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Sudden cardiac death in adult with prior history of Kawasaki disease without coronary artery involvement: A case report☆

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ABSTRACT

Current guidelines for management of Kawasaki disease (KD) recommend that patients without coronary artery involvement can be discharged from care after resolution of their acute illness. However, the long-term fate of the coronary arteries in these patients is still being understood. We present a case of a patient diagnosed with KD without coronary artery involvement in childhood who had a sudden cardiac death at 37 years old. Autopsy revealed diffuse hypoplasia of all coronary arteries with additional thickening of the intimal layer and fragmentation of the elastic lamina. These findings are consistent with the luminal myofibroblastic proliferation pattern seen as sequela of KD. This case is the first to our knowledge to describe sudden cardiac death in an adult with previous low-risk KD and suggests the need for heightened concern in all symptomatic patients with a prior history of KD.

1. Introduction

Kawasaki disease (KD) is a self-limiting, acute vasculitis of medium-sized arteries affecting children. This febrile illness is characterized by rash, conjunctivitis, mucositis, extremity changes, and lymphadenopathy. Although self-limited, coronary involvement, specifically the formation of coronary artery aneurysms, carries the greatest morbidity and mortality. KD is reported worldwide and is the leading cause of acquired heart disease in children living in developed countries [1]. American Heart Association guidelines suggest that patients without coronary involvement can be discharged from cardiology care anywhere from four weeks to 12 months after their acute illness given their low-risk [1]. However, the presence of potential chronic coronary changes in low-risk patients has been a subject of continued controversy. We describe the case of an adult female who was diagnosed with KD risk level 1 at 3 years of age who presented with exertional sudden cardiac death in adulthood. We will discuss the implications of this case in regards to long term management for KD patients deemed low-risk.

2. Case presentation

A 37 year-old athletic, Caucasian female with prior history of KD at 3 years of age presented with sudden cardiac arrest, and ensuing death. She had no history of smoking, dyslipidemia, hypertension or family history of early coronary artery disease.

Reviewing archived hospital records, the patient presented in 1982, at age 3 years to Cincinnati Children's Hospital Medical Center due to fever, fatigue, and decreased oral intake. Prior to admission, she had a 5 day history of fevers (up to 40 °C), erythematous rash, conjunctivitis, and lymphadenopathy. During her admission, she continued with fevers and developed mucositis and edema of her hands. Her laboratory evaluation was notable for an elevated erythrocyte sedimentation rate (54 mm/h), leukocytosis (26.8 k/mcl), mild anemia (Hgb 11.1 g/dl, HCT 33.4%) and thrombocytosis (529 K/mcl). She was noted to have aseptic meningitis (29 white blood cells), and urinalysis notable for sterile pyuria. She was diagnosed clinically with Kawasaki disease and started on high dose Aspirin (80–100 mg/kg/day). The patient did not receive

