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Case report

Utility of post mortem MRI in definition of thrombus in aneurismatic coronary arteries due to incomplete Kawasaki Disease in infants

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ABSTRACT

Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology that primarily affects the coronary artery (CA) and presents in childhood. The characteristic coronary arterial lesion is an aneurysm, which may lead to thrombosis, dilatation, stenosis, and occlusion. Such an aneurysm is typically calcified and generally develops five or more years after the onset of acute KD. It becomes more noticeable after ten years. KD is sometimes difficult to diagnose because of the limited clinical features, especially in infants younger than 6 months old, where the clinical presentations often do not fulfill the diagnostic criteria for KD.

We report a case of Incomplete Kawasaki Disease (IKD) causing unexpected death in infants. A seven-month-old male baby, apparently well nourished and without fever or exanthema that was unexpectedly found agonal in his bed by his parents. He died in an emergency room a few hours later in spite of aggressive resuscitation efforts. Postmortem Magnetic Resonance Images were obtained during the autopsy, with evidence of an occlusive thrombus in left and right coronary artery aneurysms. Laboratory findings were consistent with IKD. The crucial role of postmortem imaging is discussed here in order to improve diagnosis tools for preventable events.

1. Introduction

Kawasaki disease (KD) was first reported by Kawasaki in 1967 [1]. KD is an acute systemic vasculitis of unknown cause that most frequently (80% of the time) affects infants and children under 5 years of age [2]. KD before the age of three months is rare. Some reports suggest that KD is triggered by bacterial or viral infections [3–5].

KD is now known to have a worldwide distribution, having been observed on all continents and in all ethnic groups. KD is now known to be associated with coronary artery lesions in about 20% of cases. The characteristic coronary arterial lesion is an inflammatory aneurysm, which may lead to rupture or occlusive thrombosis [6]. Coronary artery aneurysms or ectasia develop in 15–25% of untreated children with the disease and may lead to myocardial infarction (MI), sudden death, or ischemic heart disease [7–11].

Careful analyses of autopsy material by Japanese investigators have documented four stages in the evolving pathology of coronary artery lesions in KD [12]. The acute inflammatory changes of arteritis are seen in the first 6–9 days in the intima and adventitia, and then involve the media to become transmural by 12–25 days. Arterial aneurysms appear subsequently by 28–32 days, but sometimes as early as within the first 2 weeks of the early phase of the disease. Marked stenosis following thrombosis and recanalization of organized thrombi and the post repair intimal fibrosis are observed after 40 days. The most frequent site for aneurysm formation is the proximal left anterior descending artery (LAD) and proximal right coronary artery (RCA), followed by the left main coronary artery (LMCA), the left circumflex artery (LCX), and finally the distal RCA and the junction between the RCA and the posterior descending coronary artery [13]. Aneurysms of the coronary vessels are rare in children and in isolated forms they are indicative of KD. In KD, aneurysms occur in 15–30% of patients, usually after an acute phase of the disease [14–16]. Resolution or regression of aneurysms is found in more than 50% of KD cases, whereas thrombosis or rupture rarely complicate the remaining cases [17]. No significant difference between KD and IKD were seen in regard to coronary artery abnormalities [18]. KD is lethal in 0.5–2% of patients and death always takes place suddenly and unexpectedly. In the acute phase of disease, death is caused by complications of coronary endarteritis (thrombosis with myocardial infarction) and myocarditis (myocardial insufficiency and arrhythmias).

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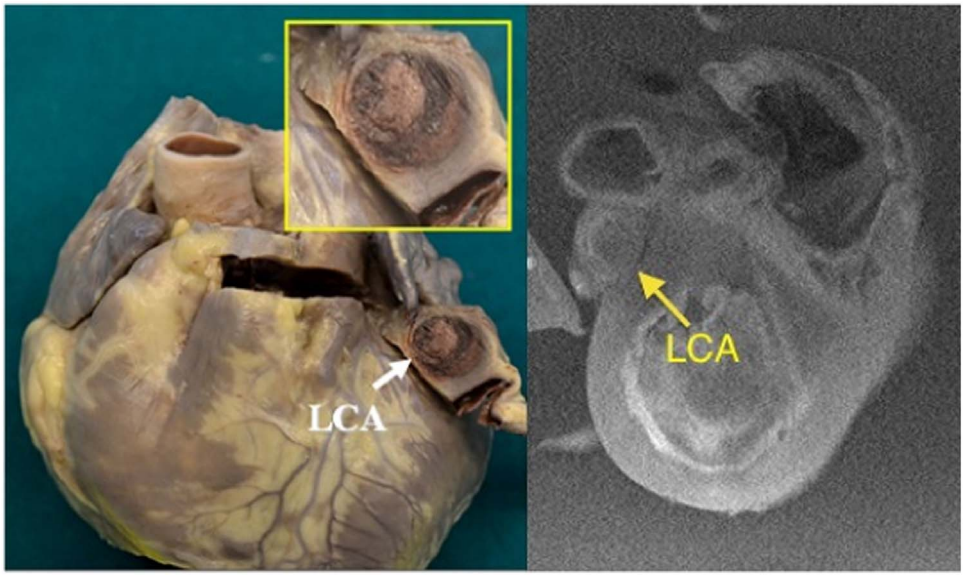

