Int J Legal Med (1999) 112 : 120–123

CASE REPORT

V. Fineschi · L. Paglicci Reattelli · G. Baroldi

Coronary artery aneurysms in a young adult: a case of sudden death. A late sequelae of Kawasaki disease?

Received: 4 May 1998 / Received in revised form: 10 July 1998

Abstract The case concerns the sudden death of a 21-year-old male during a soccer game. The autopsy revealed large, calcified saccular aneurysms at the origins of both the left anterior descending and the right coronary arteries. Histologically, the wall of the aneurysms was thin and composed of an internal fibro-calcified layer and an external thin tunica media. There was no evidence of active inflammation. The autopsy findings and a detailed medical history support the diagnosis of a late fatal sequela of Kawasaki disease.

Key words Sudden death · Coronary aneurysms · Kawasaki disease

Introduction

Kawasaki disease or mucocutaneous lymph node syndrome (MLNS) is an acute febrile exanthematic infection, resistant to antibiotics and characterized by severe vasculitis particularly involving coronary arteries and by a peculiar cutaneous and lymphonodal phlogistic state [1–3].

A more careful clinical attention and instrumental control together with immunoglobulin treatment (i.v.) have greatly improved the prognosis *quoad vitam* [4]. In fact the mortality rate has been reduced from 1–2% to 0.7% [5].

In more than 20% of the patients, severe inflammation of the vasa vasorum led to coronary arteritis with aneurysms formation, thrombosis and severe fibrous stenosis [6]. However, patients with Kawasaki disease may manifest severe, even asymptomatic, obstructive coronary disease resulting in cardiovascular symptoms and signs or sudden death [7–18].

Experience to date suggests the likelihood that Kawasaki disease plays an important role in aneurysm formation of the coronary arteries and, in the near future, this severe cardiovascular complication could be medically treated in adults [19–20].

In this case of sudden death, through gross, microscopic and clinical findings, a reconstruction of the medical history was possible supporting the diagnosis of Kawasaki disease.

V. Fineschi (✉)
Department of Forensic Sciences, University of Siena,
Policlinico Le Scotte, Viale Bracci,I-53100 Siena, Italy

L. Paglicci Reattelli
Institute of Legal Medicine, University of Perugia,
Via del Giochetto,I-75100 Perugia, Italy

G. Baroldi
Institute of Clinical Physiology, National Research Council,
Department of Cardiology "De Gasperis", Niguarda Hospital,
I-20162 Milan, Italy

Case history

A 21-year-old male suddenly collapsed while playing soccer with no previous symptoms or signs. An attempt at cardiac massage was unsuccessful and the cause of death was referred to an instantaneous cardiac arrest. A complete autopsy was performed 26 h after death.

External examination

The body was that of a well-built young man: height 182 cm, weight 78 kg with no visible external signs.

Internal examination

Examination revealed a widespread acute stasis and a heart with normal shape, dimension ($12 \times 12 \times 6$ cm.) and weight (390 g). The myocardium was normal, except for a small white area of the internal part of the anterior wall of the left ventricle. The valvular apparatus was normal.

There was a calcified saccular aneurysm (diameter 2.5 cm.) at the origin of the left anterior descending coronary branch and another similar calcified saccular aneurysm (diameter 1.5 mm.) was found 1 cm. distal to the right coronary artery orifice (Fig. 1). Cross-sections of the coronary vessels revealed a pronounced stenosis (maximum 70% lumen reduction) both of the left descending anterior branch and the right coronary artery distal to the aneurysms. The coronary ostia were unremarkable. There were no other aneurysmatic formations of arteries of any caliber. Toxicological tests were negative.

