Int J Leg Med (1994) 106:277–280

International Journal of
Legal Medicine

Sudden death caused by thrombosed coronary artery aneurysm

Two unusual cases of Kawasaki disease

Ingrid Bayer Kristensen[1], Bent Østergaard Kristensen[2]

[1] Institute of Forensic Medicine, University of Aarhus, Finsensgade 15, DK-8000 Aarhus C, Denmark
[2] Department of Cardiology, Aarhus University Hospitals, Skejby Sygehus, D-8200 Aarhus N, Denmark

Received November 2, 1993 / Received in revised form December 27, 1993

Summary. Kawasaki disease primarily affects children below 5 years of age, and fatal coronary complications usually occur within 6–12 months following the acute illness. We report 2 *unusual* fatal cases of thrombosed coronary artery aneurysms. The first case was an 11-year-old boy, who died suddenly 2 months after the acute illness. He had a classical clinical picture, but was misdiagnosed. The second case was a 29-year-old man without history of recent febrile episodes or cardiac symptoms. Both *subjects* fulfilled the stage 4 criteria of Kawasaki disease (healing stage) with extensive old myocardial damage. The cases illustrate the great variation in the clinical picture of Kawasaki disease. Teenagers can also be affected, and extensive myocardial damage may be asymptomatic for *many* years.

Key words: Kawasaki disease – Coronary artery aneurysms – Sudden death

Zusammenfassung. Die Kawasaki-Krankheit betrifft primär Kinder im Lebensalter unter 5 Jahren, und akute koronare Komplikationen entstehen normalerweise innerhalb von 6–12 Monaten nach der akuten Erkrankung. Wir berichten über 2 ungewöhnliche Fälle von thrombosierten Koronar-Aneurysmen. Im ersten Fall handelte es sich um einen 11jährigen Jungen, welcher plötzlich 2 Monate nach der akuten Erkrankung verstarb. Er hatte ein klassisches klinisches Bild, aber dieses wurde fehldiagnostiziert. Der zweite Fall war ein 29 Jahre alter Mann ohne Anamnese, mit rezenten fieberhaften Episoden oder kardialen Symptomen. Beide Personen erfüllten die Kriterien des Stadiums 4 der Kawasaki-Krankheit (Heilungsstadium) mit ausgeprägten alten myokardialen Schäden. Die Fälle zeigen, daß eine große Variation im klinischen Bild der Kawasaki-Krankheit existiert. Auch Teenager können betroffen sein, und ausgeprägte myokardiale Schäden können für viele Jahre asymptomatisch sein.

Schlüsselwörter: Kawasaki-Krankheit – Koronar-Aneurysmen – Plötzlicher Tod – Lebensalter

Correspondence to: I. Bayer Kristensen

Introduction

Kawasaki disease or the mucocutaneous lymph node syndrome was first described in 1967 by Tomisaku Kawasaki. The disease is a generalized vasculitis of unknown etiology, and is most often seen in Japan, but is diagnosed with increasing frequency in western countries [1]. It predominantly affects children under the age of five, and typical symptoms are fever, lymphadenopathy, conjunctivitis and a rash, which later desquamates in *the* hands and feet, resembling scarlet fever [2].

Approximately 30% of children with Kawasaki disease develop cardiovascular complications. Coronary artery aneurysms are seen in almost 20% of cases. Death due to myocardial infarctions or other cardiac complications, such as myocarditis, occurs in 1–2% of such children. The mortality in boys with Kawasaki disease is twice that in age-matched healthy boys, whereas girls do not suffer higher mortality [3].

Awareness of the pathology of this disorder is important for the forensic pathologist since cases may *occur* as unexpected death in childhood as well as in young adulthood [4].

We report *2* unusual cases of Kawasaki disease, undiagnosed before autopsy.

Case reports

Case 1

An 11-year-old, *previously* healthy boy *developed a* fever and a rash *2 months before death.* He was thought to have tonsillitis and was treated with penicillin. Three days before death, he was seen by the family doctor because of nausea, vomiting and abdominal pains. He was apyrexial and remained in bed the following days. On the evening before death, he was well and had been watching television. The next morning he was found dead in bed.

