Staphylococcus aureus endocarditis in a diabetic woman treated by continuous subcutaneous insulin infusion

1. Introduction

Continuous subcutaneous insulin infusion (CSII) is increasingly being used in the treatment of type 1 diabetic patients [1, 2]. As pointed out in a recent review on technical risks with CSII published in the Journal [3], cutaneous infections are the most frequent complication associated with portable pump therapy. Generally, they remain localized around the catheter needle [4–6] although exceptional toxic shock episodes have been reported [7]. Only one case of endocarditis has been mentioned in a general review of causes of mortality among diabetic patients treated with portable pumps [8]. We describe here the first case report of a CSII-treated diabetic patient who presented with a severe Staphylococcus aureus endocarditis that was successfully treated by mitral valve repair and prolonged intravenous antibiotic therapy. Although the causal relationship between CSII treatment and S. aureus endocarditis could not be proven, this complication in a diabetic patient treated with a portable insulin pump deserves further comments.

2. Clinical case

A 46-year-old woman with type 1 diabetes since the age of 15 years has been treated by CSII because of poor glycaemic control. During 4 years of CSII (using an Accucheck Spirit® pump for the last year) and soft catheters implanted in the abdominal wall (implantation changed every 3–4 days), no cutaneous infectious episodes were observed despite suboptimal blood glucose control (mean HbA1c level of 8.3%).

She was admitted in a general hospital for a flu-like syndrome, with weakness, arthralgia and fever. These symptoms had been present for 5 days and had not been favourably influenced by acetaminophen and amoxicillin oral therapy. Physical examination at admission revealed a 2–3/6 systolic murmur at the mitral area as well as peripheral oedema and purpura lesions predominating in the right leg. Clinical chemistry showed increased inflammatory markers (high CRP level), decreased haemoglobin and platelets and elevated D-dimer levels. Two consecutive blood cultures were positive for S. aureus. In the absence of clinical skin reaction, possible colonisation by S. aureus of the subcutaneous catheter was not checked. Transthoracic echocardiography revealed a 30 mm mobile mass attached to the posterior mitral valve, a finding, which was confirmed by transoesophageal echocardiography (Fig. 1). The patient received intravenous antibiotic therapy with a combination of fluclouxacillin (6 × 2 g/d) and gentamicin (3 × 80 mg/d). Three days later, a superficial skin necrosis occurred at the extremity of the fifth left toe, presumably due to peripheral embolism. Because of the size and mobility of the vegetation and the unfavourable clinical evolution, surgical treatment was considered. Coronary angiography was performed before scheduling valvular intervention because of the long-lasting and poorly controlled type 1 diabetes complicated by retinopathy and neuropathy. It revealed a 90% subocclusive stenosis on the proximal segment of left anterior descending (LAD) coronary artery. Mitral valvuloplasty (resection of the vegetation and reconstruction of the posterior leaflet) and bypass grafting between the left internal mammary artery and LAD coronary artery were performed simultaneously. Initial intravenous antibiotic administration was maintained for 4 weeks followed by 3 weeks of oral therapy. The evolution was favourable with disappearance of fever, reduction of CRP levels, and satisfactory mitral valve function without endocarditis recurrence in a recheck echocardiography. However, a retinal examination for visual defect showed arterial embolic lesion in the left eye, which was considered as sequelae of the previous active endocarditis. The patient continued CSII therapy using the same type of subcutaneous soft catheter without any further infectious adverse event during the next year of follow-up.

Fig. 1. Illustration of a 30 mm vegetation (arrow) attached to posterior leaflet of the mitral valve observed with transoesophageal echography. LA: left atrium. LV: left ventricle. Ao: aorta.
3. Discussion

The present case report describes a severe case of *S. aureus* endocarditis in a diabetic woman treated with a portable pump infusing insulin through a soft catheter implanted in the abdominal wall. Although infectious complications are not exceptional during CSII [3–5], most of them remain localised and rapidly regress with local antiseptic care and oral antibiotic administration when required. In some cases, they may lead to acute metabolic deterioration with severe hyperglycaemia and ketoacidotic episodes [9]. Only one case of fatal endocarditis was mentioned in a US series of 35 deaths among diabetic patients treated with portable pump two decades ago [8]. The key question is thus to know whether there was any relationship between CSII and *S. aureus* endocarditis in our patient? No local skin infection had been noted before the acute cardiac complication. However, it has been reported that various microorganisms, mainly *S. epidermidis* and *aureus*, contaminate most subcutaneous catheter needles even in the absence of a local skin reaction [5].

Nasal carriers of *S. aureus* have an increased risk of being infected by this pathogen [10] and diabetic patients have been shown to have higher *S. aureus* nasal carriage rates [11]. As discussed in a recent review [3], it was suggested that CSII-patients who are nasal carriers of *S. aureus* might be at higher risk of skin infections due to this microorganism [4]. Nevertheless, the nasal and perineal carriage of *S. aureus* was not found increased among CSII-treated diabetic patients and has not been considered as a risk factor in the occurrence of inflammation at the infusion site [12].

