

SUDDEN CARDIAC DEATH IN CHILDREN

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Summary. Sudden cardiac death is defined as unexpected death from cardiac causes early after or without the onset of symptoms. Having in mind that acute myocarditis may be a rare cause of sudden cardiac death in children, we have undertaken the following study: clinical, macroscopical and histopathological characteristics of the myocardium of two autopsied children who died suddenly. A number of myocardial tissue specimens were fixed in formalin and embedded in paraffin. Laboratory sections were stained with HE, Van Gieson and PAS methods. The pathohistological features of viral and acute rheumatic myocarditis were found. Coronary arteries and valves were normal. Viruses are difficult to culture from myocardial tissue, but lymphocytic and monocytic infiltrates are histological markers of viral etiology and acute Aschoff bodies of rheumatic fever.

Key words: Viral myocarditis, rheumatoid myocarditis, children, morphology

Introduction

Sudden cardiac death (SCD) is most commonly defined as an unexpected death from cardiac causes early after or without the onset of symptoms. In a vast majority of cases in children, SCD is caused by a congenital structural abnormality, hereditary or acquired abnormalities of the cardiac conduction system, myocarditis, or idiopathic dilated or hypertrophic cardiomyopathy (1-5). The ultimate mechanism of death is almost always a lethal arrhythmia (6-7). Data suggest that increased sympathetic stimulation may contribute to SCD triggering (8-10).

Myocarditis refers to general inflammation of the myocardium associated with necrosis and degeneration of myocytes. Myocarditis can occur at any age and is one of the few heart diseases that can produce acute heart failure in previously healthy adolescents and young adults (9-12). Although unusual, myocarditis can occur with a sudden onset of arrhythmias and even sudden cardiac death (13-16). Myocarditis can be caused not only by numerous infectious agents but also by hypersensitive reactions and some toxic injuries.

Viral myocarditis

Most cases of myocarditis in European countries occur without a demonstrable etiology. A majority of cases, however, are believed to be viral, although the evidence is largely circumstantial. Among these pathogens, the most prominent ones include Coxsackie's B virus and influenza virus. A viral etiology is suggested by a histological similarity between the human myocarditis and that produced experimentally by inoculation of cardiotropic viruses into animals. Patients with presumptive diagnosis

of viral myocarditis may give a history of a recent upper respiratory tract viral syndrome. The pathogenesis of viral myocarditis is believed to involve direct viral cytotoxicity or cellular mediated immune reactions directed against infested myocytes (1-6).

Rheumatic myocarditis

Rheumatic heart disease may be manifested as an isolated endocarditis, myocarditis, pericarditis or, more often, pancarditis that involves the entire heart. Myocarditis of rheumatic fever occurs in the form of typical Aschoff bodies. These inflammatory lesions begin first as infiltrates of histiocytes surrounding foci of fibrinoid necrosis in the interstitial spaces. Aschoff bodies persist for an indefinite period before they finally heal and transform into scarce (1,14).

Hypersensitivity reactions, associated with myocarditis

This type of myocarditis is associated with allergic reactions (hypersensitivity) to a particular drug, including some antibiotics, diuretics and antihypertensive agents. Several forms of myocarditis are associated with systemic diseases of immune origin, such as rheumatic fever and systemic lupus erythematosus (14).

Fiedler's myocarditis

There remains a morphologically distinctive form myocarditis of uncertain cause called *giant cell myocarditis*, characterized by a widespread inflammatory cellular infiltrate containing multinucleate giant cells interspersed with lymphocytes, eosinophils, plasma cells, and macrophages and having at least focal but fre-

quently extensive necrosis (*idiopathic giant cell myocarditis or, in the past, Fiedler's myocarditis*). The giant cells are of macrophage origin in some cases, and of myocyte origin in others (1).

The aim of this study is to report two autopsy cases of sudden cardiac death in children.

Autopsy Cases and Methods

There were two autopsy cases, one male, aged 12, and one female, aged 15. Neither of them was hospitalized. The girl died in her bed on an early morning, while the boy died at school, during a sport activity. The boy, who died suddenly while being under a physical stress, had the upper respiratory tract viral syndrome accompanied by fever three months prior to death. Since then he felt fatigue, dyspnoea and palpitations. The girl, who died at home, had fever, malaise and fatigue during one week.

Tissue autopsy specimens were embedded in paraffin and routinely processed. Myocardial sections (5 µm thick) were stained with HE, Van Gieson and PAS techniques.

