CASE REPORT

Non-atherosclerotic coronary pathology causing sudden death

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Coronary atherosclerosis is responsible for >50% of all cases of sudden death and for 90% of sudden coronary death. Four cases encountered in routine autopsy evaluation at our institute in 2004 in which non-atherosclerotic coronary pathology was responsible for sudden cardiac death are reported. The cases of a 31-year-old man with epicardial coronary arteritis, a 57-year-old man with intramyocardial vasculitis, a 45-year-old woman with spontaneous coronary dissection and a 50-year-old man with vascular fibrosis are described. Searching for non-atherosclerotic coronary disease is relevant for both the clinician and the pathologist to prevent coronary causes of sudden death going unrecognised.

Non-atherosclerotic coronary artery disease is a condition often unrecognised in the living and in the dead. In a survey of 278 cases of sudden death in Italy, 28 cases were due to non-atherosclerotic coronary artery disease.¹ Similar rates have been reported elsewhere.² In living patients with acute myocardial ischaemia, non-atherosclerotic coronary disease is occasionally recognised but only when the lesions are seen in coronary angiography as congenital abnormalities or lesions causing coronary lumen stenoses or aneurysms.^{1 3–5}

We report four cases encountered in routine autopsy evaluation at our institute in 2004 in which non-atherosclerotic coronary disease was responsible for sudden cardiac death. Box 1 lists the most common causes of sudden cardiac death.

Case 1: epicardial coronary arteritis

A 31-year-old man brought to hospital by the emergency medical services (EMS) was pronounced dead on arrival. Death had occurred suddenly, with no anticipatory symptoms of chest pain or discomfort. Medical history was non-contributory.

The gross pathological examination was mostly unremarkable, except for a mildly discoloured region of the anterolateral myocardium. Histological examination showed signs of recent ischaemic damage. Examination of the left descending anterior artery showed no evidence of intraluminal thrombus or lumen stenosis. Serial sections of the artery were taken for histological examination. Light microscopical examination after standard haematoxylin–eosin staining showed the presence of a circumferential transmural inflammatory cell infiltrate extending from the adventitia to the intima and composed predominantly of CD8+ T lymphocytes (fig 1). The remaining coronary arteries and the other (non-coronary) arteries were disease free.

In face of the early ischaemic changes—variable waviness of fibres—but no evident necrosis, the cause of death was deemed arrhythmic death secondary to myocardial ischaemia caused by non-atherosclerotic non-thrombotic coronary disease.

Case 2: intramyocardial vasculitis

A 57-year-old man was found in cardiac arrest by the EMS and pronounced dead at the scene. Death had occurred unexpectedly.

Medical history was unremarkable. Findings of the gross pathological examination were unremarkable. The left and right ventricles had a normal appearance at gross examination. The coronary arteries were free of disease along their epicardial course. Serial coronary artery and myocardial sections were studied. The light microscopical examination after standard haematoxylin–eosin staining showed the presence of a diffuse cell infiltrate in the wall of the small intramyocardial vessels. Inflammatory cells were CD4+ and CD8+ T lymphocytes. The

Box 1: Most common causes of sudden cardiac death

- **Coronary disease**
 - Atherothrombosis
 - Dissection
 - Congenital anomalies
 - Arteritis/vasculitis
 - Aneurysms
 - Intimal humps
 - Trauma
 - Myocardial bridging
- **Myocardial pathology**
 - Myocardial scarring (ischaemic)
 - Dilated cardiomyopathy (any aetiology)
 - Hypertrophic cardiomyopathy
 - Right ventricular dysplasia
 - Myocarditis
 - Aortic stenosis
 - Congenital heart disease
- **Functional diseases**
 - Long QT syndrome (congenital or acquired)
 - Catecholaminergic polymorphic ventricular tachycardia
 - Pre-excitation syndromes (ie, Wolf–Parkinson–White)
 - Brugada syndrome
 - Complete heart block (sinoatrial or atrioventricular block)
- **Pathology of the great vessels**
 - Aortic dissection
 - Pulmonary embolism
 - Pulmonary artery dissection
- **Miscellaneous**
 - Mixoma
 - Cardiac metastases
 - Pericardial effusion/tamponade

Figure 1 (A) Epicardial coronary arteries with circumferential transmural periadventitial inflammatory cell infiltrate, composed mainly of CD8+ T lymphocytes (B). (C, D) Intramyocardial vasculitis, showing the lymphocytic infiltrate in the small intramyocardial vessel wall. (D) Immunohistochemical detection showing CD4+ T lymphocytes. (E, F) Intimal "humps" with variable degrees of luminal stenosis of the intramyocardial arterioles of the ventricular septum.

epicardial coronary arteries were spared, as were the other (non-coronary) arteries. The cause of death was considered arrhythmic death secondary to myocardial ischaemia caused by non-atherosclerotic non-thrombotic coronary disease. Figure 1 shows the lymphocytic infiltrate in the small intramyocardial vessel wall.