Fig. 1. Gross examination and post mortem RMI showed aneurysmatic and thrombotic left coronary vessel.

Although no specific laboratory tests exist that can definitively identify KD, there are clinical and laboratory findings that guide diagnosis and treatment [19]. The currently accepted clinical diagnostic criteria for KD include: fever for at least five days with five of the following criteria: 1) polymorphic exanthema; 2) changes in the peripheral extremities, that is, erythema and/or indurative edema of the palms and soles (acute phase) or desquamation around the finger tips (convalescent phase); 3) bilateral non-exudative conjunctival injection; 4) changes in the oropharynx, that is, injected or fissured lips, strawberry tongue, and injected pharynx; and 5) acute nonsuppurative cervical lymphadenopathy (> 1.5 cm in diameter).

KD is sometimes difficult to diagnose because of the limited clinical features [19,20], especially in infants younger than 6 months old, where the clinical presentations often do not fulfill the diagnostic criteria for KD. Such cases are thus termed as incomplete Kawasaky disease (IKD) [20–24]. IKD, however, should not be thought of as mild KD, because the risk of coronary artery aneurysm is similar to conventional KD [25]. Laboratory studies show leukocytosis, elevation of acute phase reactants, such as erythrocyte sedimentation rate and C-reactive protein and thrombocytosis. As cases of KD may be rarely found in forensic pathology observation and tend not to be an obvious cause of death, especially in atypical presentation, showing findings of several infant cases may positively impact knowledge of such pathology.

Rates of recurrence and familial occurrence of KD are best documented in the literature from Japan; these rates may be lower in other races and ethnicities. In Japan, the recurrence rate of KD has been reported to be 3%. [26].

The reported occurrence of KD in children of parents who themselves had the illness in childhood also supports the contribution of genetic factors [27–30]. Early diagnosis of the disease may avoid mortality or negative patient outcomes. Treatment of KD in the acute phase is directed at reducing inflammation in the coronary artery wall and preventing coronary thrombosis, whereas long-term therapy in individuals who develop coronary aneurysms is aimed at preventing myocardial ischemia or infarction.

The post mortem MRI such us the post mortem CT [31] is a convenient tool in the screening performed to determine the cause of death and it is useful in cases of infant sudden death for the detection of a typical coronary arteries lesion Kawasaky related.

In this case the post mortem RMI of the heart showed an occlusive thrombus in a left and right coronary artery aneurysms as confirmed at autopsy.

2. Case history

A 7-month-old baby, who had a full-term normal delivery, weighed 3100 g and was 49.5 cm in crown-heel length at birth. Conception/delivery for mother was eventless, and the family history was normal. He had no abnormal health problems on medical examinations at 1 and 3 months of age.

The baby, apparently well nourished and without fever or exanthem, was unexpectedly found agonal in his bed by his parents. He was admitted in an emergency room where laboratory test showed only an increase of platelets (651.000/mm^3) and troponina T (1.96 ng/ml) but 2 h later in spite of aggressive resuscitation efforts he died.

3. Post-mortem magnetic resonance findings

The post mortem interval between MRI and the medico legal autopsy was of two hours.

MRI was performed using a 1.5-T scanner (GE Excite HDxt, Milwaukee, WI) with an eight-element (four anterior and posterior) phased-array receiver surface coil. The images were obtained by acquiring T2-weighted short-tau inversion recovery (T2w-STIR). The following parameters were used: thickness 3 mm, no gap, matrix 512×512, field of view (FOV) 28 cm, TI 120 ms. Post mortem MRI images of the heart showed an occlusive thrombus in a left and right coronary artery aneurysms (Figs. 1 and 2). A post mortem CT and/or plain x-ray was not performed.

