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Systemic Sarcoidosis Resulting In Sudden Death: An Autopsy Case Report

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ABSTRACT

Introduction

Systemic sarcoidosis is a multisystem granulomatous disease that can remain clinically silent, with cardiac involvement often under-recognized despite its potential to cause sudden death. **Case report:** We report a case of sudden, unexpected death of a 31-year-old healthy gentleman who collapsed at home and pronounced dead shortly afterward. **Results:** Autopsy showed a slightly overweight adult male subject with no external deformity or injury. The heart revealed cardiomegaly with extensive firm, whitish lesion affecting the interventricular septum, with patchy similar lesions in the free wall of the right ventricle. Multiple nodular whitish lesions of various size were present in the liver and spleen. Microscopically, all the lesions have similar findings; showing non-caseating granulomas composed of lymphocyte infiltrates, epithelioid histiocytes and multinucleated giant cells. Asteroid body was also present in a few giant cells. The cause of death was certified as systemic sarcoidosis. The mechanism of death was attributed to cardiac dysfunction, as granulomatous inflammation of the myocardium can disrupt normal conduction pathways or impair contractility, potentially leading to fatal arrhythmias. **Conclusions:** This case emphasizes the diagnostic value of autopsy in systemic sarcoidosis. It also highlights the

importance of considering sarcoidosis in unexplained deaths and demonstrates the key role of histopathology in securing the diagnosis.

Keywords: Sarcoidosis; Cardiac Sarcoidosis; Sudden Death; Granulomatous disease; Autopsy

Introduction

In Malaysia, cardiovascular disease remains the leading cause of sudden death, accounting for approximately 75% of all cases.[1] Sarcoidosis-related deaths are exceedingly rare, likely due to under-recognition or the absence of comprehensive studies. In contrast, U.S. data indicate increased mortality among sarcoidosis patients at younger ages, particularly between 20 and 40 years. The disease is twice as common in females and consistently more prevalent in Black patients compared to Caucasians.[2,3]

Sarcoidosis is defined as multisystem granulomatous disorder of unknown aetiology.[2] Clinically, sarcoidosis presents with a broad spectrum of manifestations, ranging from asymptomatic forms to severe multisystem involvement. Fatal outcomes are most often associated with pulmonary, cardiac, or neurological complications. Cardiac sarcoidosis is among the most severe extrapulmonary manifestations and has been implicated in 25–50% of sarcoidosis-related deaths, primarily through fatal arrhythmias, conduction abnormalities, or sudden cardiac arrest.[4,5] Neurosarcoidosis, although less common, can also lead to devastating outcomes such as hydrocephalus, seizures, and brainstem dysfunction.[6] Sarcoidosis remains clinically silent in up to 45% of cases, making early detection particularly challenging. Despite its often subtle presentation, it is implicated in up to 80% of sarcoidosis-related fatalities.[2,7] In some instances, the diagnosis is only made post-mortem, reflecting the insidious nature of the disease.

We report a case of sudden, unexpected death in a young, apparently healthy adult male, in whom systemic sarcoidosis involving the heart, lungs, liver and spleen was identified during post-mortem examination.

Case Presentation

A 31-year-old man with no known medical history was found unresponsive on the bathroom floor of his house. He had last been seen by his wife about an hour earlier when he informed that he was going to take a bath. When he did not emerge, his wife became concerned and notified his father, who forcibly entered the bathroom and discovered the man lying in a prone position, unconscious and unresponsive. He was rushed to the Emergency Department of a nearby hospital where cardiopulmonary resuscitation was initiated. Despite resuscitative efforts, he was pronounced dead shortly thereafter. The body was transferred to the Forensic Department for a medico-legal autopsy. In the days leading up to the incident, the patient had experienced a productive cough for three days but did not seek medical attention. He did not report any associated symptoms such as fever, chest pain, palpitations, abdominal pain, diarrhoea, or vomiting.