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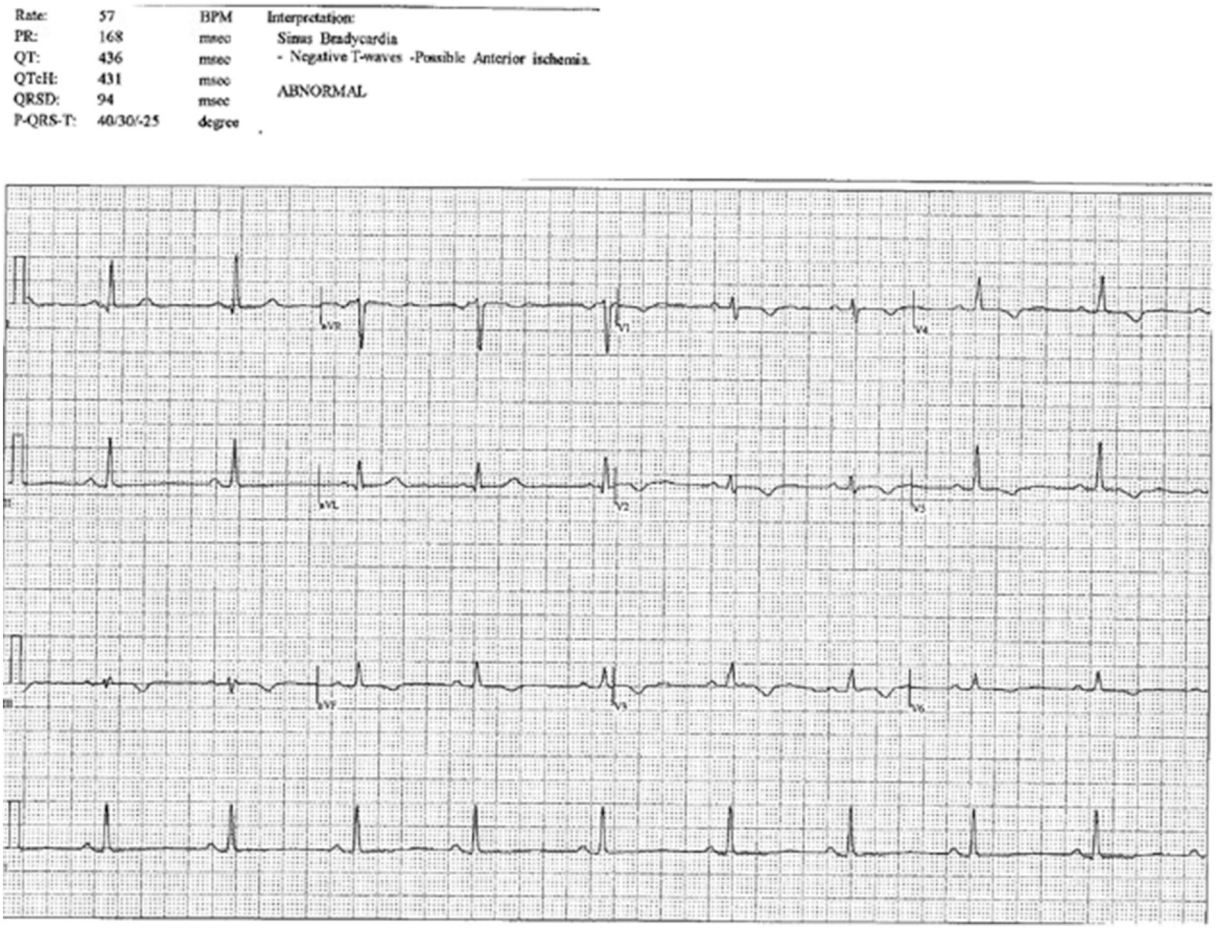

Fig. 1. Resting EKG completed prior to arrest showing T wave inversion concerning for myocardial ischemia.

intravenous immunoglobulin as this was not standardly given during this era. While hospitalized, she underwent a normal electrocardiogram and echocardiogram. She was discharged after 7 days, with documented desquamation of her fingertips at the time of discharge.

Follow up echocardiogram 2 months after presentation revealed normal cardiac structure and function without pericardial effusion. The patient also underwent cardiac catheterization the next day. Left and right coronary arteriograms showed normal anatomy and no evidence of aneurysms nor obstruction.

The patient did not have subsequent pediatric cardiology follow up. She was relatively healthy with multiple sclerosis (MS) diagnosed in her 30's but was stable on interferon beta 1a and cholecalciferol. She had no history of smoking, diabetes mellitus, hypertension or dyslipidemia. She was a half-marathon runner and a few months prior to her death, she

