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A Case of Sarcoidosis in a Forensic Setting – What Has Been Found as Case of Death

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Sarcoidosis is a multisystem inflammatory disease of unknown etiology with a particular clinical and pathological picture. Pathologically can be confirmed with the finding of non-caseating (non-necrotizing) granulomas containing epithelioid cells and large multinucleated giant cells. Sarcoidosis is associated with an increased risk of premature death; it is twice as high as the general population. The common cause of death includes: cardiac failure due to cardiac sarcoidosis, lung disease associated with pulmonal hypertension, infection etc. In this case presentation we show finding of another and not so common cause of cardiac death in a patient with sarcoidosis i.e. bacterial myocarditis represented by clusters of bacterial colonies throughout the myocardial tissue.

Key words: sarcoidosis, cardiac sarcoidosis, bacterial myocarditis

Introduction

Sarcoidosis is a multisystem inflammatory disease of unknown etiology. Mainly it is considered as autoimmune disease, where T-cells play a central roll with the excessive cellular immune reaction. Microbial, environmental and genetic factors have been proposed so far as possible agents. Pathologically is manifested with non-caseating (non-necrotizing) granulomas containing epithelioid cells and large multinucleated giant cells. They are predominantly found in lungs and lymph nodes, but the disease is also visible to skin (erythema nodosum), eyes (conjunctivitis and uveitis), spleen (splenomegaly), liver, kidneys, bone marrow and especially involves the metabolism

of calcium, nervous and musculoskeletal system [8]. Löfgren syndrome, characterized by fever, bilateral hilar lymphadenopathy and acute onset of erythema nodosum and migratory polyarthritis is also characteristic of sarcoidosis [6].

The sarcoidosis is generally considered as non-fatal disease with very diverse incidence, from 1-5 per 100,000 in East Asia countries to 14-16 per 100,000 in Scandinavian countries and Canada. In Southern Europe, estimates are lower than in the North. The average age at diagnosis is around 50 years. Several studies, but not all, show a bimodal distribution of age primarily related to sex. Even though many studies report a female to male ratio of 1:1, more males than females are diagnosed at 20–45 years old, whereas incidence peaks in females later (at 50–65 years old) [1].

As possible risk factors are considered: genetic predisposition, infection, occupation, environmental factors [1].

In 5 to 10% of cases sarcoidosis is asymptomatic and can be found only by autopsy [3].

Although described more than 100 years ago (by Boeck, the Norwegian dermatologist), the knowledge about the involvement of myocardium i.e. the cardiac sarcoidosis is more recent [2].

Cardiac sarcoidosis occurs in at least 25% of patients with sarcoidosis in the USA, and accounts for as many as 13–25% of deaths from sarcoidosis [1]. In Japan, sarcoid heart disease is more common and responsible for as many as 85% of deaths from sarcoidosis [1]. The characteristics and the comprehensiveness of the clinical picture in cardiac sarcoidosis depend on the location and extent of the glaucomatous inflammation and the subsequent fibrosis in the myocardium and especially depend on the involvement of the conduction system [7].

According to some authors, sarcoidosis should be suspected in any patient, younger than expected, presenting with complete heart block or heart failure [5], which is of great forensic medicine importance.

Hence, in a forensic setting, the importance of sarcoidosis, and particularly of cardiac sarcoidosis, comes from its occurrence as a possible cause of sudden death in relatively young persons, 30 to 50 years old.

In this case presentation we show finding of another and not so common cause of cardiac death in a patient with sarcoidosis i.e. bacterial myocarditis represented by clusters of bacterial colonies throughout the myocardial tissue.

Presentation of the case

By the order of the public prosecutor, a body of the 42 years old man, the foreign citizen with temporary residence in our country, has been admitted to the Institute of forensic medicine for forensic autopsy, because of sudden unexpected death and unknown cause of death.

He was found unresponsive in his apartment and was urgently transmitted to hospital, where he died after several hours of intensive care and cardio pulmonal resuscitation. He died under the clinical picture of cardiotonic shock. Uncertain data have been received that he suffered of sarcoidosis during alive.

Autopsy finding

Macroscopic feature of organs

On autopsy we found a body of a 42 years old male, with asthenic osteomuscular constitution.

