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Case Report

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# Simultaneous Occurence of Pheochromocytoma and Sarcoidosis

***(Running title: Coexistence of pheochromocytoma and sarcoidosis)***

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**Abstract**

Sarcoidosis is a systemic granulomatous disease that can affect multiple organs, while pheochromocytoma is a rare tumor of the adrenal gland that secretes catecholamines. The coexistence of these two conditions is exceedingly rare and poses unique diagnostic challenges. We present a case of a patient simultaneously diagnosed with both sarcoidosis and pheochromocytoma, emphasizing the need for a high index of suspicion along with the importance of multidisciplinary care. A 28 year old male was admitted for tachycardia, headache, and facial flushing. Chest x-ray revealed bilateral hilar lymph adenopathy and infiltrations in both middle lung zones. Abdominal ultrasound and CT showed a 3 cm nodule in the left adrenal gland. Pathologic examination of the involved organs was compatible with sarcoidosis and pheochromocytoma. This case report aims to consolidate current knowledge on the relationship between pheochromocytoma and sarcoidosis. Understanding this association is critical for timely diagnosis and effective management.

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## Introduction

Sarcoidosis and pheochromocytoma are two distinct clinical entities with vastly different pathophysiologies and clinical manifestations. Sarcoidosis is characterized by the formation of non-caseating granulomas in affected organs, while pheochromocytoma is a catecholamine-secreting tumor arising from chromaffin cells in the adrenal medulla. Although both diseases are rare, their coexistence in a single patient can pose diagnostic and therapeutic challenges due to overlapping symptoms and potential interactions between treatment strategies. Synchronous coexistence of both conditions in a single patient is extremely rare, with only a few reported cases available in the literature (1-5).

This case report aims to enlighten the simultaneous occurence of sarcoidosis and pheochromocytoma by focusing on the clinical features and the diagnostic approach along with the treatment strategy to elucidate the connection between these two disorders and the clinical considerations that arise in their management. As the presentation and symptoms of both display notable similarities their coexistence appears as a diagnostic challenge in clinical practice.

## Case Presentation

A 54-year-old female with a history of hypertension and asthma presented to the outpatient clinic with complaints of worsening dyspnea, fatigue, facial flushing, and intermittent palpitations. Initial evaluation revealed elevated blood pressure readings, and further inquiry into her symptoms suggested episodes of sweating and tachycardia. Physical examination was notable for bilateral anterior cervical lymphadenopathy and crackles on lung auscultation. Serum biochemistry was within normal limits except for an elevated ACE level 92 IU/ml. A chest X-ray demonstrated bilateral hilar lymphadenopathy and ground glass opacities in the middle zones of both lungs raising suspicion for sarcoidosis (Figure 1).

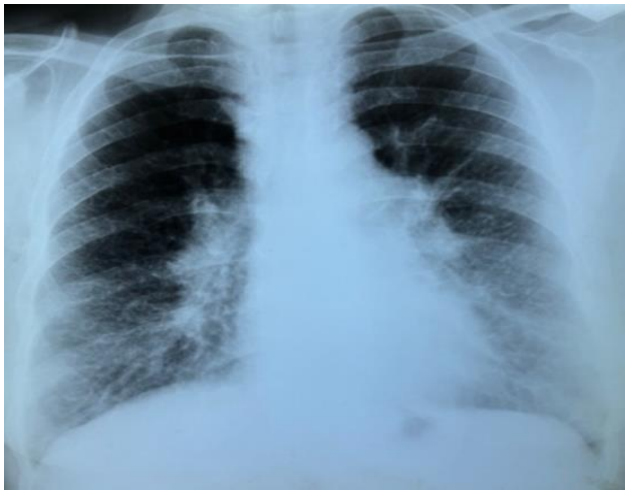

**Figure 1:** Chest x-ray showing stage II sarcoidosis with bilateral hilar lymphadenopathy and ground glass opacities in both middle lung parenchyma.

Given her symptoms of palpitations and elevated blood pressure, further investigation for pheochromocytoma was warranted. A 24-hour urine collection revealed significantly elevated levels of metanephrines. A subsequent abdominal ultrasound and CT scan showed a 3 cm left adrenal mass, consistent with pheochromocytoma (Figure 2).

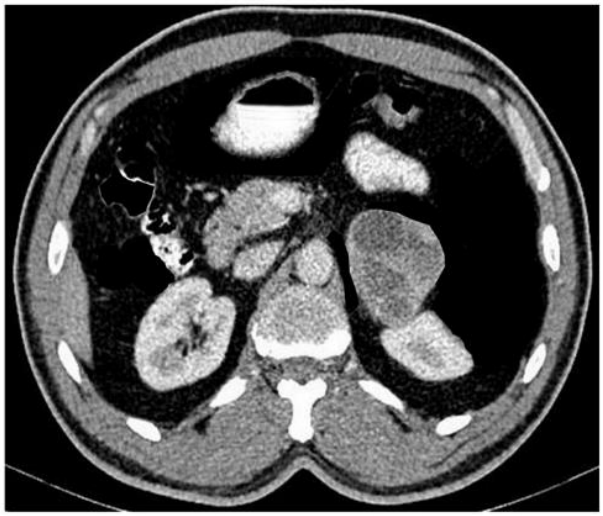

**Figure 2:** Abdominal CT revealing a 3 cm left adrenal tumor.

Histopathologic examination of the cervical lymph node and the TBB biopsy samples revealed non-caseating granulomas consistent with sarcoidosis. Serum ACE was 86 IU/L while BAL cytology revealed lymphocytosis. Pathologic evaluation of the adrenal gland biopsy performed under CT revealed pheochromocytoma. Following a multidisciplinary consultation including endocrinology, pulmonology, and surgery it was decided to proceed with laparoscopic adrenalectomy. The patient was commenced on a non-selective beta-blocker to manage hypertensive episodes and to stabilize cardiovascular status prior to surgical intervention. After successful removal of the left adrenal tumor, it was confirmed as a benign pheochromocytoma by histopathologic assessment. Following surgical resection, blood pressure normalized along with significant resolution of adrenergic symptoms. The patient was started on oral 32 methylprednisolone for sarcoidosis that had led to persistent dyspnea in exertion and dry cough.