Autopsy findings

Autopsy showed a lean adult male, measuring 178 cm in length and 85 kg in weight, with a body mass index of 26.8 kg/m^2. There was no injury of congenital deformity seen. Bilateral conjunctivae were markedly congested. Postmortem changes such as lividity and rigor mortis were present. Bluish discolouration of the fingernail beds was prominent, indicating cyanosis. Internal

examination showed an intact skull, with the brain weighed 1620 gm. Cut surfaces of the cerebrum, cerebellum and brainstem showed congested blood vessels with no apparent pathology. Examination of the thoracic region showed intact musculoskeletal structures with multiple enlarged cervical and paratracheal lymph nodes. The heart weighed 455 gm, denoting cardiomegaly. There was no congenital abnormality seen. All the coronary arteries were patent. The right and left ventricular walls measured 3 mm and 12 mm in thickness, respectively, while the interventricular septum was markedly thickened at 18 mm. Cut sections revealed diffuse, firm, whitish lesions predominantly involving the interventricular septum, as well as the posterior wall of the left ventricle and the right ventricle (Fig. 1A). The right and left lungs were slightly heavier than normal, weighing 560 gm and 490 gm respectively. Inter-fissure adhesions were present on the right lung. Cut sections of the lungs showed marked vascular congestion and pulmonary oedema. There was no whitish lesion, cavitation, abscess or cheesy-like material present (Fig. 1B). Examination of the abdominopelvic organs revealed the presence of patchy, well-defined, firm whitish lesions of various sizes at the liver surface and the hepatic parenchyma (Fig. 1C and D). Similar lesions were also seen in the spleen (Fig. 1E). The liver and spleen weighed 1880 gm and 510 gm respectively, denoting hepatosplenomegaly.

Several postmortem specimens were obtained for laboratory investigations. Blood and tissue cultures revealed the presence of *Klebsiella pneumoniae* in both aerobic and anaerobic blood cultures as well as liver tissue, suggesting possible systemic involvement. Other organisms isolated —*Enterococcus faecium*, *Pantoea agglomerans*, *Streptococcus parasanguinis*, and mixed flora from the spleen—are likely contaminants or of no clinical significance. Lung swab cultures yielded no pathogenic growth. Forensic toxicology analysis showed no ethyl alcohol or common drugs detected.