Autopsy findings: The deceased was 166 cm tall and weighed 31 kg. All organs *were normal* except the heart, *which* weighed 186 g. *Aneurysms with thromboses were found* in the right coronary artery (RCA) and left anterior descending coronary artery (LAD)

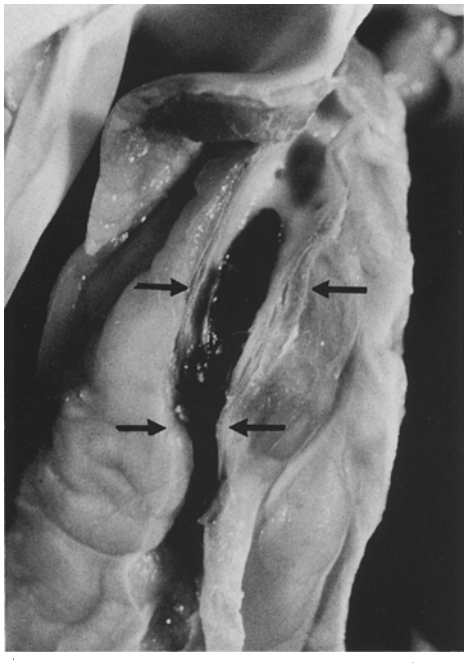

Fig. 1. Aneurysm of the left anterior descending coronary artery *(arrows)* with luminal thrombus from the 11-year-old boy

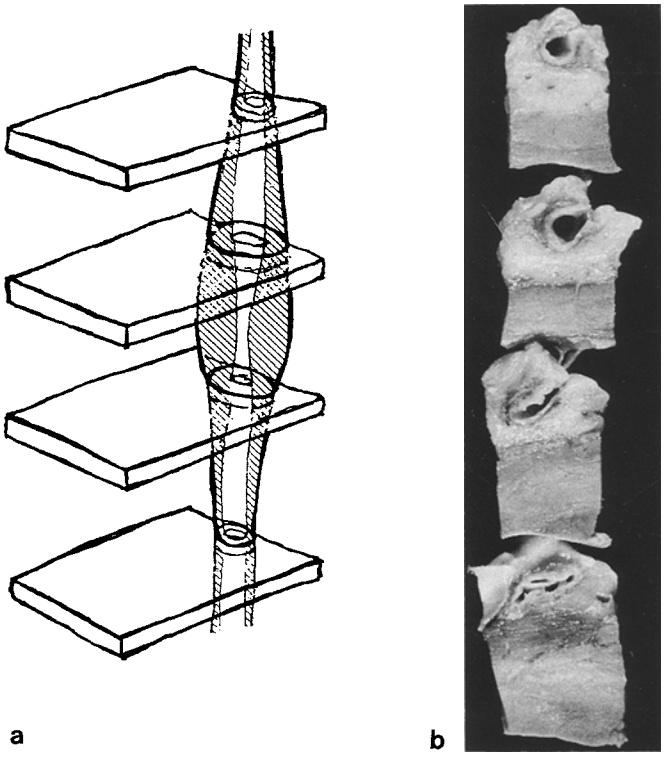

Fig. 2. Serial cross-sections through *the aneurysm in the* left anterior descending coronary artery (LAD) from the 29-year-old man. **a** Drawing of the aneurysmatic LAD. The lines indicate the sections in b. **b** Aneurysm in LAD with surrounding epi- and myocardium

(Fig. 1) and accordingly a fibrous infarct was seen in the septum. The left circumflex artery was normal. Histologically, the affected arteries showed intimal proliferative fibrosis, medial thinning with loss of elastic membranes and occlusive luminal thromboses. There were no signs of acute arteritis and no signs of acute infarction, but extensive septal fibrosis *was found.*

Case 2

During a family party a 29-year-old, previously healthy man (truck-driver) with no history of recent infectious diseases, cardiac pains or arrhythmias suddenly collapsed with cardiorespiratory arrest. Attempts at resuscitation were unsuccessful.

Autopsy findings. The deceased was 183 cm tall and weighed 82 kg. There were no traumatic lesions and no alcohol intoxication (blood-alcohol concentration: 0,22 promille). All organs were normal except the heart, *which* was enlarged (weight: 515 g) and showed fibrosis of the endo- and myocardium in the anterior part of the left ventricle.