During the external examination dominated a feature of dehydration, asthenia, livid colorization of the skin, especially on head and neck, but also livid to pink colorization of the skin of the entire body. Also, apparent conjunctivitis and uveitis has been found.

During the examination of the internal organs, there dominated the finding of granulomatous lymphadenitis. The hilar lymph node enlargement has been found, with a diameter of until 3 cm. The lymph nodes have been well demarcated, with lack of central necrosis and on their cut surface they appeared to be grayish to yellowish **(Fig. 1A).**

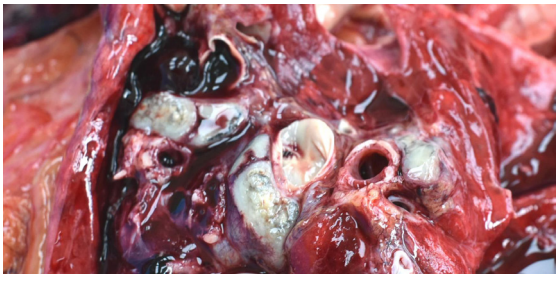


Fig. 1A

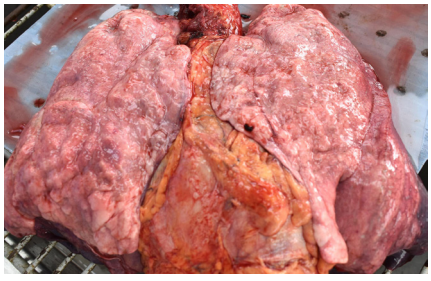


Fig.1B

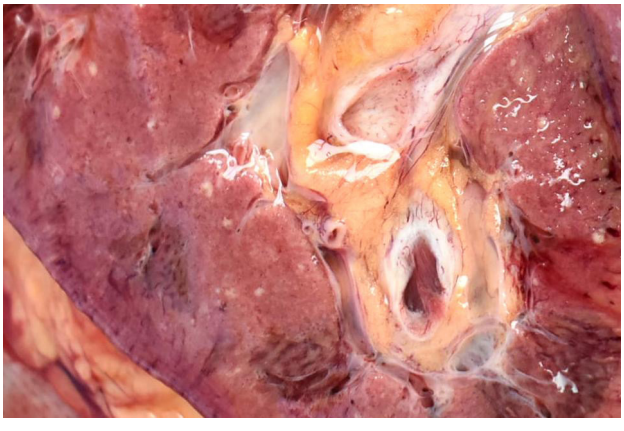
Fig. 1. **A**. Granulomatous lymphadenitis characteristic for sarcoidosis; **B**. Gross appearance of the lungs.

The surface of the lungs was uneven and somewhat cloudy. In some places there were found fibrous whitish changes, due to which in some places there are irregularities on the surface of the lungs **(Fig. 1B).**

Regarding to the extrapulmonary disease, it has been found hepatomegaly of 2040 grams and splenomegaly of 470 grams.

The brain has been swollen with a reddish colorization of the meninges due to the obvious hyperemia.

The macroscopic appearance of the heart has been non-specific. The heart enlargement has been found and pericardial adhesions and thickening of the endocardium. Macroscopically, no specific feature has been found on myocardium.



Specific feature has been found on kidneys. Tiny whitish granuloma-like formations with the diameter of 0,1 to 0,2 cm have been found disseminated throughout the kidney tissue. **(Fig. 2).**

Fig. 2. Tiny whitish granuloma-like formations in the kidney tissue.

The stomach contained around 200 ml of dark brown contents with a coffee ground appearance and around 50 ml of dark red coagulated blood have been found in the duodenal bulbus, but only small amount of blood streaking the intestinal contents has been found in the intestinal lumen. Erosions of the gastral and duodenal mucosa have been obvious.

Microscopical findings

Sarcoidosis has been presented with non-caseating epithelioid granulomas with tightly packed epithelioid cells, Langhans giant cells and lymphocytes, mostly seen in pleura and connective tissue septa (**Fig. 3A, B**).