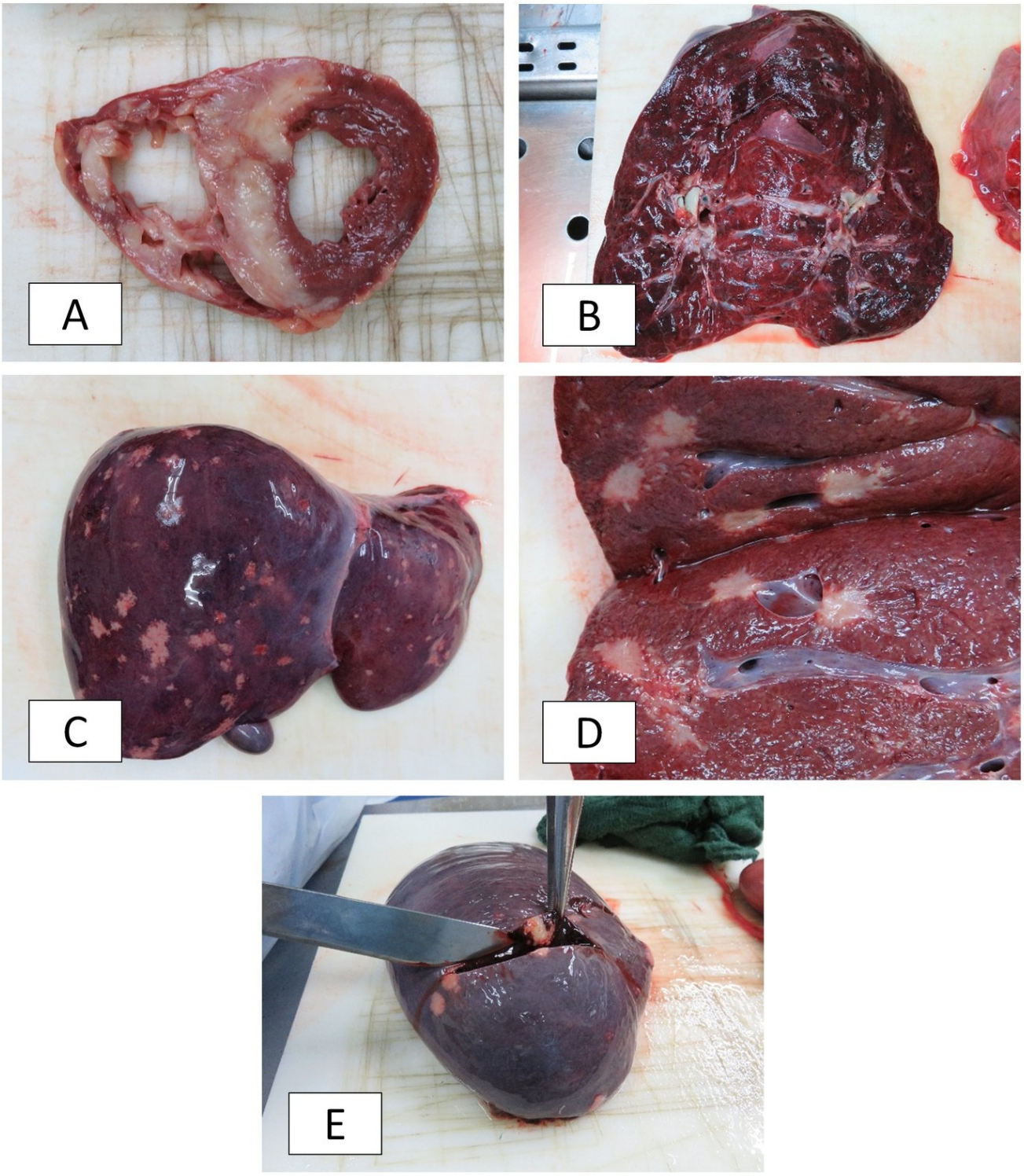


Fig. 1 A Cut section of the myocardium reveals a diffuse, firm, whitish lesion involving the interventricular septum, along with patchy similar lesions in the free wall of the right ventricle. B Bisection of the right lung shows fairly normal parenchyma apart from vascular congestion and oedema. C & D The liver surface exhibits scattered, irregular, whitish lesions of varying sizes. On cut section, the liver parenchyma reveals patchy, well-circumscribed, firm, whitish lesions distributed throughout. No areas of necrosis or haemorrhage are observed. E Multiple whitish lesions are also present on the surface of the spleen. On incision, these lesions are confirmed to originate within the parenchyma and extend to the surface.

Microscopic findings

Representative tissue specimens from the brain, heart, lungs, liver, kidneys, spleen and lymph nodes were obtained for histological evaluation. Sections were processed and stained with routine hematoxylin and eosin (H&E). Histopathological examination of the heart, lungs, lymph nodes, liver and spleen revealed consistent findings of non-caseating granulomatous inflammation, characterized by well-formed aggregates of epithelioid histiocytes and multinucleated giant cells, including both Langhans-type and foreign body-type forms (Fig. 2A-D). The granulomas were typically ‘naked’, with minimal surrounding lymphocytic infiltration. Occasional intracytoplasmic inclusions such as asteroid bodies were noted within giant cells (Fig. 2E). Ziehl-Neelsen staining for acid-fast bacilli and special stain for fungal organisms such as Grocott’s Methenamine Silver (GMS) was negative, effectively excluding tuberculosis or infectious causes. No significant histopathological changes were observed in the brain or kidney samples. Although pathogenic microorganisms were identified in blood and liver tissue cultures, histological examination revealed no evidence of active bacterial inflammation in any organ.

