Letter to the Editors

Valvular heart disease in a patient taking
3,4-methylenedioxymethamphetamine (MDMA,
'Ecstasy')

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3,4-methylenedioxymethamphetamine, (MDMA, 'Ecstasy'), an amphetamine-derived drug, is a psychoactive stimulant used as a recreational drug. *In vitro* experiments have suggested that ecstasy can lead to fenfluramine-like proliferation of cardiac valves through activation of 5-hydroxytryptamine 2B (5-HT_{2B}) receptors and can induce mitogenic responses in human valvular interstitial cells [1]. We report the first observation of valvular heart disease (VHD) with pathological confirmation after long term use of ecstasy.

A 33-year-old male patient was admitted for shortness of breath and chest pain. The only risk factor reported was active smoking. He reported long lasting exposure to ecstasy (several pills week⁻¹ since the age of 17 years). At examination a systolic and diastolic mitral murmur was diagnosed. Mean blood pressure was 106/70 mmHg. ECG showed sinus rhythm (91 beats min⁻¹) with a right bundle branch block. Echocardiography revealed a slight left ventricular dilation (end-diastolic diameter of 55 mm) with an ejection fraction of 55% and typical features of mitral valve disease. There was a left atrial enlargement (area of 42 cm²) thick mitral valve with decreased opening of the mitral valve leaflets. Mean pressure gradient across the mitral valve was of 14.7 mmHg with mitral valve areas of 1.56 cm². These moderate to severe mitral stenosis features were associated with severe mitral regurgitation (regurgitant orifice area = 0.49 cm²) with a central blood jet. Other valves and heart chambers were normal. This patient had pulmonary hypertension (40 mm Hg) without right

heart failure. Coronary angiogram showed normal coronary arteries with a decreased cardiac index and post capillary pulmonary hypertension. Surgery was decided. Macroscopic analysis made the surgeon hypothesize about a possible cardiac tumour. Mitral valve leaflets and the chordae tendinae were markedly thickened and fibrous. The chordae tendinae were retracted (Figure 1). After resection, the surgeon decided to perform mitral valve replacement with a mechanical Saint Jude prosthesis despite severe damage of the mitral annulus. At histology, the endocardium on both sides was fibrous up to 2 mm thick. It was stratified with layers of collagen bundles and spindle cells. Density of spindle cells was heterogeneous, but more frequently low. In this abundant extracellular matrix, rare foci contained abundant elastic fibres. No inflammation or myxoid matrix accumulations were observed, ruling out rheumatic and Barlow diseases (Figure 1B, C). Common disease (Osler endocarditis, carcinoid syndrome, rheumatic fever, autoimmune disease...) or intake of other drugs (ergot derivatives, appetite-suppressant drugs including benfluorex) known to affect cardiac valves were not found. One month later, the patient came back with chest pain, fatigue and loss of weight. Trans-thoracic echocardiography showed a paraprosthetic leak with prosthesis dehiscence. The patient underwent re-operation with fixation of his prosthesis. At follow-up there were no complications.

This is the first case of VHD with pathological confirmation related to long term exposure to ecstasy. Except for an

Figure 1

Anatomical and histological findings. (A) a short leaflet mitral valve (left) and a large leaflet mitral valve with a part of the left ventricle which was also removed (right). (B) Gross pathology of the mitral valve: on this section the valve is markedly thickened and fibrous as well as the chordae tendinae (arrow). (C) Histopathology of the mitral valve: this figure shows a huge fibrous thickening of the endocardium. The cell density is low in an abundant extracellular collagenous matrix exhibiting a stratified pattern (H&E, $\times 50$). Left inset: the cells are spindle shaped and organized in parallel (H&E, $\times 100$). Right inset: most of the spindle cells in the thickened endocardium express alpha-smooth muscle actin and are considered as activated interstitial cells (alpha-smooth muscle actin immunohistochemistry, $\times 100$).

in vitro study [1], few data are available [1]. Among 29 subjects using ecstasy, eight had abnormal mitral valve echocardiography vs. 0 in controls [2]. The fact that the lesions in our patient were very similar to those described with appetite-suppressant drugs [3] and the ability of

ecstasy to activate 5-HT_{2B} receptors, like fenfluramine [1, 4], suggests its role in the pathophysiology of this VHD. VHD is unusual in young subjects.

The present work allows the addition of ecstasy to the list of substances able to induce VHD [5]. The data also underline the important (and probably underestimated) harm associated with the now large use of ecstasy in young subjects. Information must be given about this risk.

Competing Interests

There are no competing interests to declare.

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