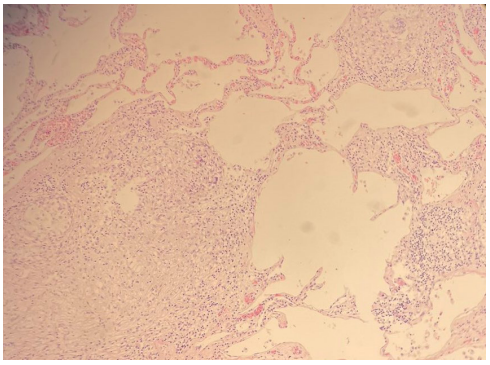


Fig. 3A

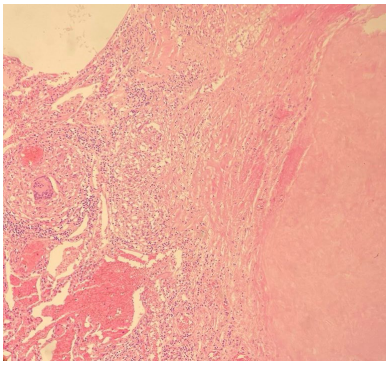


Fig. 3B

Fig. 3. Non-caseating granulomas in lung. Hematoxylin-Eosin Staining. A.×100; B.×400

There have been found large confluent epithelioid granulomas in hilar lymph nodes with broad areas of hyalinization. The granulomas are composed of epithelioid histiocytes with intermingled mature lymphocytes. The histiocytes show oval nuclei and abundant eosinophilic cytoplasm. Occasional giant cells are seen (**Fig. 4 A, B**). The Ziehl-Neelsen stain was found to be negative.

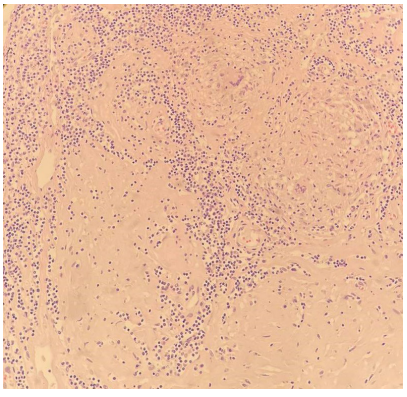


Fig. 4A

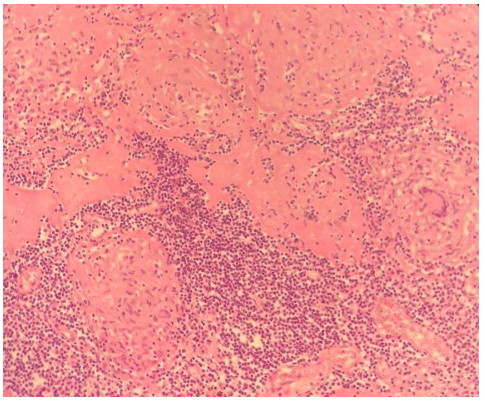


Fig. 4B

Fig. 4. Sarcoid granulomas in mediastinal lymph nodes. Hematoxylin-Eosin Staining. A.×100; B.×400

Multifocal areas of bacterial colonies were found in the myocardium and both kidneys with abscess formation (**Fig. 5 and Fig. 6**).

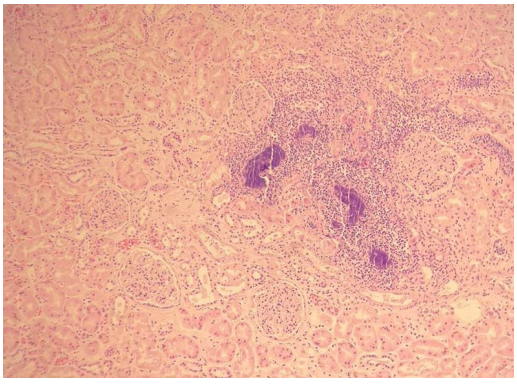


Fig. 5A

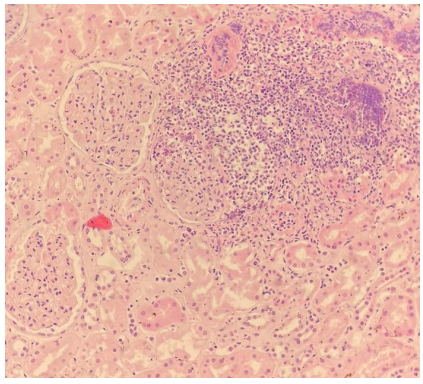


Fig. 5B

Fig. 5. Acute pyelonephritis. Colony of bacteria with abscess formation. Hematoxylin-Eosin Staining. A.×100; B.×400