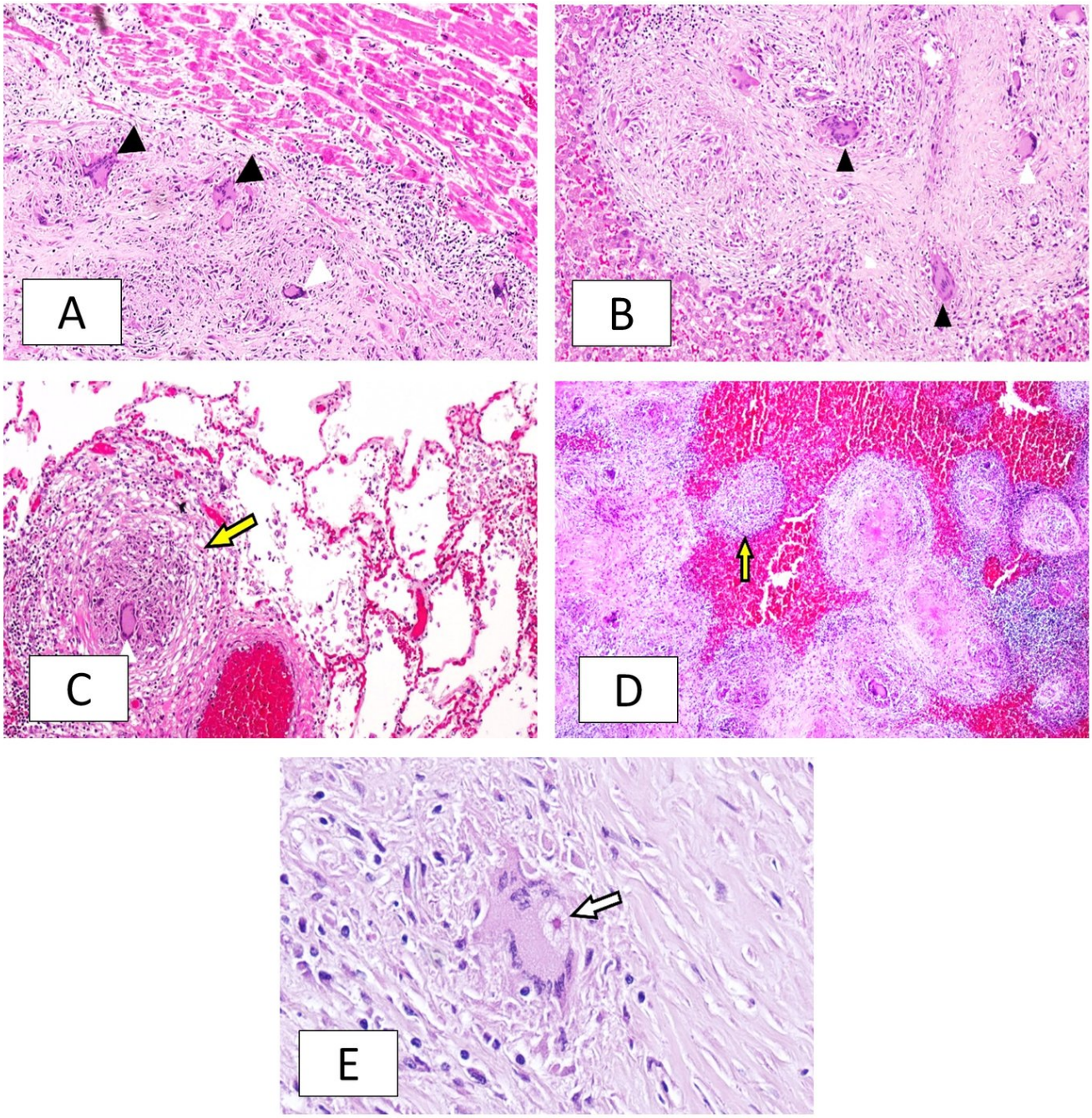


Figure 2A Cardiac tissue shows extensive non-caseating granulomas disrupting cardiac parenchyma, with scattered Langhans and foreign body-type giant cells (white and black arrowheads). B Liver lesion exhibits similar non-caseating granulomas with Langhans and foreign body-type giant cells (white and black arrowheads). C Lung parenchyma shows multiple non-caseating granulomas (red arrow) with Langhans-type giant cells (white arrowhead), despite no visible lesions macroscopically. D Spleen displays multiple extensive non-caseating granulomas (red arrow). E Asteroid body within a multinucleated giant cell (white arrow).