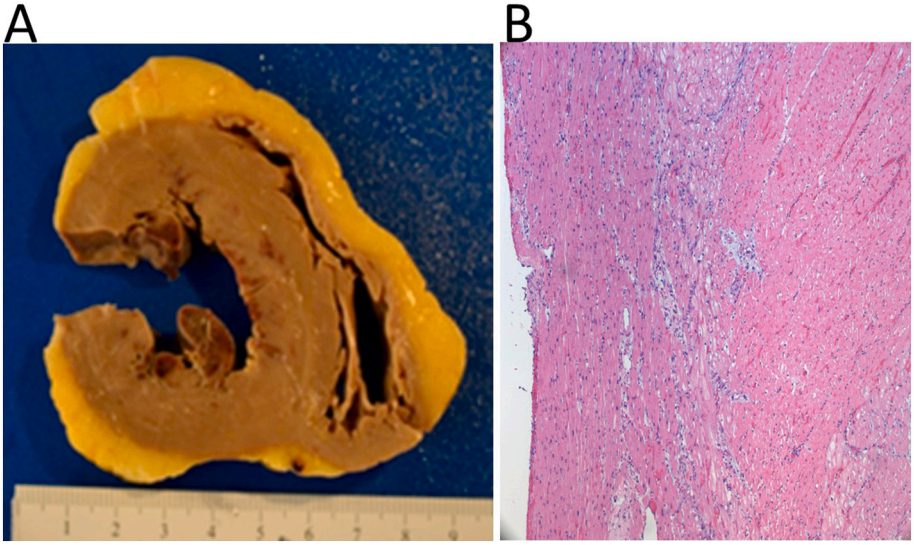

Fig. 2. Gross (A) and microscopic (B) evidence of circumferential sub-endocardial infarction.

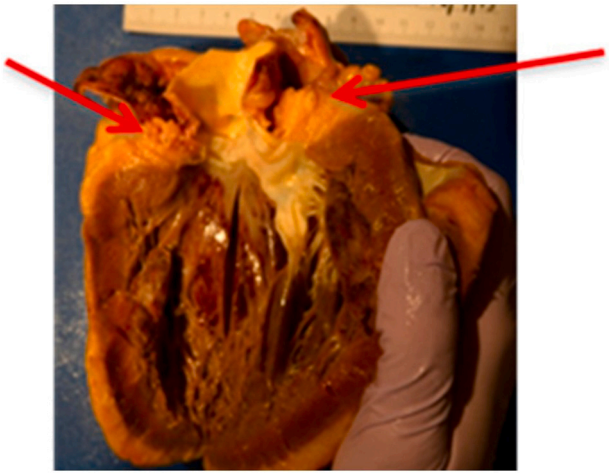

Fig. 3. Gross specimen with arrows demonstrating the proximal coronaries. Coronary artery distribution was normal; however, the caliber of the vessels was significantly decreased.

experienced nausea, vomiting, chest tightness, and heart fluttering with strenuous exercise. She was evaluated by an adult cardiologist at an outside institution, with a resting EKG which was notable for T wave inversion in inferior and lateral leads (Fig. 1). Stress echocardiogram four days later showed normal segmental wall motion with a resting ejection fraction of 60%. There were isolated unifocal premature ventricular contractions as well as persistent T wave inversion during and post exercise.

Two days following evaluation, she presented in cardiac arrest following exercise. Paramedic reports noted ventricular fibrillation progressing to pulseless electrical activity and asystole. Following 45 min of resuscitation, she experienced return of spontaneous circulation. She was admitted to the ICU under hypothermic protocol, ventilated and on inotropic support. Care was withdrawn due to brain death and an autopsy was performed.

Heart only autopsy (Figs. 2–5) revealed normal cardiac configuration with normal cardiac chamber sizes without any valvar abnormalities. The left ventricular wall grossly had a circumferential subendothelial mottled appearance, which histologically corresponded to recent myocardial infarction with myocyte necrosis and abundant, primarily neutrophilic, inflammation. On gross evaluation of the coronary arteries, there was notable hypoplasia of the left and right main, left anterior descending and circumflex arteries. On cross-section there was luminal narrowing (50–80%) of all coronary arteries. Histologically, there was circumferential vessel wall thickening due to expansion of the intimal layer by proliferation of myofibroblastic cells and deposition of collagen. The internal elastic lamina was focally disrupted. These findings are compatible with the luminal myofibroblastic proliferation pattern seen as sequela of KD and differ from the histologic appearance of atherosclerosis in coronary arteries (usually eccentric luminal narrowing characterized by intimal expansion of stromal cells, foamy macrophages, and lymphocytes in a matrix with cholesterol clefts and calcifications).