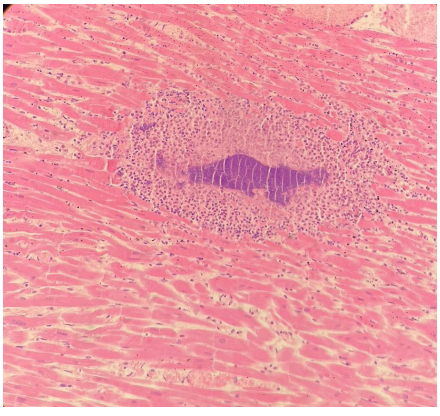


Fig. 6A

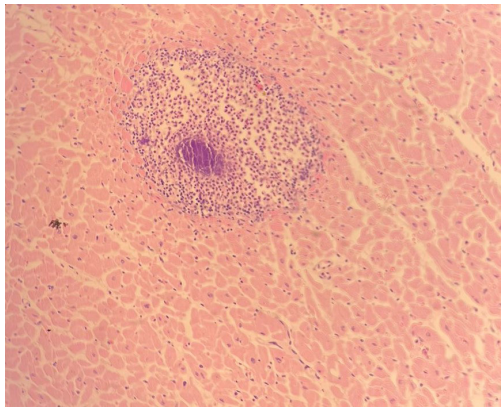


Fig. 6B

Fig. 6. Acute bacterial myocarditis. Colony of bacteria with abscess formation. Hematoxylin-Eosin Staining. A.×100; B.×400

Toxicology results

Ante-mortem toxicology analyses performed in the hospital had been qualitative and had shown the presence of cannabis and cocaine. During hospitalization of several hours, the deceased has been treated with atropine and corticosteroids. Exactly the atropine and corticosteroids have been found on post-mortem toxicology with no traces of psychoactive substances.

Post-mortem biochemistry investigation pointed on the high value of enzymes characteristic for myocardial necrosis: Troponin I>50000,0; Creatine kinase (CK) of 80148,34 and Creatine kinase MB (CK-MB) of 4359,19.

Discussion and concluding the cause of death

The ante-mortem information about sarcoidosis in the analyzed autopsy case, has been unofficial and the diagnosis of sarcoidosis had to be carried out.

As by the literature, clinically and pathologically Sarcoidosis is described as a multisystem inflammatory disease characterized by the formation of noncaseating granulomas in affected organs, most of it in lungs and thoracic lymph nodes which are engaged in more than 90% of all cases [4]. However, virtually every organ can be involved: the eyes (keratitis and uveitis), skin (erythema nodosum) and liver are affected in 15%–30% of cases. Sarcoidosis of the nervous system and heart is less common (2%–10%). Sarcoidosis mimics several diseases, making the diagnosis challenging. Of note, 10%–15% of patients are asymptomatic, and diagnosis is incidental, for example, following a chest radiograph. Lofgren syndrome (acute onset of fever, erythema nodosum, ankle arthritis, and bilateral hilar adenopathy) is characteristic finding for sarcoidosis.

There have been also described certain radiological criteria for the diagnosis of sarcoidosis.: bilateral and symmetrical lymphadenopathy localized in the hila and mediastinum, ground-glass opacities and consolidations, and interlobular septal thickening. Fibrotic progression is marked by loss of lung volume, honeycombing with traction bronchiectasis, bullae, and coarse septal bands [3].

According to the previously noted, the complete clinical and pathological picture of sarcoidosis has been found in our autopsy case (lymphadenopathy, lung changes, keratitis and uveitis etc). But, the exact cause of death had to be carried out.