## Discussion

Sarcoidosis is a multisystem granulomatous disorder of unclear etiology, primarily affecting the lungs, lymph nodes, skin, and eyes (6-13), while pheochromocytoma is a neuroendocrine tumor of the adrenal medulla that secretes catecholamines, leading to life-threatening hypertensive crises (14-16). Sarcoidosis has a global prevalence of approximately 10-20 per 100,000 people (17-20) while pheochromocytoma, on the other hand, is much rarer, with an estimated annual incidence of 0.8 per 100,000 individuals (21,22). Coexistence of sarcoidosis and pheochromocytoma is exceptional with few documented cases in the literatüre (1-5). Although occurrence of sarcoidosis and pheochromocytoma is rare but significant due to their distinct pathophysiological mechanisms and the potential clinical challenges posed by their overlapping presentations. The mechanisms underlying this association remain unclear, although both conditions can have overlapping pathophysiological pathways involving immune dysregulation and inflammation. Coexistence of these conditions may complicate diagnosis, management, and treatment outcomes. This case report has enlightened the current understanding of sarcoidosis and pheochromocytoma disclosing the possible pathophysiological links between the two disorders of which the simultaneous occurrence is a great diagnostic and treatment challenge for clinicians.

Coexistence of sarcoidosis and pheochromocytoma is rare and represents a complex clinical scenario. While no definitive pathophysiological link has been established between the two conditions, there are several potential underlying mechanisms that may explain their coexistence such as immune system dysregulation with aberrant immune responses could lead to both the granulomatous inflammation seen in sarcoidosis and the development of pheochromocytoma. Chronic inflammation of sarcoidosis may lead to changes in the regulation of neuroendocrine cells or adrenal tissue, increasing the susceptibility to developing adrenal tumors such as pheochromocytoma. Sarcoidosis may affect the neuroendocrine system, and the adrenal glands can occasionally be involved (1,2). This could increase the risk of pheochromocytoma in patients with sarcoidosis due to granulomatous inflammation in the adrenal glands, potentially leading to abnormal cell proliferation and neoplastic transformation along with alteration of local hormonal environments by granulomatous inflammation that may influence adrenal gland function that may predispose individuals to tumor formation.

Some genetic syndromes that predispose patients to pheochromocytoma such as MEN 2, neurofibromatosis type 1, or von Hippel-Lindau syndrome can also lead to overlapping features with conditions like sarcoidosis or sarcoid-like reactions, Mutations in certain oncogenes or tumor suppressor genes (e.g., VHL, RET) theoretically could affect immune regulation, predisposing individuals to both tumors and granulomatous disease. The shared genetic susceptibility might be more relevant in syndromic cases where both pheochromocytoma and sarcoidosis-like granulomas occur. Sarcoidosis has been associated with endocrine dysfunction, including adrenal insufficiency and hypothalamic-pituitary axis involvement (4,5). Though not directly linked, sarcoidosis-induced hormonal imbalances could hypothetically contribute to the development of adrenal tumors like pheochromocytoma (14,16).

Sarcoidosis is thought to result from an exaggerated immune response to an unknown antigen, leading to the formation of non-caseating granulomas. The immune dysregulation in sarcoidosis primarily involves T-helper cells (Th1 and Th17), macrophages, and pro-inflammatory cytokines, such as TNF-alpha and interferon-gamma while pheochromocytomas arise from chromaffin cells of the adrenal medulla or extra-adrenal paraganglia, which produce and secrete catecholamines (23). The exact mechanisms underlying the simultaneous occurrence of sarcoidosis and pheochromocytoma are not well understood. Although a direct connection between the two conditions has not been identified, several mechanisms may contribute to their coexistence. Chronic inflammation and immune dysregulation seen in sarcoidosis may create a tumorigenic environment leading to the development pheochromocytoma.

## Conclusions

This case illustrates the rare but simultaneous coexistence of sarcoidosis and pheochromocytoma that emphasizes the significance of a comprehensive assessment in patients presenting with constitutional manifestations. Clinicians should maintain a high level of suspicion for pheochromocytoma in patients with atypical presentations of hypertension and systemic symptoms, particularly when other diagnoses, such as sarcoidosis, are established. As the underlying mechanisms of both disorders may overlap and one may closely relate to or influence the emergence or development of the other, their coexistence may emerge as a diagnostic challenge for clinicians. Early identification with a multidisciplinary management is crucial for optimal outcomes in these patients.

### Author contributions

Cuneyt Tetikkurt contemplated and wrote the case report.
Muammer Bilir prepared the laboratory findings of the patient.
Halil Yanardag analyzed the imaging findings.

### Conflicts of interest

All authors declare that they do not have any conflicts of interest associated with this study. Authors confirm that there does not exist any supporting or funding agencies for this research

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