Morphology

1. Boy, 12 years of age: At autopsy, the heart was focal firm and dilated, with myocardial pseudo hypertrophy. Microscopically, multifocal interstitial infiltrate composed principally of lymphocytes and macrophages was seen (Fig. 1). The myocardial fibres were disrupted by both the infiltrate and fibroblast proliferation. The inflammatory process was subacute-healed and associated with areas of replacement-type fibrosis.

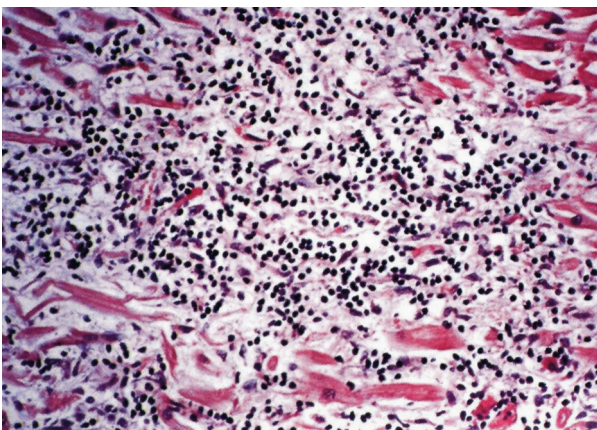


Fig. 1. Interstitial infiltrate composed principally of lymphocytes and macrophages HE×200

2. Girl, 15 years of age: The gross appearance of the heart was not distinctive, and the weight ranged within normal values. Histological examination of myocardial tissue demonstrated pathologic substrate such as focal non-specific myocarditis in which macrophages predominate, although a few neutrophils and eosinophils were also evident (Fig. 2). Mucoïd oedema and fibrinoid degeneration of collagen was a characteristic finding. Initially, the pattern of the Aschoff body, which con-

sisted of perivascular focus of swollen eosinophilic collagen surrounded by lymphocytes, plasma cells and macrophages (Fig. 3), was also conspicuous. The most important finding was neural fibres destruction by dense macrophage infiltration (Fig. 4). Coronary arteries were normal in both cases.

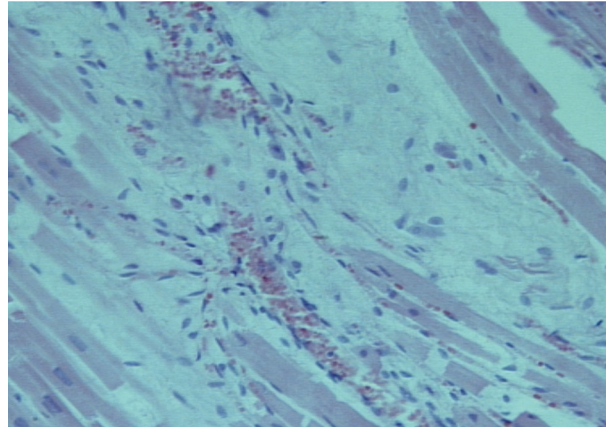


Fig. 2. Macrophages predominate HE×250

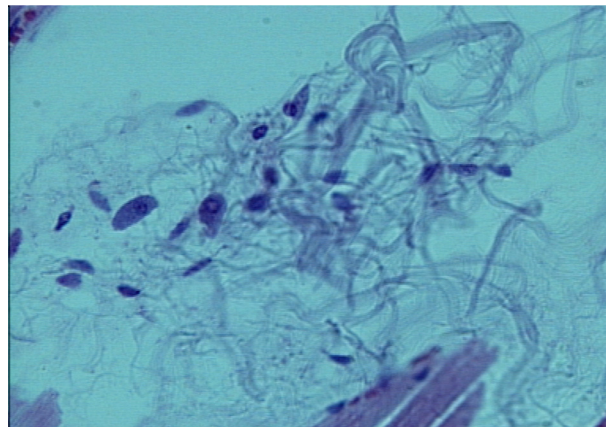


Fig. 3. Mucoïd oedema and fibrinoid degeneration of collagen surrounded by lymphocytes, plasma cells and macrophages PAS×300

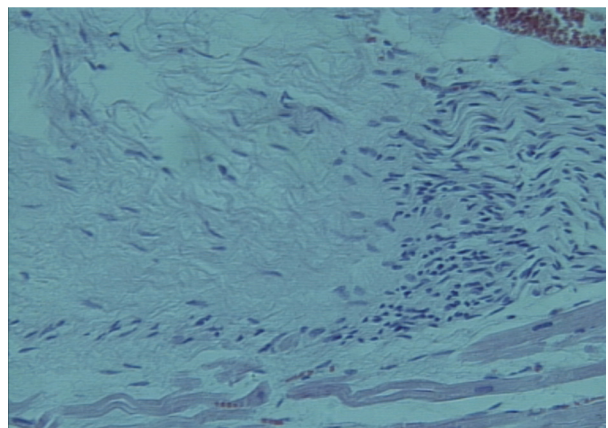


Fig. 4. Neural destruction by dense macrophage infiltration HE×200

Significant findings were confined also to the brain and lungs, in both cases. The brain appeared heavy and oedematous and showed signs of tonsillar herniation. Diffuse cerebral oedema was confirmed histologically. The lungs appeared heavy and congested and microscopically showed diffuse pulmonary oedema. Alveolar walls were irregularly paved by a mixed infiltrate, and chronic inflammatory cells, but no significant necrosis or hyaline membrane, were seen.