Regarding to the cause of death in sarcoidosis patients, reference data show that sarcoidosis is associated with an increased risk of premature death, by some references it is twice as high as the general population. Respiratory failure due to extensive pulmonary disease is a common cause of death up to 60% of deaths. Nonfatal cardiac sarcoidosis and ischemic heart disease leading to heart failure is present 20% of deaths in sarcoidosis. Risk of infection is also high in sarcoidosis, especially because of the immunosuppressant treatment in some patients [1]. Opportunistic infections are rarely seen in these patients but can cause serious complications. Sarcoidosis-associated pulmonary hypertension diagnosed in up to 3%–20% of patients with sarcoidosis is also associated with high morbidity and mortality [1].

Speaking about the case, after the exclusion of the toxicology finding, most of the autopsy findings were obviously pointing to a cardiac death i.e. the cyanosis, dark red blood in the body, congestion and also the clinical data obtained ante-mortem.

Where the heart failure is involved in a patient with diagnosed sarcoidosis, the diagnosis of cardiac sarcoidosis has to be considered as a possible cause of death. The diagnosis of cardiac sarcoidosis is clinical and pathological. For the clinical diagnosis three or more of four major criteria are involved: high-grade atrioventricular block or fatal ventricular arrhythmia; basal thinning of the ventricular septum or abnormal ventricular wall anatomy and LV contractile dysfunction. Clinical diagnosis is confirmed when the criterion of positive myocardial uptake of 67 Ga citrate scintigraphy or 18 F-FDG PET. Histological diagnosis is confirmed when endomyocardial biopsy demonstrates non-caseating epithelioid cell granulomas [7].

In the case analyzed here, dysfunctional elements for the clinical diagnosis of cardiac sarcoidosis obviously couldn't have been perceived on autopsy and the

hospitalization time has been too short for detailed investigation. Also, the presence of non-caseating epithelioid cell granulomas in the myocardium tissue has not been confirmed by histology. Instead, clear proof of bacterial myocarditis has been perceived histologically by clusters of bacterial colonies with abscess formation. Very similar finding has been seen in kidneys where abscess formations could have been perceived even macroscopically on a cut surface. Therefore, bacterial myocarditis has been established as a diagnosis.

In conclusion, this interesting case shows that sarcoidosis is very complex disease, even it is generally considered as non-fatal. However, it has been shown previously that sarcoidosis patients are twice as much prone to death comparing them to the general population. The specific cause of death in those cases can be found among lung disease, cardiac sarcoidosis but also the infection, especially when the corticosteroid therapy is involved. In our analyzed case death has been attributed to cardiac failure due to histologically proved bacterial myocarditis.

References

1. **Arkema, E. V., Y .C. Cozier.** Sarcoidosis epidemiology: recent estimates of incidence, prevalence and risk factors. – *Curr. Opin. Pulm. Med*., **26**(5)**,** 2020, 527–534.
2. **Doughan, A.R., B. R. Williams.** Cardiac sarcoidosis. General cardiology. – *Heart,* **92,** 2006, 282–288.
3. **Nikolova, S**. Distinctive manifestations of pulmonary sarcoidosis on high resolution computed tomography. *KNOWLEDGE – International Journal*, **57**(4), 2023, 451-456.
4. **Rossides M., P. Darlington, S. Kullberg, E. V. Arkema.** Sarcoidosis: Epidemiology and clinical insights. – *Journal of Internal Medicine*, **293**, 2023, 668–680.
5. **Smedema, J. P., G. Snoep, M. P. G. Kroonenburgh, R. J. Geuns, W .R. M. Dassen, A. P. Gorgels, H. J. G. M. Crijns.** Cardiac involvement in patients with pulmonary sarcoidosis assessed at two university medical centers in the Netherlands. – *Chest,* **128**(1), 2005, 30-35.
6. **Tana, C.** Sarcoidosis: An old but always challenging disease. – *Diagnostics,* **11**(4), 2021a, 696.
7. **Tana, C., C. Mantini, I. Donatiello, L. Mucci, M. Tana, F. Ricci, F. Cipollone, M. A. Giamberardino.** Clinical features and diagnosis of cardiac sarcoidosis. – *J. Clin. Med.,* **10**(9), 2021b, 1941.
8. **Tana, C., M. Drentb, H. Nunese, V. Kouranosf, F. Cinettog, N. T. Jessurund, P. Spagnoloi.** Comorbidities of sarcoidosis. – *Annals of Medicine,* **54**(1), 2022, 1014–1035.