The first case of takotsubo cardiomyopathy associated with sodium tetradecyl sulphate sclerotherapy

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The present article describes the case of a 70-year-old woman who developed a classic type takotsubo cardiomyopathy after receiving cosmetic sclerotherapy for varicose veins of the legs with sodium tetradecyl sulphate (STS) injections. The patient was in her usual state of health before the injections, and described no apprehension leading up to the procedure and no pain during the procedure. However, a few minutes after the completion of the procedure, the patient had severe chest pain of sudden onset and an electrocardiogram highly suggestive of ST elevation myocardial infarction. The patient was referred for emergent coronary angiography, which was normal. Subsequent ventriculography confirmed the suspected apical ballooning typical of takotsubo cardiomyopathy. Ventricular function returned to near-normal within three days of presentation. The present article describes what is believed to be the first case of takotsubo cardiomyopathy associated with the use of STS. A review of adverse events ascribed to STS revealed visual disturbances and transient ischemic attacks, suggesting the possibility of a common underlying vasospastic pathophysiology and an under-recognized vasoactive potential of STS that merits further investigation. In the interim, the present case advocates for the recommendation of universal pretreatment test dosing.

Key Words: Kounis syndrome; Sclerotherapy; Sodium tetradecyl sulphate; Stress cardiomyopathy; Takotsubo

We present the case of a 70-year-old woman who developed takotsubo cardiomyopathy ('apical ballooning syndrome') after receiving cosmetic sclerotherapy for varicose veins of the legs with sodium tetradecyl sulphate (STS) injections.

CASE PRESENTATION

The patient was in overall good health, apart from gastroesophageal reflux and well-controlled arterial hypertension for which she was prescribed hydrochlorothiazide 25 mg daily. She was scheduled for elective outpatient injections of an STS sclerosing detergent in a private clinic for the treatment of asymptomatic varicose veins in the lower extremities. The patient was in her usual state of health immediately before the administration of STS. Importantly, she denied experiencing any apprehension leading up to the procedure. The patient further stated that the procedure itself was associated with minimal, if any, pain. However, 5 min after the injection, while the patient was getting dressed, she experienced a sudden, hot, flushing sensation followed swiftly by severe transfixing chest pain, which did not abate despite repeated doses of sublingual nitroglycerin. Acetylsalicylic acid was administered empirically at the clinic and she

Le premier cas de cardiomyopathie takotsubo associée à une sclérothérapie au tétradécylsulfate de sodium

Le présent article décrit le cas d'une femme de 70 ans qui a présenté un cas classique de cardiomyopathie takotsubo après avoir subi une sclérothérapie plastique pour traiter des varices dans les jambes par des injections de tétradécylsulfate de sodium (TSS). La patiente présentait son état de santé habituel avant les injections et ne décrivait ni appréhension avant l'intervention, ni douleur pendant l'intervention. Toutefois, quelques minutes après l'intervention, elle s'est soudainement mise à souffrir de graves douleurs thoraciques, et l'électrocardiogramme était fortement indicateur d'un infarctus du myocarde avec élévation du segment ST. La patiente a été aiguillée vers une coronarographie émergente, qui a donné des résultats normaux. Une ventriculographie subséquente a confirmé le ballonnement apical présumé, caractéristique de la cardiomyopathie takotsubo. La fonction ventriculaire est redevenue presque normale dans les trois jours après la présentation. Le présent article décrit ce qu'on croit être le premier cas de cardiomyopathie takotsubo associée à l'utilisation de TSS. Une analyse des effets indésirables attribués au TSS révèle des troubles de la vision et des crises ischémiques transitoires, ce qui laisse supposer la possibilité d'une physiopathologie vasospastique transitoire et un potentiel vasoactif sous-évalué du TSS qui justifie des explorations plus approfondies. Entre-temps, le présent cas plaide pour la recommandation d'un essai de posologie avant le traitement.

Figure 1) Presenting electrocardiogram revealing an acute ST segment elevation in the anterolateral leads

was rushed to the hospital. Serial electrocardiograms on arrival to the emergency department revealed an evolving acute anterolateral ST segment elevation myocardial infarction (Figure 1). The patient

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Figure 2 Coronary angiography of the right (A) and left (B) circulation

was quickly transferred to the cardiac catheterization laboratory for an emergency coronary angiogram and probable primary percutaneous coronary intervention. Loading doses of acetylsalicylic acid and clopidogrel were given, along with a 4000 unit bolus of intravenous heparin and as-needed fentanyl. Hydrocortisone 500 mg was administered intravenously in the emergency room before transfer to the catheterization laboratory because of a history of iodine allergy.