The cause of death was certified as systemic sarcoidosis, supported by the presence of multiple whitish macroscopic lesions in the heart, liver, and spleen, along with characteristic microscopic findings of non-caseating granulomas containing multinucleated giant cells. Extensive cardiac lesions indicated significant myocardial involvement. The mechanism of death was attributed to

cardiac dysfunction, as granulomatous inflammation of the myocardium can disrupt normal conduction pathways or impair contractility, potentially leading to fatal arrhythmias.

Discussion

Sarcoidosis is a systemic granulomatous disease of unknown aetiology, most commonly affecting the lungs in up to 92% of cases. Other frequently involved sites include the skin and lymph nodes, while the liver, spleen, eyes, and heart are less commonly affected. Cardiac involvement, though clinically apparent in only 2 to 5% of patients, may be present in up to 45% based on imaging or autopsy studies.[2,8] The disease is characterized histologically by non-caseating, non-necrotizing granulomas across multiple organ systems. Systemic involvement is common, with up to 68% of sarcoidosis-related natural deaths showing evidence of multiorgan disease.[2] The exact cause of sarcoidosis remains unknown, but experts believe it may result from the immune system reacting to an unidentified substance. Research indicates that infectious agents, chemicals, dust, or an abnormal immune response to the body's own proteins (self-proteins) could trigger granuloma formation in individuals with a genetic predisposition.[9] This case involved a young adult male with no known medical history who collapsed suddenly at home and was pronounced dead shortly after, consistent with the epidemiological profile of sarcoidosis.

Autopsy remains a valuable tool for identifying the extent of systemic sarcoidosis, particularly in clinically silent or undiagnosed cases. While only about 5% of sarcoidosis patients show clinical signs of cardiac involvement, postmortem studies reveal myocardial involvement in at least 25% of cases.[10] At autopsy, sarcoidosis typically presents as multiple firm, whitish lesions on the surface and within the parenchyma of affected organs. Gross sectioning often reveals the extent of tissue involvement. Clinical presentation varies by organ system and can mimic infectious, inflammatory, or neoplastic conditions.[11] In the heart, granulomatous inflammation frequently affects the epimyocardium and interventricular septum[2] leading to manifestations such as heart failure, arrhythmias, or conduction abnormalities like bundle branch block.[2,9,12] However, many patients remain asymptomatic or present with nonspecific symptoms, making diagnosis difficult. In some cases, sarcoidosis is only detected at autopsy following sudden or unexplained death.[9] In the present case, cardiac involvement was the predominant finding, with extensive granulomatous infiltration affecting the entire interventricular septum and right ventricular wall, highlighting the central role of cardiac pathology in systemic sarcoidosis. Involvement of the liver and spleen was also observed, which contrasts with previous studies that report these organs as being less commonly affected. Notably, although pulmonary involvement is reported in up to 95% of sarcoidosis cases, no grossly visible lesions were identified in the lungs. Instead, non-caseating granulomatous inflammation was confirmed only on microscopic examination, emphasizing the potential for clinically and macroscopically silent disease.

Sarcoidosis is histologically characterized by the formation of non-caseating granulomas, which represent well-defined and compact accumulations of immune cells.[7,13] These granulomas are primarily composed of epithelioid histiocytes, exhibiting abundant cytoplasm, and are distinguished by the absence of significant necrosis, a key feature differentiating sarcoidosis from other granulomatous conditions. Within these granulomas, multinucleated giant cells, including both Langhans and foreign-body types based on nuclear arrangement, are frequently observed. A surrounding infiltrate of lymphocytes, predominantly CD4+ T-cells, is typically present, although its density can vary depending on the stage of the disease and prior treatment. Furthermore, the

inflammatory infiltrate generally lacks substantial eosinophils or neutrophils, aiding in the differentiation from other inflammatory processes.