Community-acquired *S. aureus* bacteremia frequently develops in the absence of primary focus of infection and is more likely to result in endocarditis and secondary metastatic foci of clinical infection as compared to non community-acquired bacteremia [13]. *S. aureus* was the most common pathogen (31.4%) among the 1779 cases of definite infective endocarditis in the recent International Collaboration on Endocarditis Prospective-Cohort Study [14]. Patients with *S. aureus* endocarditis exhibited distinct characteristics compared with patients with endocarditis due to other pathogens, with more frequent diabetes, chronic diseases or health care contact. Infection associated with various medical interventions was the most common form of *S. aureus* endocarditis (ranging from 26 to 54% across various countries), and most patients with health care-associated *S. aureus* endocarditis acquired the infection outside of the hospital. This may be the case for our diabetic woman chronically treated with CSII. However, approximately 20% of patients with *S. aureus* endocarditis developed their infection in the absence of identifiable health care contact [14]. It is important to note that, besides CSII, no other predisposing factors for endocarditis were identified in the present case.

4. Conclusion

We report the exceptional case of severe *S. aureus* endocarditis in a young diabetic woman treated by CSII. Even if we have no direct proof of a causal relationship between CSII therapy and infective endocarditis, the high prevalence of asymptomatic *S. aureus* catheter needle colonisation in CSII-treated patients, on the one hand, and the observation that health care-associated infection is the most common form of *S. aureus* endocarditis, on the other hand, suggest a plausible link between CSII and *S. aureus* endocarditis. The established fact that infection reactions are the most frequent complication in diabetic patients treated with insulin portable pump emphasises the need for careful aseptic measures while changing the subcutaneous needle or catheter during CSII therapy.

References


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Soluble vascular cell adhesion molecule-1 is independently associated with soluble tumor necrosis factor receptor 2 in Japanese type 2 diabetic patients

The major clinical consequence of type 2 diabetes is mortality and morbidity from atherosclerotic vascular disease. Although it remains to be clarified which factors are responsible for the evolution of atherosclerosis, the earliest morphological evidence of atherosclerosis is the attachment of monocytes to the cell surface of vascular endothelium. Monocytes attach at the cell surface of adhesion molecules such as vascular cell adhesion molecule 1 (VCAM-1). Jager et al. [1] have shown that increased levels of soluble VCAM-1 are associated with risk of cardiovascular mortality independently of traditional risk factors, homocysteine, and C-reactive protein in type 2 diabetic patients. The mechanisms underlying the development of atherosclerosis, however, are unclear in type 2 diabetic patients.

Along with insulin resistance, tumor necrosis factor (TNF) seems to account for the development of atherosclerosis in type 2 diabetes. Shai et al. [2] demonstrated that soluble TNF receptor 2 (sTNF-R2) is strongly associated with risk of coronary heart disease in type 2 diabetic patients. We recently demonstrated that soluble TNF receptors are not associated with insulin resistance but are associated with albuminuria or aortic stiffness measured by brachial-ankle pulse wave velocity in Japanese type 2 diabetic patients [3–5]. To the best of our knowledge, however, the relationships between VCAM-1 and TNF system activities including soluble TNF receptors were not yet investigated in type 2 diabetic patients. In this regard, the problem is that insulin therapy or the degree of overweight per se affects the concentrations of VCAM-1 and TNF system activities. We therefore recruited insulin naïve type 2 diabetic patients who were not massively obese and investigated the relationships between VCAM-1 and TNF system activity in type 2 diabetic patients.

Fifty-four Japanese type 2 diabetic patients were enrolled. Their age, BMI, fasting glucose, and HbA1c were 62.5 ± 1.7 years (mean ± S.E.M.), 23.6 ± 0.4 kg/m², 137 ± 4 mg/dl, and 6.8 ± 0.1%, respectively. Along with VCAM-1, glucose, insulin, lipids, homocysteine, TNF-α, sTNF-R1, sTNF-R2, high sensitive C-reactive protein (hsCRP), interleukin-6 (IL-6), and leptin were measured in the morning after an overnight fast as described previously in [3,6–8].

With univariate analysis, VCAM-1 was positively correlated with age ($r = 0.355$, $P < 0.01$), sTNF-R1 ($r = 0.562$, $P < 0.0001$), and sTNF-R2 ($r = 0.701$, $P < 0.0001$) in our patients. Serum levels of VCAM-1, however, were not associated with homocysteine, TNF-α, glucose, insulin, BMI, hsCRP, IL-6, or leptin. Multiple regression analyses revealed that VCAM-1 was independently predicted by sTNF-R2 ($F = 38.7$), which explained 38.2% of the variability of VCAM-1 in our patients.

Thus, it may be suggested that VCAM-1 is associated with TNF system activity in Japanese type 2 diabetic patients.

References