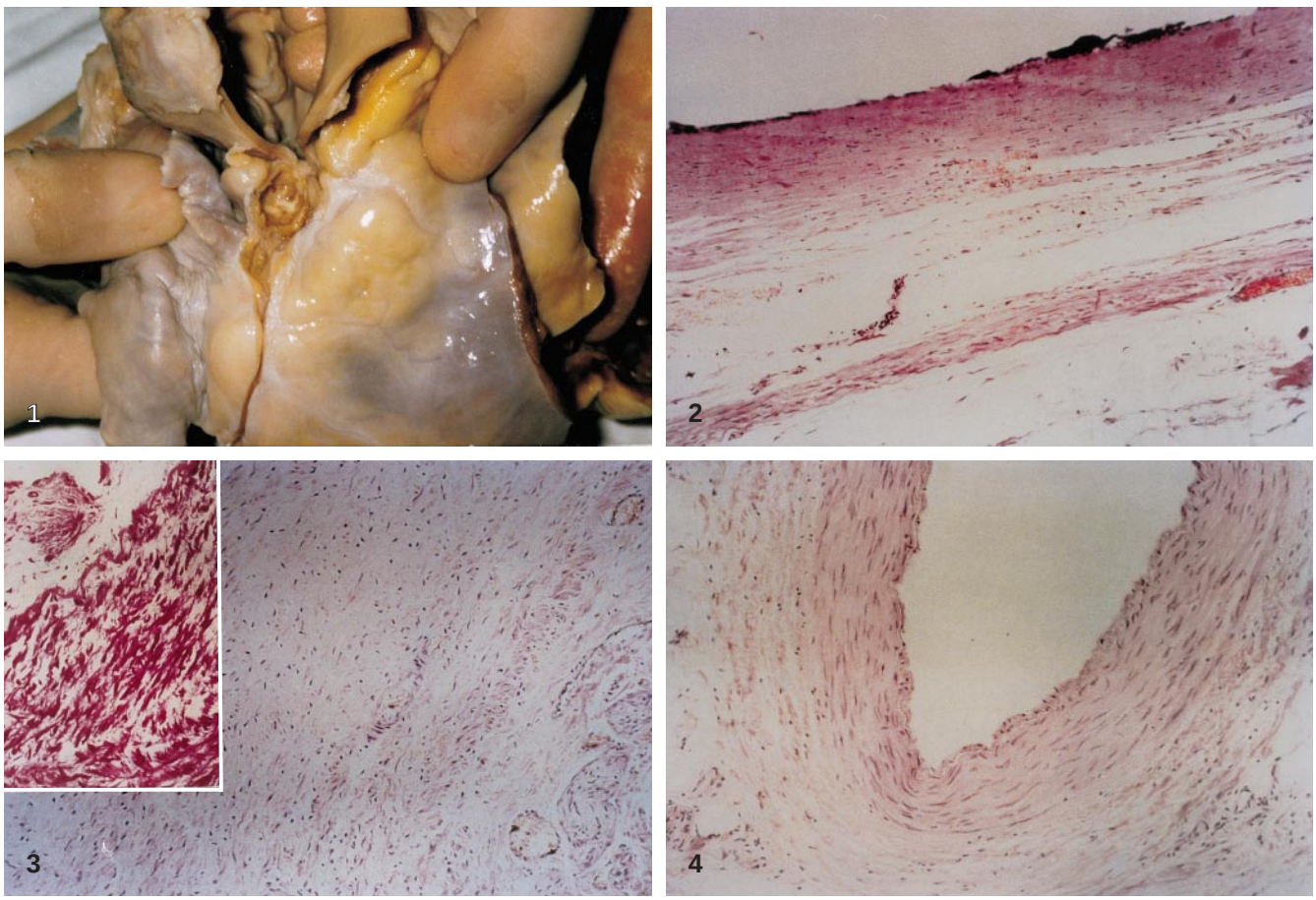

Fig. 1 Calcified aneurysm at the origin of right coronary artery

Fig. 2 Aneurysm wall. Several sections of the two aneurysms showed the same histologic pattern: a thin wall with an internal fibrous-calcified layer and thin external tunica media (H & E × 100)

Fig. 3 Subocclusive intimal thickening of left anterior descending branch distal to the aneurysm. The intimal thickening is formed by smooth muscle cell hyperplasia (insert: Mallory × 250) minimal elastic-fibrous network and proteoglycan accumulation. In the intimal thickening small arterioles are seen (H & E × 250)

Fig. 4 Branching (left) of the left circumflex branch from the aneurysmatic wall of the left descending branch. Note the absence of intimal thickening in this vessel (H & E × 80)

Histological findings

Coronary arteries

The aneurysm wall was thin and formed by an internal fibro-calcified layer and an external thin tunica media (Fig. 2). An advanced vascularized and organized thrombus, filling a small part of the lumen, was present in the left aneurysm. The arterial wall of the left descending branch and right coronary artery distal to the aneurysm assumed the typical pattern of obliterative intimal thickening with a lumen area reduction ranging from 60% to 70%. This thickening was mostly constituted by marked proliferation of smooth muscle cells, minimal elastic and fibrous network and minimal interstitial proteoglycan accumulation (Fig. 3). In contrast, the circumflex branch did not reveal the physiological intimal thickening normally present in all extramural arteries of normal males and females (Fig. 4). No inflammatory processes of any type were detected.