Coronary artery aneurysms were found in the left main *artery* and in the RCA. The RCA aneurysm was calcified and the lumen occluded. In the left main coronary artery, an 8 mm long aneurysm with intimal thickening and segmental stenosis involving the offspring of the left circumflex branch was found (Fig. 2). The first diagonal branch was normal. Histologically, the RCA was almost occluded by organized thrombus material. In the LAD, an aneurysm without thrombus was seen (Fig. 3). There was extensive myocardial fibrosis, but no evidence of acute infarction. There were no signs of acute arteritis, atheromatosis or myocarditis.

Discussion

The most serious complication of Kawasaki disease is the formation of coronary artery aneurysms, predominantly localised in the LAD and in the RCA [5]. Other cardiac manifestations include myocarditis, pericarditis, endocarditis with valvulitis and *lesions in the* conduction system [6]. The vascular lesion *can be* histologically described in 4 stages [7]:

Stage 1 (0–11 days): perivasculitis and/or vasculitis of arterioles, venules, capillaries and small arteries with infiltration of mononuclear and polymorphonuclear cells. In larger arteries, there is perivaculitis without inflammation of media, as well as pericarditis, interstitial myocarditis, and endocarditis.

Stage 2 (12–25 days): in this period intensive panarteritis and aneurysm formation in the medium-sized arteries are found. Stenosis and thrombotic obstruction in the coronary arteries can also be seen. Usually fibrinoid necrosis in the media is not detected in contrast to periarteritis nodosa.

Stage 3 (26–40 days): *this* stage is characterized by the disappearance of the acute inflammation, with only minimal cell infiltrations of the perivascular area. Marked intimal thickening causing stenosis of the vascular lumen or thrombus formation and coagulation necrosis in the myocardium are seen.

Stage 4 (healing phase): More than 40 days after onset. This period is characterized by calcification or recanalization of the obstructed portions of the coronary artery. Myocardial fibrosis and endocardial fibroelastosis also develop in this stage.

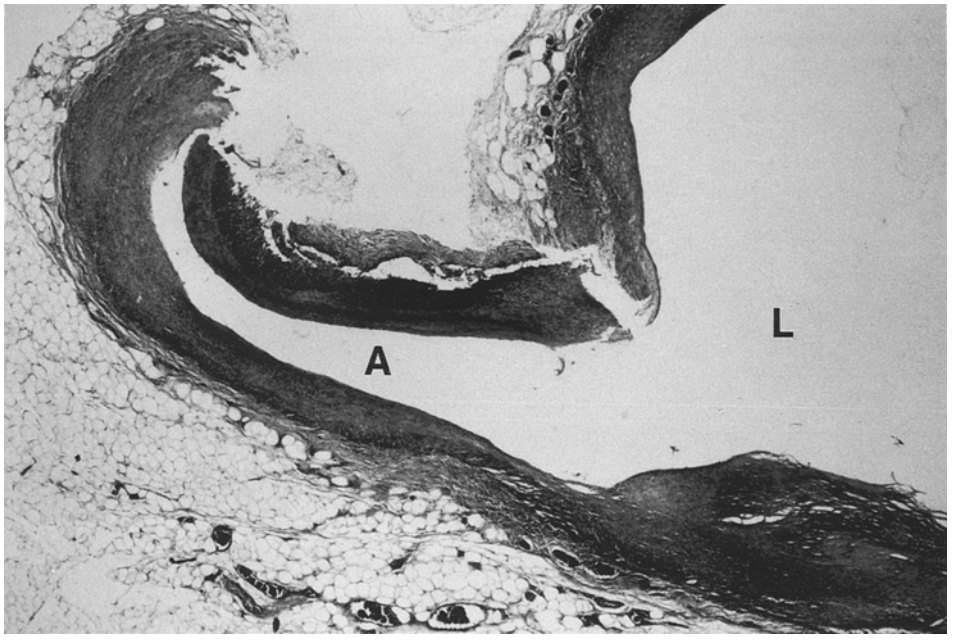

Fig. 3. Histological cross-section corresponding to section 3 in Fig. 2b. L = the coronary artery lumen. *A* = the aneurysm. (H & E.; magnification 20×)

Histologically, our cases fulfilled the diagnostic criteria for the healing stage of Kawasaki disease. Importantly the 29-year-old man had no signs of atheromatosis. A congenital origin in this case seem*ed unlikely,* since the wall of the aneurysms consist*ed* largely of fibrous tissue [8]. Despite extensive myocardial damage, the *patient* remained asymptomatic, *which* has also been reported by others [9]. The immediate cause of death remain*ed* uncertain from our study. Since the alcohol concentration in the blood was rather low, this was presumably not a precipitating factor. The most likely explanation seem*ed* to be arrhythmias, probably induced by silent ischemic myocardium [9].