Discussion

Infectious heart diseases in childhood - with less than 1% of hospital admissions - are rare, but serious. Among several causes of myocarditis in our region, virus myocarditis plays the most important role. Myocarditis was diagnosed according to the Dallas criteria (6) by the presence of inflammatory infiltrates of the myocardium with degeneration and/or necrosis of adjacent myocytes. Myocarditis can occur at any age and is one of the few heart diseases that can produce acute heart failure in previously healthy adolescents or young adults (14-16). Although unusual, it can manifest itself with a sudden onset of arrhythmias and even sudden cardiac death (1,14).

In patients with acute or chronic myocarditis, arrhythmias are a common and usual clinical symptom in the natural course of the disease. Factors responsible for the increased incidence of cardiac arrhythmias are structural changes, parameters of ventricular dynamics and vascular changes (10). On the one hand, inflammatory processes in the cardiac myocytes and interstitium can lead directly to fluctuations in membrane potential. Fibrosis and scarring of the myocardial tissue and secondary hypertrophy and atrophy myocytes favor the development of ectopic pacemakers, late potentials and reentry as a result of inhomogeneous stimulus condition. In addition, vascular factors can further increase the arrhythmogenicity of the inflamed myocardium through disturbance of micro- and macrovascular perfusion and

the resulting myocardial ischemia (10). A viral etiology is suggested by the histological similarity of the human myocarditis to that produced experimentally by the inoculation of cardiotropic viruses into animals (4-5,8).

Patients with a presumptive diagnosis of viral myocarditis have a history of a recent upper respiratory tract viral syndrome, with a positive throat culture for a specific virus. However, it is not usual for viruses to be cultured from the heart, even when endomyocardial biopsy or autopsy tissues studied. The pathogenesis of viral myocarditis is believed to involve direct viral cytotoxicity or cell-mediated immune reactions directed against infected myocytes (13-18).

In most patients with viral myocarditis, the symptoms begin a few weeks after the initial infection, which is confirmed by this report. The disease may be unusually severe in infants and in pregnant women, accompanied by a fulminant course with malignant arrhythmias (10).

We were unable to discover the cause. But, we hope that our report will help in this process by raising the level of awareness for the need of vigilance for future outbreaks, improved case reporting, and further refinement of diagnostic tools.

Rheumatic heart disease encompasses myocarditis during acute rheumatic fever and residual chronic valvular deformities. In severe cases of rheumatic fever, the heart tends to be dilated, and a few patients die in the acute stage of the disease. The mortality of acute rheumatic carditis is low, and the main cause of death is heart failure from myocarditis, and this is pointed out in our report (1,3,16).

Conclusion

- The diagnosis of both viral and rheumatic acute myocarditis remains difficult and it generally depends on clinical and histological criteria.

- Arrhythmia is one of the reasons of sudden death.

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IZNENADNA SRČANA SMRT KOD DECE

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Kratak sadržaj: *Iznenadna srčana smrt se definiše kao neočekivana smrt srčanog porekla koja nastaje neposredno nakon ispoljene simptomatologije, ili bez pojave bilo kakvih simptoma. Imajući u vidu da akutni miokarditis može biti redak uzrok iznenadne srčane smrti kod dece, pratili smo kliničke, makroskopske i histopatološke promene miokarda kod dva autopsijska slučaja iznenada preminule dece. Fiksirani su brojni isečci srčano-mišićnog tkiva u formalinu i kalupljeni u parafin. Laboratorijski isečci su obojeni HE, Van Gieson i PAS metodom. Nadjene su patohistološke karakteristike akutnog virusnog i reumatoidnog miokarditisa. Nalaz na koronarnim arterijama i valvulama je bio normalan. Viruse je teško izolovati iz srčano-mišićnog tkiva, ali limfocitni i monocitni infiltrati su histološki markeri miokarditisa virusne etiologije, dok su Aschoff-ova tela markeri reumatske groznice.*

Ključne reči: *Virusni miokarditis, reumatoidni miokarditis, deca, morfologija*