Case 3: spontaneous coronary dissection

A 45-year-old woman was admitted to hospital with severe hepatic failure. A few days after admission, cardiac arrest occurred. At autopsy, coronary dissection of the left main coronary artery extending to the left anterior descending and circumflex arteries was noted. Histological examination showed a multistage process, as granulation tissue consistent with subacute changes was present in the left main coronary artery, whereas acute haemorrhage was present in the left anterior descending and circumflex arteries. The coronary

lumen was almost completely occluded (fig 2). Ischaemia-induced lethal arrhythmia was considered to be the cause of death.

Case 4: intramyocardial vascular humps

A 50-year-old man was found unresponsive by the EMS and brought to hospital. The patient was pronounced dead on arrival. The toxic screen was negative for commonly used drugs of misuse. Gross examination of the heart and coronary arteries was unremarkable. The only finding was the presence of a prominent medial and fibrointimal thickening of the intramyocardial vasculature at histological examination. There was a range of arterial changes, including eccentric intimal obstructive humps that were periodic acid-Schiff positive and Congo Red negative. The myocardium showed "patchy" fibrosis adjacent to the small vessels (fig 1). Cardiac arrhythmia was considered the cause of death.

Figure 2 Spontaneous coronary dissection. (A) Coronary dissection in the left main coronary artery extending to the left anterior descending and circumflex arteries. (B, C) Acute haemorrhage in the left anterior descending (C) and circumflex arteries (B). Panel B highlights the coronary lumen almost completely lost by “ab extrinseco” compression by the false lumen. (C) Concentric haematoma between the media and the adventitia.

DISCUSSION

In the four cases presented here, non-atherosclerotic coronary artery disease was identified as the cause of sudden death of otherwise healthy adults.

Coronary vasculitis is usually a feature of coronary involvement in the setting of more widespread vasculitis such as Takayasu's type and panarteritis nodosa.⁶ Most classifications of systemic vasculitis are based on the size of the blood vessels involved, the anatomical site, histology and clinical manifestations.⁷ As only medium and small-sized coronary arteries were affected and no other organs had signs of inflammation, we were able to exclude most forms of vasculitis. Not meeting the criteria for polyarteritis nodosa, Kawasaki disease or microscopic polyangiitis, atypical isolated coronary vasculitis was diagnosed. Similarly, isolated involvement of intramyocardial vasculature, as found in case 2, is atypical.⁸

In the third case, spontaneous coronary dissection was observed. Spontaneous coronary artery dissection remains a rare but important cause of acute coronary syndromes and sudden cardiac death. The true incidence is probably underestimated as most of cases are diagnosed after death. It occurs in three major groups: in young women in the peripartum period, in patients with atherosclerotic disease and in an idiopathic group. There are several associated conditions, but the pathogenesis remains unclear.^{9–10}

In the fourth case, the intramyocardial small arterioles showed prominent medial and fibrointimal thickening, so-called intimal humps, with variable degrees of luminal stenosis of the intramyocardial arterioles of the ventricular septum. In the presence or even in the absence of myocardial damage, the abnormally small vessels may result in poor blood flow, inadequate perfusion, arrhythmias and sudden death. Intramyocardial small vessel abnormalities are not commonly recognised. Small vessel disease has been reported as an isolated cardiac anomaly in individuals with sudden death and may also be associated with other cardiac conditions.¹¹

In conclusion, in all cases, the probable mechanism of sudden death was ventricular arrhythmia due to myocardial ischaemia secondary to non-atherosclerotic coronary disease.

In all cases, other causes of sudden cardiac death (involvement or infiltration of the conduction system, coronary anomalies, myocarditis, aortic or pulmonary artery dissection and other) were excluded by a thorough pathological examination. Clinicians and forensic pathologists, in particular, should be aware of the possibility of non-atherosclerotic coronary disease causing myocardial ischaemia and death. Non-atherosclerotic causes of myocardial ischaemia, although rare, should be considered when assessing the pretest likelihood of coronary disease. Moreover, in sudden unexplained deaths, signs of non-atherosclerotic coronary disease should be sought.

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