Myocardium

An area of old fibrosis was observed in the myocardium of the anterior left ventricle with a size corresponding to 20% of the histologically examined area. The myocardial fibrosis was situated in the internal half of the wall as a massive confluent process with few small islands of fatty tissue in the center. In addition, foci of myocardial contraction band necrosis or coagulative myocytolysis were visible in all regions of the heart. This change is formed by paradiscal and pancellular lesions with a number of foci of 49 × 100 mm^2 and a number of damaged myocells of 78 × 100 mm^2 in the anterior left ventricle. There were 33 foci and 78 myocells in the posterior left ventricle, 3 and 6 in the right ventricle and 1 and 2 in the interventricular septum, respectively.

The intramural vessels were normal and no pathological changes in the cardiac valves, aorta or pulmonary arteries were observed.

Clinical history

Examination of the medical records showed that at the age of 3 years the subject was hospitalized for pharyngotonsillitis with a febrile state lasting over 30 days, a non-purulent conjunctivitis, extreme cutaneous dehydration with dry mucosa and lip fissurae, strawberry tongue, a cutaneous rash limited to the torso and a right laterocervical lymphadenopathy. Diarrhea, moderate jaundice and frequent colic-like abdominal pains were also reported. The heart rate was 120/min and regular, the blood pressure was 115/50 mm Hg, the heart size was normal. The liver, kidneys and spleen were not palpable. Chest x-ray examination (anteroposterior) revealed clear lung fields. Hematochemical data showed a raised erythrocyte sedimentation rate of 88 mm in the first hour, thrombocytosis (620.000/mm^3.), hemoglobin: 11.8 g/dl; polymorphonuclear leuko-

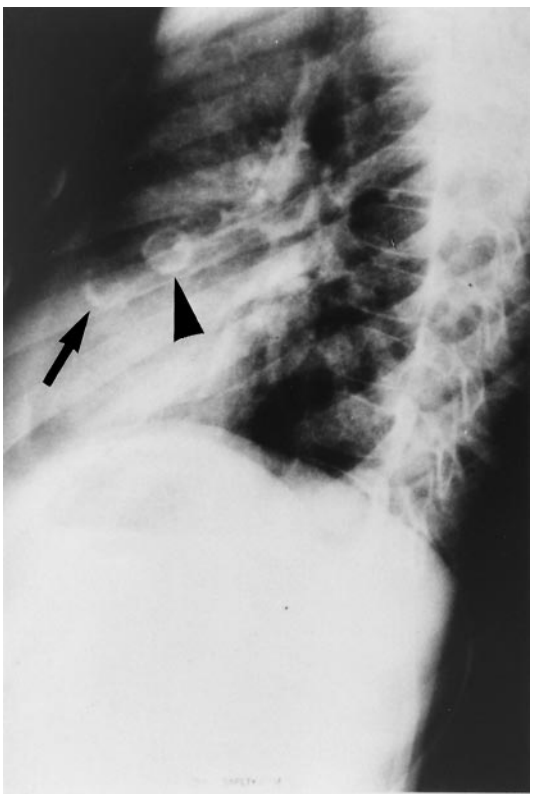

Fig. 5 Chest X-ray examination at the age of 18. Lateral view reveals two ring calcifications: aneurysms of the left descending anterior branch (*arrow*) and of the right coronary arteries (*arrowhead*)

cytosis : 14.8000/mm^3. Serial blood, urine, throat and stool cultures were negative. Skin tests were negative for tuberculosis, coccidioidomycosis and histoplasmosis. He was treated with intravenously administered penicillin and cephaloridine. In 10 days the rash gradually faded but the fever persisted and there was no response to the therapy. Antibiotic drugs were changed to gentamycin sulfate and tetracycline without response: the fever persisted 32 days. After 43 days of gradual recovery the child was discharged.

At the age of eight, an X-ray examination of the chest revealed two annular calcifications interpreted as the result of peribronchial lymphadenopathy. After 1 year, another x-ray examination confirmed these circular imagings, interpreted as stratifications of fibrin due to a pericarditis.

An electrocardiogram and an echocardiography taken at the age of 18, during screening for participation in competitive sports, were negative. A chest x-ray confirmed the previous finding which was clearly evident but not interpreted (Fig. 5).