4. Medico legal autopsy findings

A systematic autopsy was performed. The autopsy showed an oral mucositis, cervical lymphadenopathy. The baby was 69 cm in height and 7.550 kg in weight. The heart weighed 75 g (reference normal value 35 g). Aneurysmal dilatation (9 mm diameter) of the left coronary (common trunk) and right coronary with thrombotic occlusion of both (Figs. 1 and 2) as confirmed by the images on postmortem MR investigation of the heart. No abnormalities were detected in other organs.

5. Histological findings

The histological examination of coronary aneurysm tissue samples stained with Hematoxylin-Eosin, Veighert-Van Gieson and Massons thrichromic showed lymphomonocytic necrotizing panarteritis with

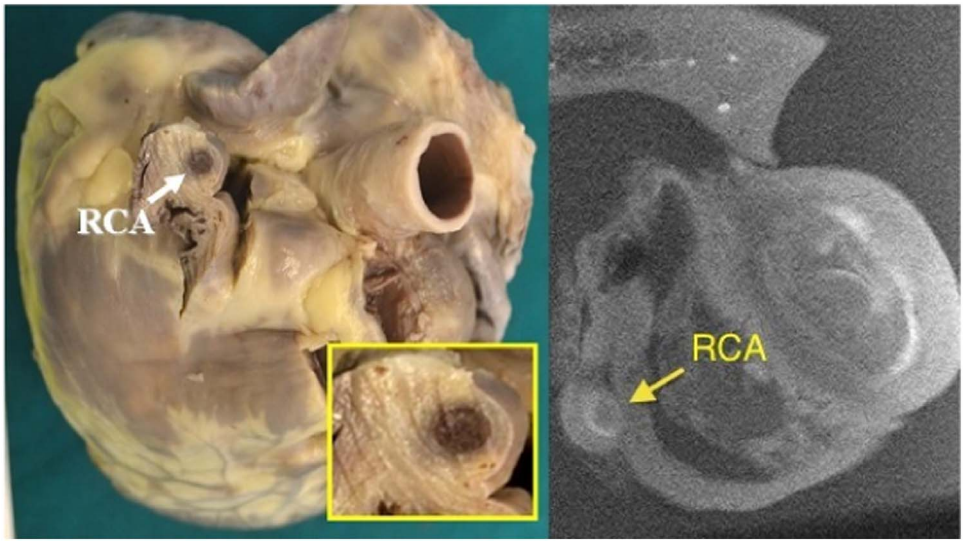

Fig. 2. Gross examination and post mortem RMI showed aneurysmatic and thrombotic right coronary vessel.

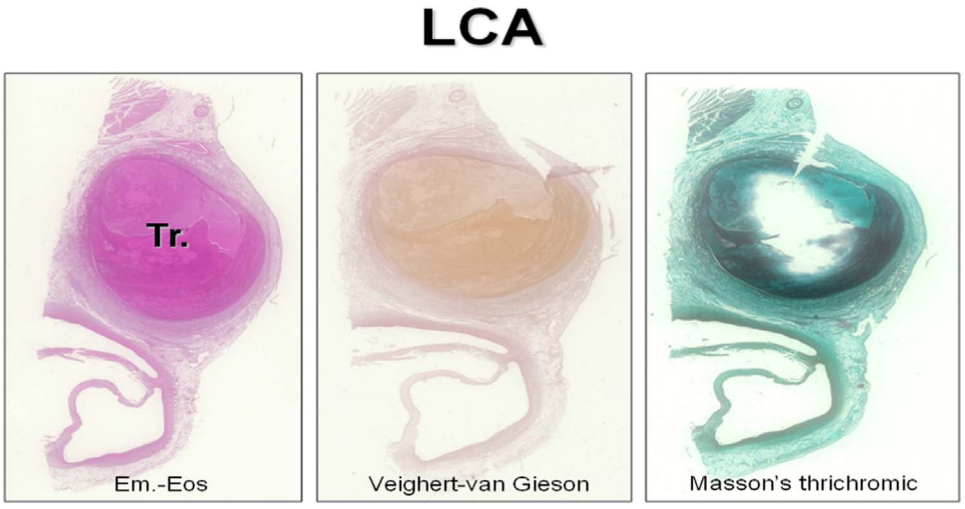

Fig. 3. Aneurysmatic and thrombotic left main coronary artery (2X).