Beyond the granulomas themselves, several associated histological features are commonly encountered in sarcoidosis. Fibrosis, or scarring, is a frequent finding, particularly in chronic cases, where it can lead to the replacement of normal tissue architecture and subsequent organ dysfunction. Additionally, characteristic but non-specific inclusions, such as Schaumann and asteroid bodies, may be identified within the giant cells. While the fundamental histological features remain consistent across organ systems, variations in the distribution and specific characteristics of these granulomas can occur, such as the predilection for the epimyocardium and septum in cardiac sarcoidosis or the compact nature of granulomas in neurosarcoidosis. Ultimately, the definitive diagnosis of sarcoidosis necessitates the identification of these non-caseating granulomas in affected tissues,[11,12,14] coupled with the exclusion of alternative causes of granulomatous inflammation through appropriate investigative modalities and careful clinicopathological correlation.

In this case, typical findings of sarcoidosis were confirmed histologically. Based on the characteristic gross and microscopic findings—non-caseating granulomatous inflammation with multinucleated giant cells—and exclusion of infectious causes, the cause of death was determined to be systemic sarcoidosis.

Conclusions

This case highlights the value of autopsy in diagnosing systemic sarcoidosis, revealing extensive non-caseating granulomas in the heart, lung, liver, spleen and lymph nodes. Cardiac granulomatous inflammation likely led to fatal arrhythmias. These findings illustrate the importance of considering sarcoidosis in unexplained deaths and emphasize the role of histopathology in confirming the diagnosis.

Declarations

Ethics approval and consent to participate

We seek for waiver of ethical review and approval since the data were not directly indicative of the individual subject, observatory in nature and the research involved no risk to the deceased subject.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors contributed substantially to the autopsy examination and manuscript write-up. Razuin Rahimi led the drafting of the manuscript. Mohamad Rusydi Mazlan and Nur Fatimah Ahmad

Zairin contributed to the case presentation and the write-up of the autopsy findings. Nur Arina Ahmad was responsible for the histopathology section and the preparation of accompanying photographs. All authors reviewed the manuscript critically for important intellectual content and approved the final version.

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What's New in This paper

What is already known on this topic?

Sarcoidosis is a multisystem granulomatous disorder of unknown aetiology that most commonly affects the lungs and lymphatic system but may involve virtually any organ. Cardiac involvement, although clinically under-recognised, is a significant cause of morbidity and sudden death. Most published data focus on clinical presentation, imaging findings, and biopsy-based diagnosis, while comprehensive autopsy-based descriptions of extensive multiorgan and cardiac involvement remain relatively limited.

What question did this study address?

This study addressed whether systemic sarcoidosis with extensive cardiac and multiorgan involvement could be definitively characterised through complete autopsy and histopathological examination, and how direct pathological assessment clarifies the extent of organ involvement—particularly myocardial infiltration—as a mechanism of sudden or unexpected death.

What does this study add to our knowledge?

This report provides a detailed autopsy-confirmed case of systemic sarcoidosis demonstrating widespread non-caseating granulomatous inflammation involving the heart and multiple extracardiac organs. It underscores the critical role of post-mortem examination in identifying clinically occult cardiac sarcoidosis, illustrates the pathological basis for fatal arrhythmia or conduction disturbance, and highlights the diagnostic challenges when systemic sarcoidosis presents without prior clinical suspicion.

Suggestions for further development

Further studies incorporating larger autopsy series or multicentre registries are needed to better define the true prevalence and pathological spectrum of cardiac involvement in systemic sarcoidosis. Integration of histopathology with molecular studies, advanced imaging correlation, and genetic or immunological profiling may improve early detection, risk stratification, and understanding of mechanisms underlying sudden cardiac death in sarcoidosis.