Discussion

In general the gross and microscopic features of coronary aneurysms, although not diagnostic, are characteristic of the delayed complications of an acute coronary artery vasculitis [21]. In the present case the pathogenesis of the aneurysms can be related to Kawasaki disease. In fact, a clinical diagnosis of the latter can be made in the presence of five of the following six symptoms:

1. Fever persisting for five days or longer
2. Reddening of palms and soles with desquamation
3. Polymorphous exanthema
4. Bilateral conjunctivitis
5. Strawberry tongue, reddened lips and oropharyngeal mucosa
6. Acute non-suppurative cervical lymphadenopathy.

A diagnosis of Kawasaki disease is accepted in patients with only four symptoms when a coronary aneurysm is detected by coronary angiography or echocardiography [22]. Several studies have also identified abnormalities in the T lymphocytes and in the various ratios of OKT3+, OKT4+ and OKT8+ cells in patients with and without vasculitis. Such abnormalities may serve to identify those patients likely to develop coronary involvement [23].

In our case five out of six diagnostic clinical criteria of Kawasaki disease were present. Furthermore, several years after the acute clinical episode, two uninterpreted calcified rings were shown by chest x-rays. A recent review indicated that the radiographic evidence of an annular calcification represents a calcium sediment in the walls of a coronary artery aneurysms which was observed in 36% of the patients[24–25].

Coronary angiographic studies found coronary artery aneurysms in more than 23% of the Kawasaki patients which occurred in the initial tract of the coronary arteries [26–27], the right coronary artery being more frequently involved and occluded [25]. In clinical angiographic studies prominent collateral vessels were specifically described in approximately 44% of these patients [25]. Clinical studies on the dimension and type of aneurysm report that the risk of ischemic heart disease increases when the aneurysm diameter is more than 8 mm with a shape saccular in type [19], a finding confirmed by postmortem quantitative morphometry [28].

Our case seems important for various reasons. First, from a forensic viewpoint, it emphasizes that long-term sequelae of Kawasaki disease may be fatal many years following the acute phase [29–31], most of acquired aneurysms, in both children and adults, being due to Kawasaki disease [21]. However, in the absence of a complete clinical history, a definitive pathology diagnosis is impossible [20]. Second, by the misinterpreted radiographic documentation of the calcified aneurysms. Third, it shows myocardial focal necrosis, namely coagulative myocytolysis (or contraction band necrosis), typical of catecholamine myocytotoxicity, linked with ventricular fibrillation and sudden death. [32–35].

References

1. Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H (1974) A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. Pediatrics 54: 271–276
2. Wortmann DW (1992) Kawasaki syndrome. Semin Dermatol 11:37–47
3. Fukushige J, Nihill MR, McNamara DG (1980) Spectrum of cardiovascular lesions in mucocutaneous lymph node syndrome. Am J Cardiol 45:98–107

