3,4-Methylenedioxymethamphetamine (MDMA, Ecstasy) Intoxication in a Young Adult with Giant Coronary Aneurysms from Kawasaki Disease

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ABSTRACT

Kawasaki disease is an acute vasculitis of unknown etiology that usually occurs in children less than five years old. Coronary artery aneurysm due to arteritis is the most common cardiac complication. Chronic aneurysms are associated with an increased risk of developing luminal thrombosis and ischemic myocardial injury.

We present a case of an 18-year-old male with a history of Kawasaki disease complicated by chronic giant aneurysms of the right and left coronary arteries. Serial echocardiographic studies and treadmill electrocardiogram stress tests as recent as 1.5 years before death revealed excellent cardiac function by clinical criteria. The decedent sustained a witnessed collapse after ingesting 3,4-methylenedioxymethamphetamine (MDMA) and ethanol. He was pronounced dead in the emergency department after unsuccessful resuscitative efforts.

Autopsy revealed large aneurysms of the three main epicardial coronary arteries with extensive foci of severe stenosis by intimal fibrosis and organizing thrombus. Microscopic examination revealed multifocal severe myocyte hypertrophy. There were remote microinfarcts in the anterior and posterior aspects of the left ventricle and a recent, healing microinfarct in the posterior aspect of the left ventricle. Toxicology examination of postmortem femoral blood revealed MDMA, ethanol, and amiodarone.

This case illustrates the residual, lasting effects of cardiac disease due to Kawasaki disease and a potential complication in the setting of use of an illicit stimulant, MDMA, an amphetamine derivative that produces sympathetic activation and cardiovascular effects including tachycardia, vasoconstriction, dysrhythmias, and coronary artery spasm. Kawasaki disease-related abnormalities of the heart likely resulted in a lower threshold for developing a fatal cardiac dysrhythmia under the circumstance of stimulant use. *Acad Forensic Pathol.* 2018 8(3): 752-762

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INFORMATION

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INTRODUCTION

Kawasaki disease is a vasculitis of unknown etiology that usually occurs in children less than five years old. The disease commonly presents as an acute febrile syndrome with conjunctivitis, polymorphous skin rash, cervical lymphadenopathy, oral mucositis, and skin desquamation (1). Children of Asian/Pacific Islander descent have an increased risk of developing Kawasaki disease (2). Prompt initiation of treatment with intravenous immunoglobulin (IVIG) decreases the risk of developing cardiac complications of the disease. Kawasaki disease is currently the most common cause of acquired heart disease in children in developed countries.

Coronary artery aneurysm due to arteritis is the most common cardiac complication and develops within eight to 12 days of disease onset (3). Aneurysms are reported to develop in 5% of treated patients and 20% of untreated patients (3). Over time, these aneurysms may spontaneously regress, remain the same size, expand, or rupture (4). Histologically, the coronary artery aneurysms demonstrate medial thinning, focal destruction of the internal elastic lamina, calcification, organized mural thrombi, recanalization, and a variable amount of residual inflammatory cells (3). Luminal myofibroblastic proliferation resulting in progressive asymmetric stenosis has been described (5). The size of the aneurysm is predictive of the clinical course, with giant aneurysms (defined as an absolute dimension $\geq 8\text{mm}$) conferring the highest risk for subsequent coronary artery thrombosis, stenosis, myocardial infarction, and cardiac death (6). Coronary angiogram and intravascular ultrasound are used to characterize the aneurysms (7). Patients are often followed with serial echocardiography.

CASE REPORT

We present a case of an 18-year-old male with a history of Kawasaki disease complicated by giant aneurysms of the right and left coronary arteries. Serial echocardiographic studies and treadmill electrocardiogram (EKG) stress tests as recent as 1.5 years before death revealed excellent cardiac function with no evidence

of dyskinesia and a normal cardiovascular response to exercise. The decedent sustained a witnessed collapse after ingesting 3,4-methylenedioxymethamphetamine (MDMA) and ethanol. He was transported to the emergency department and pronounced dead after unsuccessful resuscitative efforts.

RESULTS

Autopsy revealed large aneurysms of all three main epicardial coronary arteries. The maximum arterial diameter was 2 cm (**Image 1A**). Histologically, the aneurysmal areas had intimal fibrosis with foci of calcification and organized mural thrombi. There were extensive foci of severe stenosis with areas of pinpoint luminal narrowing (**Images 1B to D**). Microscopic examination of the coronary arteries revealed diffuse fibrocalcific plaques with prominent recanalization and a recent plaque hemorrhage of the right coronary artery (**Image 2**). These findings were highly consistent with the history of Kawasaki disease. The heart demonstrated left ventricular hypertrophy with biventricular dilatation and mild biatrial dilatation. Microscopic examination of the myocardium revealed multifocal severe myocyte hypertrophy, related to the coronary artery disease. There were remote microinfarcts in the anterior and posterior aspects of the left ventricle and a recent, healing microinfarct in the posterior aspect of the left ventricle (**Image 3**).

Toxicology examination of postmortem femoral blood revealed MDMA at 414 ng/mL, ethanol at 43 g/dL (0.043%), and amiodarone (administered during resuscitation). Toxicology examination of postmortem urine revealed MDMA and examination of the vitreous fluid revealed ethanol.

Autopsy examination also revealed resuscitation-related blunt force injuries. The remainder of the autopsy examination revealed no abnormalities.

CONCLUSION

This case illustrates the residual, lasting effects of cardiac disease due to Kawasaki disease in the setting of the use of an illicit stimulant, MDMA, an amphet-

Image 1A: Segment of the right coronary artery including the aneurysmal dilatation.

Image 1B: Cross section of the right coronary artery aneurysm.

Image 1C: Cross section of the left anterior descending coronary artery aneurysm.

Image 1D: Cross section of the left circumflex coronary artery aneurysm. All coronary artery cross sections demonstrate severe narrowing by fibrosis and organizing thrombus.

Image 2A: Photomicrograph of the right coronary artery revealing intimal fibrosis with calcification and organizing mural thrombus with recanalization (H&E, x20).

amine derivative that produces sympathetic activation (8). Drug-induced sympathetic activation can cause cardiovascular effects including tachycardia, vasoconstriction, blood pressure alterations, dysrhythmias, and coronary artery spasm (8). In this case, Kawasaki

disease-related structural abnormalities of the heart likely resulted in a lower threshold for developing a fatal cardiac dysrhythmia under the circumstance of stimulant use.

Image 2B: Photomicrograph of the right coronary artery revealing intimal fibrosis with calcification and organizing mural thrombus with recanalization (H&E, x100).

Image 2C: Photomicrograph of the right coronary artery revealing focal recent plaque hemorrhage with hemosiderin-laden macrophages (H&E, x20).

Image 2D: Photomicrograph of the right coronary artery revealing focal recent plaque hemorrhage with hemosiderin-laden macrophages (H&E, x600).

Image 3A: Anterior left ventricle showing a remote microinfarct with adjacent severe myocyte hypertrophy (H&E, x100).

Image 3B: Posterior left ventricle showing a subendocardial healing microinfarct (H&E, x100).

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