3. Discussion

This case is the first to our knowledge to describe sudden cardiac death in an adult patient with prior KD and without prior evidence of coronary involvement. This patient on autopsy demonstrated no evidence of aneurysmal coronary dilation but had a luminal

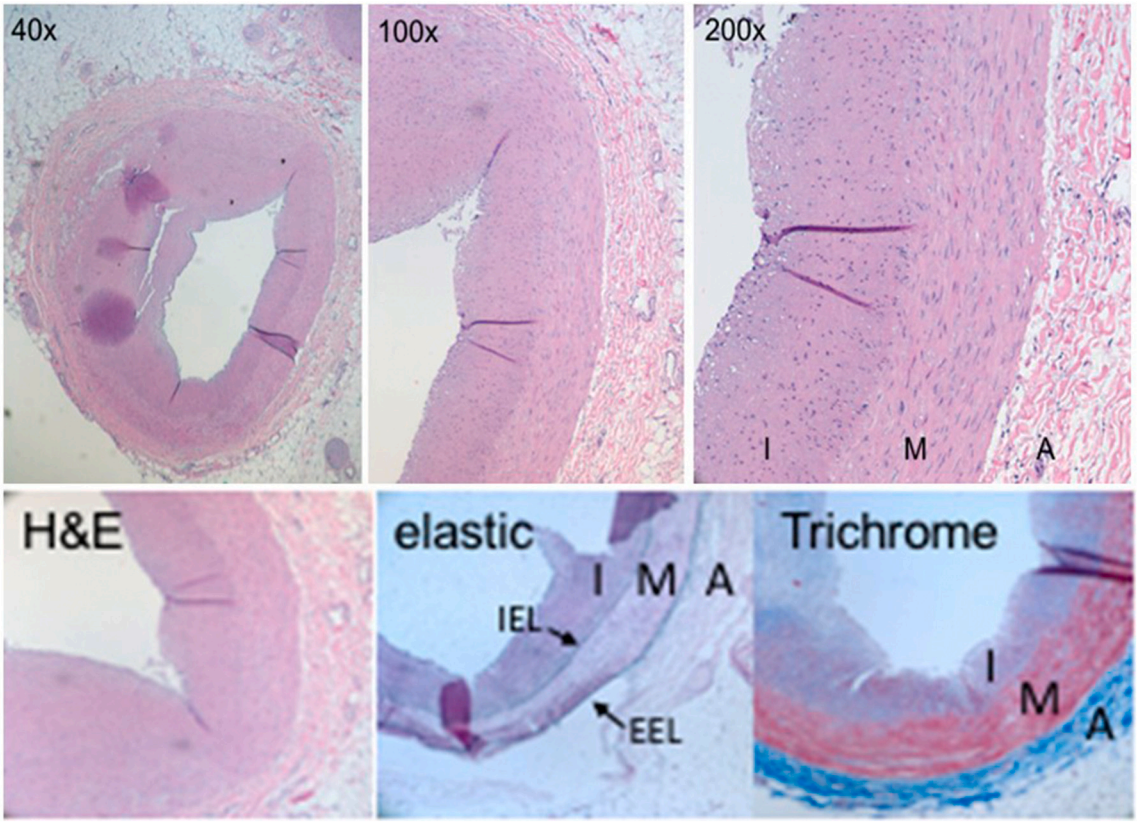

Fig. 4. Microscopic examination revealed dysplastic coronary arteries (LAD is shown) with significantly thickened intima (I), with increased cellularity and matrix deposition, highlighted with Trichrome staining. Media (M) and adventitia (A) are labeled. Furthermore, the internal elastic lamina (IEL) was fragmented, and thickening of intima.