Diagnostic angiography, however, revealed near-normal coronary arteries without any evidence of a stenotic lesion capable of producing such a clinical and electrocardiographic picture (Figure 2). Therefore, ventriculography was performed, which demonstrated classic takotsubo cardiomyopathy (Figure 3). The typical apical ballooning was confirmed the following day by transthoracic echocardiography (Figure 4), with a left ventricular ejection fraction of 45% and an otherwise normal heart. Medical management was modified to include an angiotensin-converting enzyme inhibitor. Follow-up echocardiography just three days later showed the almost complete normalization of the regional wall-motion abnormalities described and a left ventricular ejection fraction of greater than 60%.

Figure 3 Ventriculography in diastole (A) and systole (B) revealing the typical apical ballooning of takotsubo cardiomyopathy

DISCUSSION

Classic takotsubo cardiomyopathy consists of hyperdynamic basal segments with akinesis or dyskinesis of the apex, resulting in 'apical ballooning' (giving rise to a shape reminiscent of the traditional Japanese pot used to trap octopus, for which the cardiomyopathy is named), and a clinical and electrocardiographic picture that is often indistinguishable from acute myocardial infarction (1). Although its exact mechanism is not understood, it is believed to be due to an excessive adrenergic discharge that may result in diffuse vasospasm of the coronary microcirculation. It has been described in situations of substantial physical or psychological stress such as brain trauma or the loss of a loved one. This association has resulted in takotsubo cardiomyopathy also being known as stress-induced cardiomyopathy or 'broken heart' syndrome. Treatment is supportive and the majority of patients recover normal left ventricular function within weeks of presentation (1).

STS is a detergent sclerosing agent and its use has been described in the literature for various indications. It produces intraluminal thrombosis and rapid vessel wall damage through lipid disruption

Figure 4) Transthoracic echocardiographic four- (A) and two-chamber (B) views in systole confirming takotsubo cardiomyopathy

within minutes in its foam formulation. The use of STS in the treatment of varicose veins has been established for some time (2). Adverse reactions are typically minor, and include local reactions such as pain, itching and discolouration. Mastocyte degranulation is believed to cause allergic reactions to STS. Test dosing before sclerotherapy has been recommended and caution should be exercised in treating patients with a history of atopy. In addition, there is some suggestion that serum albumin plays a role in mitigating STS effects on circulating blood cells (the serum albumin level of the patient described here was normal). Although rare, anaphylaxis has been described (3) and may lead to life-threatening cardiorespiratory arrest. Deep venous thrombosis and pulmonary embolism have also been described, as have cases of accidental injection into the

interstitium and arterial system, resulting in skin necrosis and even limb loss (2). Although chest pain has been described following STS treatment in one patient (2), we believe the present report provides the first description of takotsubo cardiomyopathy associated with this treatment.

It is interesting to note that, although quite rare, a survey (4) of the use of STS sclerotherapy for varicose veins in the United Kingdom reported cases of stroke and transient ischemic attack. Temporary visual disturbances have been described (2) following STS sclerotherapy, consisting of diminished visual acuity or scotomata. The pathophysiological mechanism of these neurological complications is not known definitively. One possible explanation is that this is the result of central nervous system vasospasm that occurs transiently following STS therapy. This vasospasm would be akin to the supposed mechanism underlying the apical ballooning syndrome. It has been suggested that such a vasospasm can result from mast cell degranulation. In fact, clinical myocardial infarction with normal underlying coronary arteries has been described in the setting of anaphylactic reactions and has been termed the Kounis syndrome (5). Given reports of anaphylaxis following STS therapy (3), it is possible that the central nervous system events described in the STS literature (2,4) and the present case of takotsubo cardiomyopathy are the result of a common mastocyte-mediated vasospastic phenomenon that may or may not be generalized enough to have associated anaphylaxis, resulting in the Kounis syndrome. As such, migraines, transient ischemic attacks, takotsubo cardiomyopathy and the Kounis syndrome following exposure to agents known to cause mastocyte degranulation would be part of the same pathophysiological spectrum.

Although one may not conclusively infer a causal link between STS and the takotsubo cardiomyopathy experienced by the present patient, the temporal relationship of the events described remains highly suggestive and should underscore the need to pursue test dosing of STS in all patients as recommended to avoid rare but potentially life-threatening complications such as anaphylaxis or left ventricular failure. Furthermore, the pathophysiological mechanism underlying the visual disturbances associated with STS sclerotherapy and the vasoactive potential of this agent deserve further attention in the literature.

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