4. Newburger JW, Takahashi M, Burns JC, Beiser AS, Chung KJ, Duffy CE, Glode MP, Mason WH, Reddy V, Sanders SP (1986) The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med 315:341–347
5. Yanagawa H, Yashino M, Nakamura Y, Kawasaki T, Kato H (1995) Results of 12 nationwide epidemiological incidence surveys of Kawasaki disease. Jpn Arch Pediatr Adolesc Med 149: 779–783
6. Harrison DC (1996) Nonatherosclerotic coronary artery disease. In: Fuster V, Ross R, Topol EJ (eds) Atherosclerosis and coronary artery disease. Lippincott-Raven, Philadelphia, pp 757–772
7. Trillo AA, Scharyj M, Prichard RW (1980) Coronary artery aneurysm and myocardial infarction resulting in sudden death of a 6-year-old child. Am J Forensic Med Pathol 1:349–354
8. Kegel SM, Dorsey TJ, Rowen M, Taylor WF (1977) Cardiac death in mucocutaneous lymph node syndrome. Am J Cardiol 40:282–286
9. Kohr RM (1986) Progressive asymptomatic coronary artery disease as a late fatal sequela of Kawasaki disease. J Pediatr 108:256–259
10. Gorgels APM, Brat SHGJ, Becker AE, Raab THJM, Boehmer AG, Da Costa AJ, Van Der Poel AJM, Wellens HJJ (1986) Multiple aneurysms of the coronary arteries as the cause of sudden death in childhood. Am J Cardiol 57:1193–1194
11. Rowley AH, Gonzales-Crussi F, Gidding SS, Duffy CE, Shulman ST (1987) Incomplete Kawasaki disease with coronary artery involvement. J Pediatr 110:409–413
12. McCowen C, Henderson DC (1988) Sudden death in incomplete Kawasaki's disease. Arch Dis Child 63:1254–1256
13. Loubser MD, Hoh MC, Sreeram N (1989) Sudden death in incomplete Kawasaki disease. Arch Dis Child 64:637–638
14. Schultz TC (1989) Coronary artery aneurysms in a young adult. Am J Forensic Med Pathol 10:63–66
15. Murai T, Kuroda N, Shinozuka T, Kurihara K, Yanagida J, Watanabe H, Saito K, Maurai N, Imai M (1989) Coronary aneurysms in a young adult: report of a case suspected of Kawasaki disease. Med Sci Law 29:59–63
16. Burke AP, Farb A, Virmani R, Godin J, Smialek JE (1991) Sports-related and non-sports-related sudden cardiac death in young adults. Am Heart J 121:568–575
17. Subramaniam S, Boo K (1992) Sudden death in a young adult due to coronary artery aneurysm secondary to suspected Kawasaki disease. Malays J Pathol 14:49–51
18. Bayer Kristensen I, Østergaard Kristensen B (1994) Sudden death caused by thrombosed coronary artery aneurysm. Int J Legal Med 106:277–280
19. Kato H (1987) Cardiovascular involvement in Kawasaki disease: evolution and natural history. Prog Clin Biol Res 250:277–286
20. Pounder DJ (1985) Coronary artery aneurysms presenting as sudden death 14 years after Kawasaki disease in infancy. Arch Pathol Lab Med 109:874–876
21. Virmani R, Robinowitz M, Atkinson JB, Forman MB, Silver MD, McAllister HA (1986) Acquired coronary arterial aneurysms: an autopsy study of 52 patients. Hum Pathol 17:575–583
22. Lie JT (1997) Kawasaki disease. In: Bloom S (ed) Diagnostic criteria for cardiovascular pathology acquired diseases. Lippincott-Raven, Philadelphia, pp 193–194
23. Terai M, Kohmo Y, Niwa K, Toba T, Sakurai N, Nakajima H (1987) Imbalance among T-cell subsets in patients with coronary arterial aneurysms in Kawasaki disease. Am J Cardiol 60:555–559
24. Doi YL, Hamashige N, Odowara H, Kuzume O, Chikamori T, Ozawa T (1987) Ring-calcification of coronary artery aneurysms in an adolescent. Chest 92:1118–1120
25. Burns JC, Skike H, Gordon JB, Malhotra A, Schoenwetter M, Kawasaki T (1996) Sequelae of Kawasaki disease in adolescents and young adults. J Am Coll Cardiol 28:253–257
26. Suzuki A, Kamiya T, Kuwahara N, Ono Y, Kohata T, Takahashi O, Kimura K, Takamiya M (1986) Coronary arterial lesions of Kawasaki disease: cardiac catheterization findings of 1100 cases. Pediatr Cardiol 7:3–9
27. Sakai Y, Takayanagi K, Inoue T, Yamaguchi H, Hayashi T, Morooka S, Takabatake Y, Sato Y (1988) Coronary artery aneurysms and congestive heart failure-possible long-term course of Kawasaki disease in an adult -A case report. Angiology 39:625–630
28. 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
29. Smith BA, Grider DJ (1993) Sudden death in a young adult: sequelae of childhood Kawasaki disease. Am J Emerg Med 11: 381–383
30. Wreford FS, Conradi SE, Cohle SD, Lie JT, Dana SE, Puri S (1991) Sudden death caused by coronary artery aneurysms: a late complication of Kawasaki disease. J Forensic Sci 36:51–59
31. Quam JP, Edwards WD, Bambara JF, Luzier TL (1986) Sudden death in an adolescent four years after recovery from mucocutaneous lymph node syndrome (Kawasaki disease). J Forensic Sci 31:1135–1141
32. Baroldi G, Falzi G, Mariani F (1979) Sudden coronary death. A postmortem study in 208 selected cases compared to 97 “control” subjects. Am Heart J 98:20–25
33. Baroldi G, Silver MD (1995) Sudden death in ischemic heart disease. An alternative view on the significance of morphologic findings. Landes Publ, Austin Texas, Springer, Heidelberg New York, pp 131–133
34. Fineschi V, Wetli CW, Di Paolo M, Baroldi G (1997) Myocardial necrosis and cocaine. A quantitative morphologic study in 26 cocaine-associated deaths. Int J Legal Med 110:193–198
35. Zack F, Terpe H, Hammer U, Wegener R (1996) Fibromuscular dysplasia of coronary arteries as a rare cause of death. Int J Legal Med 108:215–218