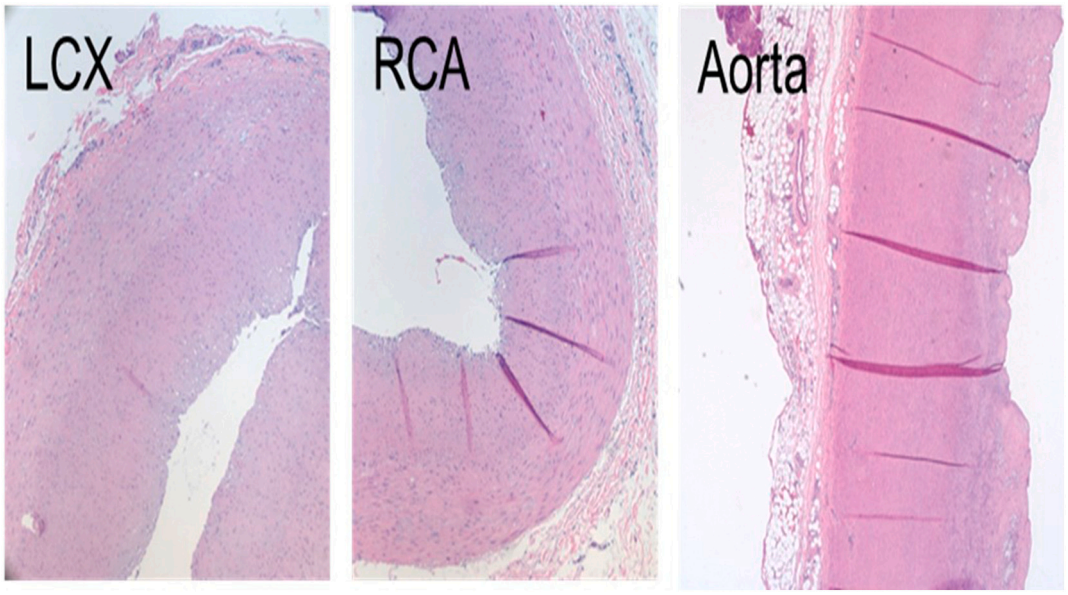

Fig. 5. This was a global finding involving both left and right coronary arteries, while the aorta was unaffected (one focus of early atherosclerotic changes was seen and is illustrated in the figure).

myofibroblastic proliferation pattern indicative of late KD sequelae. Previous descriptions of KD vasculopathy include self-limited necrotizing arteritis, followed by subacute/chronic vasculitis and luminal myofibroblastic proliferation, the latter two processes which may occur over months to years [2]. A previous case report of a 16 month-old with sudden infant death syndrome following KD diagnosis at 3 months of age without coronary involvement also illustrates this point. This patient's autopsy was notable for coronary artery intimal thickening consistent with subacute/chronic vasculopathy [3]. Large scale epidemiology studies have previously demonstrated no increased risk of mortality in KD patients compared to the general population [4]; however, data have shown reduced myocardial flow reserve on PET imaging in KD patients without history of coronary involvement emphasizing that these late vasculopathic processes may place individual patients at risk [5].

Long-term surveillance of KD patients is tiered based on coronary artery dilation, with low-risk (i.e. no acute coronary artery involvement) patients often discharged between 4 weeks to 12 months following the diagnosis [1]. This recommendation is based upon the long-term epidemiology data as well as studies suggesting long-term echo follow up is not cost effective [4,6–8]. One complicating factor is that the number of KD patients who are reaching adulthood has grown, and in addition to the subacute and chronic vasculopathy, accelerated atherosclerosis may put these patients at increased risk [9]. The Japanese Circulation Society suggested that adult patients with KD and no coronary involvement should have noninvasive testing every 3–4 years, however, the benefit and cost effectiveness of such a strategy has not been evaluated [10]. Our institution has begun exercise stress testing KD risk level 1 patients in the second decade of life to determine if this is an effective strategy to uncover chronic vasculopathy cases.

There are two important points to emphasize in our particular patient which may limit current generalizability to all low-risk KD patients. One point was that our patient was born in an era prior to routine IVIG administration. It is unclear whether receiving IVIG could have affected the subacute/chronic vasculopathy. In addition, this patient was diagnosed with MS. There is evolving recognition of cardiovascular risk factors in patients with MS. Investigations are ongoing, but a potential mechanism involves systemic inflammation resulting in atherosclerosis [11]. Our patient demonstrated diffuse coronary vessel disease with a pattern classically attributed to KD; however, the MS diagnosis certainly requires recognition. Our case is not intended to direct long-term management guidelines for low-risk KD patients but demonstrates that the previous diagnosis of KD is important in symptomatic patients regardless of previous acute coronary involvement. Patients and families when presenting with cardiac symptoms should alert providers of their history of KD, and providers should have a lower threshold for diagnostic evaluation.

In conclusion, although risk-level 1 KD is deemed a relatively low-risk disease without long-term complications on the population level, there have been reports of subacute/chronic vasculopathy and concern for late complications. The necessity of long-term surveillance of all low-risk patients is unclear; however, symptomatic patients with a previous diagnosis of KD should have heightened evaluation given the above observations.

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Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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