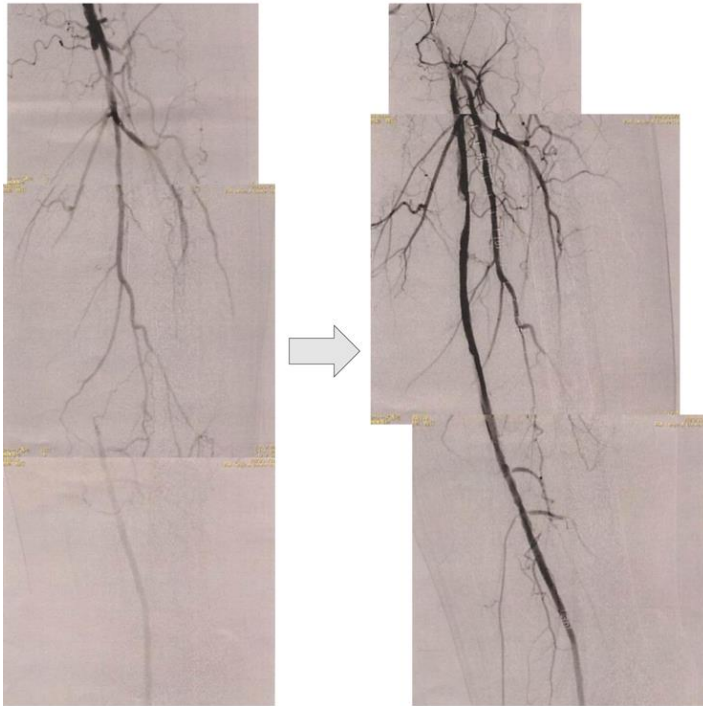
Figure 3: Changes in blood stream for left lower extremity left: before intervention, right: after intervention.

After confirming that the symptoms of intermittent claudication in the left lower limb have disappeared, similar treatment for right lower limb revascularization will be considered for future plan. For anti-coagulation therapy, oral administration of aspirin 100mg and clopidogrel 3.75mg will be continued for two months. After that, clopidogrel was discontinued and only aspirin will be continued. Oral ezetimibe will be continued for the control of dyslipidemia.

Medical Problems

From mentioned above, this case had a variety of medical problems. He was diagnosed as T2D at the age of 35 years, and developed other complicated pathophysiology such as hypertension, dyslipidemia and chronic kidney disease (CKD) stage G3a. As diabetic complication, he has CVA, IHD and PAD associated with related operation about these three major macroangiopathy. Furthermore, he has also microangiopathy for slight neuropathy, nephropathy (diabetic kidney disease, DKD) and simple diabetic retinopathy (SDR).

Ethical Standards

Current case report is complied with the ethical guideline of the Declaration of Helsinki. Moreover, some comments were associated with the regulation related to the personal information. The principle was along with ethic rule for clinical research for human being. Adequate guidelines are presented from Japanese government. The case includes Ministry of Health, Labor and Welfare, Japan and Ministry of Education, Culture, Sports, Science Technology, Japan. The author et al. established the ethical committee as to this case. The meeting existed in the Yoshinogawa

Hospital, Tokushima prefecture, Japan. The established committee includes several related hospital regular staffs and professional legal person. They consist of the president of the hospital, physician and surgeon in charge, head nurse, registered pharmacist and legal professional. We discussed enough for current protocol and agreed the proposal. The informed consent was obtained from the patient by the document.

Discussion

This case has been characterized for its several severe complications related to T2D. In particular, macroangiopathy includes cerebral legion such as CVA, IHD and PAD. Several related perspectives are described in this discussion.

This patient has been on insulin therapy for 12 years since the age of 45 in order to obtain good glycemic control. Does insulin treatment affect cardiac events in patients with T2D? As to the cardiac event for T2D patients, systematic review and meta-analysis were conducted. Out of 8091 patients and 10139 control cases in 6 RCTs, large data were analyzed [16]. As a result, insulin therapy did not increase or reduce the risk of all-cause mortality, major adverse cardiac events (MACE) or hospitalization for heart failure (HHF). This patient has gained about 10 kg in the last 10 years. Another report was found concerning the relationship between weight changes and event of IHD in patients with T2D [17]. As a result, weight gain or loss more than 5% for 2 year becomes the influence for MACE in T2D.

In this case, TIA and CVA were found a few times, and episodes of loss of consciousness and memory were observed. Consequently, the procedure of STA-MCA bypass was carried out in January 2023. The decision to perform this procedure is evaluated based on the situation and recurrence [18,19]. Slightly earlier implementation is recommended [20]. No particular episodes of TIA or CVA were observed postoperatively, and careful follow-up will be necessary in the future. As to the treatment of PAD, SFA is involved in self-expanding stents by in-stent restenosis (ISR). It will be beneficial for multiple overlapping devices and long lesions [21]. Some stent designs are found such as SMART, Zilver and Ever Flex, in which comparative research are conducted.

In addition to macroangiopathy of CVD, IHD and PAD, current case has shown microangiopathy of neuropathy, nephropathy and retinopathy. He showed persisting obvious proteinuria for years, suggesting CKD stage G3a. During current 18 months, he has several events of macroangiopathy. For this period, serum creatinine level has increased from 1.03 mg/dL to 1.67 mg/dL, with decreased eGFR from 59 mL/min/1.73m^2 to 35 mL/min/1.73m^2 (Figure 1). As to the report for diabetic nephropathy and several categories of eGFR, 35 thousand T2D cases were analyzed for 3 years [22]. The results showed the prevalence as follows: nephropathy 31.6%, impaired eGFR 16.9% and albuminuria 22.0%. The results of eGFR categories 1-5 showed the prevalence of 36.0%, 47.1%, 15.7%, 1.1% and 0.1%, respectively. The

existence of diabetic nephropathy showed strong relationship with previous history of CVA and IHD. Furthermore, it showed significant association with smoking, obesity, non-HDL value, suboptimal BP and HbA1c control.

Future prediction models of DKD have been tried to be established from clinical research data. Using electronic medical records (EMR) (n=816), data was analyzed for 3 years [23]. The increased risk for developing DKD during 3 years as shown in the case of low albuminemia, poor glycemic control, lower eGFR and high bicarbonate. Concerning developing risk of CKD/heart failure (HF) for T2D patients, novel machine learning (ML) model was used for prediction [24]. Out of 217 thousand patients, 17 thousand cases were analyzed in detail. Then, 5-year prediction area under the curve (AUC) for CKD/HF was proved to be 0.718/0.837, respectively. Consequently, this model can contribute the prognosis by involving in earlier diagnosis and intervention.

Certain limitation may be present in this report. Current case has long history of T2D associated with macroangiopathy and microangiopathy. For latest 18 months, the case showed exacerbation of CVA, IHD and PAD associated with receiving some types of the operations. Various aggravating factors might influence such clinical progress until now and also from now.

In summary, 57-year-old T2D male showed various macroangiopathic and microangiopathic complications, and received the operations of CVD, IHD and PAD. Continuous adequate treatments and careful attention would be required in the clinical progress. Current report is expected to become a reference for diabetic practice and research.

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