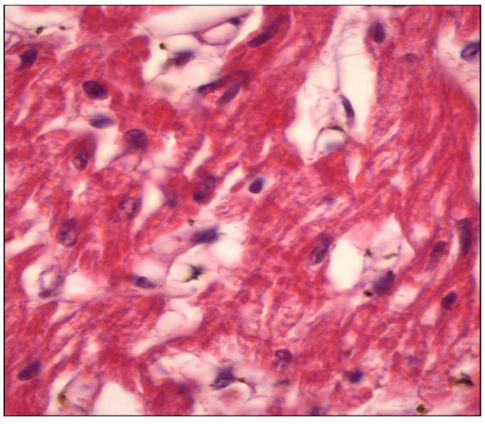

Fig. 4. Contraction bands necrosis in both ventricles with platelets thrombi in the small coronary arteries (HE X40).

intimal ulceration and endoluminal thrombus, partially fragmented consist mainly platelets, fibrin embedding lymphomonocytes and red blood cells (Fig. 3). Diffuse contraction bands necrosis in both ventricles with platelets thrombi in the small coronary arteries. The epicardium showed a focal chronic inflammation (Fig. 4). The histological study also revealed a sinus histiocytocis and cortical follicular hyperplasia of the lymphatic nodes and hypoplasia of megariocytic cells in the bone marrow. In the other organs only acute congestion was observed. Laboratory findings were consistent with IKD and the cause of death was sudden cardiac arrest due to coronary thrombus in the aneurismatic LCA and RCA without rupture.

6. Other examinations

The test for antistreptolysin O antibody in the cardiac blood was negative. Antibody tests for infectious agents (such as Mycoplasma pneumonia, Chlamydia, Adenovirus, Epstein-barr virus, Influenza virus A, B, Parainfluenza virus 1, Respiratory syncytial virus, Rotavirus, Echovirus, Coxsackie virus B group 5, Mumps, Measles, Rubella, and Cytomegalovirus) were all negative. Neither drugs nor ethanol were detected by toxicological examination.

7. Discussion

IKD should be considered in all children with unexplained fever for ≥5 days associated with 2 or 3 of the principal clinical features of KD [18].

The major sequelae of KD are related to the cardiovascular and,

more specifically, the coronary arterial system. Autopsy studies of KD patients have demonstrated a systemic inflammatory process involving many tissues and organs, but most strikingly affecting the coronary arteries.

The cause of death in the presented case in accord to post-mortem MRI, autopsy and histopatological findings was attributed to cardiac arrest due to coronary thrombus in the aneurismatic LCA and RCA without rupture. The patient was initially diagnosed as sudden infant death syndrome and subsequently diagnosed as IKD after additional examination such us post mortem MRI imaging and histopathological analysis of the autopsy materials. Forensic pathologists should therefore consider the possibility of KD in patients who show any feature of KD (such as high fever and skin changes) and focus on the cardiac pathology such as myocardial changes and coronary artery aneurysms.

Recent developments in the field of postmortem imaging [32] could be an alternative methods for the detection of coronary disease in KD; the use of RMN screening in infant with suspected IKD - in contrast to PMTC - can provide more information about the diameter of vessel and early ischemic changes of myocardium at an earlier stage than traditional autopsy and routine histology [33,34].

It is known the growing use of cross-sectional imaging in childhood death [35–38].

Recent data confirm that postmortem MRI is likely to become the standard for postmortem imaging in children. A recent benchmark prospective validation study of postmortem imaging in foetuses and children at a specialist children's hospital in London found a > 90% concordance rate between noninvasive postmortem assessment (including postmortem MRI and ancillary investigations not requiring invasive procedures, such as placental examination) and conventional full autopsy findings in 400 cases (277 foetuses, 123 children) [39].

The routine use of post mortem CMR (cardiac magnetic resonance) in sudden unexpected infant death will help to identify rare but important causes of death such us Kawasaki disease. This approach could therefore allow a triage process in which initial postmortem MRI and other investigations are performed with progression to full or modified autopsy as indicated by the results of the noninvasive postmortem findings. This approach is likely to be useful in improving the uptake of postmortem evaluation for parents in whom current approaches are unacceptable.

8. Conclusion

This case highlights the use of post mortem MR in sudden infant death, particularly as fewer parents agree to invasive autopsy.

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