The abdominal pains reported by the boy a few days before death were most likely of myocardial ischemic origin.

Ischemic symptoms and lethal complications such as thromboses have been related to the localization and size of the aneurysms [5]. *It has been suggested, that* RCA aneurysms with focal and segmental narrowing *are* accompanied by earlier development of *a* sufficient number of collaterals than LAD aneurysms, thereby protecting against severe myocardial damage, particularly in infants and children below 5 years of age [10]. Exceptions are cases of obstructive lesions in the feeding artery (e.g. left coronary artery) [11]. In our cases, both the RCA and the LAD were effected. In the 29-year-old man, there was no history of recent febrile episodes, suggesting that *the* acute phase might have been sometime in infancy or childhood. The development of *a* sufficient number of collaterals at that time might explain why he remained asymptomatic until death. The boy, with the same degree of coronary affection, apparently had symptoms a few days before death. This might be explained by an inability to develop *a* sufficient number *of* collaterals in *this* age group.

Long-term follow-up of patients with Kawasaki disease and myocardial infarctions, however, have shown that severe stenosis of the left main coronary artery or the proximal part of LAD are most serious and sometimes fatal [10].

Coronary artery aneurysms can be diagnosed non-invasively by echocardiography. This method is also used, together with the clinical picture and laboratory tests, in monitoring the effect of the recommended treatment – immunoglobulins and acetylic salicylic acid, which seems to prevent formation of coronary artery aneurysms [12]. The aneurysms usually develop during the third and fourth weeks after the acute onset of the disease. If Kawasaki disease had been suspected in the early phase of the disease in the boy, correct diagnosis might have been made and most likely life-saving treatment could have been initiated. This is in contrast to the 29-year-old man, who remained asymptomatic until death.

References

1. Melish ME (1991) Clinical and epidemiologic aspects of Kawasaki Disease. Clin Cardiol 14 [Suppl II]:3–10
2. Gersony WM (1991) Diagnosis and management of Kawasaki Disease. JAMA 265:2699–2703
3. Nakamura Y, Yanagawa H, Kawasaki T (1992) Mortality among children with Kawasaki Disease in Japan. New Engl J Med 326:1246–1249
4. Wreford FS, Conradi SE, Lie JT, Dana SE, Puri S (1991) Sudden death caused by coronary artery aneurysms: a late complication of Kawasaki Disease. J Forensic Sci 36(1):51–59
5. Fujiwara T, Fujiwara H, Hamashima Y (1987) Frequency and size of coronary arterial aneurysm at necropsy in Kawasaki Disease. Am J Cardiol 59:808–811
6. Fujiwara T, Fujiwara H, Nakano H (1988) Pathological features of coronary arteries in children with Kawasaki Disease in which Coronary arterial aneurysm was absent at autopsy. Quantitative analysis. Circulation 78:345–350
7. Hamashima Y (1980) Kawasaki's Disease. In: Pain SL (ed) Clinics in rheumatic diseases. The necrotizing vasculitides. W.B. Saunders, London, pp 319–338

8. Schultz TC (1989) Coronary artery aneurysms in a young adult. Am J Forensic Med Pathol 10:63–66
9. Tatara K, Kusakawa S, Itoh K, Kazuma N, Lee K, Hashimoto K, Shinohara T, Kondoh C, Hiroe M (1989) Long-term prognosis of Kawasaki Disease patients with coronary artery obstruction. Heart Vessels 5:47–51
10. Shiraishi I, Onouchi Z, Hayano T, et al (1991) Asymptomatic myocardial infarction in Kawasaki Disease: long-term prognosis. Pediatr Cardiol 12:78–82
11. Onouchi Z, Hamaoka K, Kamiya Y, Hayashi S, Ohmochi Y, Sakata K, Shiraishi I, Hayano T, Fukumochi H (1993) Transformation of coronary artery aneurysm to obstructive lesion and the role of collateral vessels in myocardial perfusion in patients with Kawasaki Disease. J Am Coll Cardiol 21:158–162
12. Koren G, Rose V, Lavi S, Rowe R (1985) Probable efficacy of high-dose salicylates in reducing coronary involvement in Kawasaki Disease. JAMA 254:767–769