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(CASE REPORT)

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Neurosarcoidosis presenting as transient ischemic attacks: A Case Report

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Abstract

Sarcoidosis is a multi-organ granulomatous disease of unknown etiology characterized by the presence of non-caseating granulomas. It has the potential to affect multiple organs including the nervous system. Neurosarcoidosis is present in around 5% of sarcoidosis patients. The clinical manifestations of neurosarcoidosis are heterogeneous, as granulomas can affect the brain, spinal cord and peripheral nervous system, separately or in different combinations. We report a case of neurosarcoidosis with pulmonary involvement in a young female patient presented with multiple episodes of transient ischemic attacks (TIAs). She was treated with boluses of cyclophosphamide followed by azathioprine which led to marked clinical and radiological improvement.

Keywords: Neurosarcoidosis; Transient ischemic attacks; Pulmonary sarcoidosis; Cyclophosphamide; Azathioprine

1. Introduction

Sarcoidosis is a systemic disease identified pathologically by the presence of non-caseating epithelioid granulomas. It primarily affects patients in their middle years , with a slight female predominance. The lungs and intrathoracic lymph nodes are typically the organs most affected [1]. The diagnosis of sarcoidosis relies on three main criteria: a compatible clinical presentation, evidence of non-necrotizing granulomatous inflammation, and the exclusion of other potential causes [2].

Neurosarcoidosis, characterized by nervous system involvement, is present in approximately 5 % of cases .

The presentation of neurosarcoidosis varies widely and depends on the location and extent of the CNS involvement. Common clinical features headache, facial weakness, vision and hearing loss, seizures, and cognitive impairment [3]. The onset of symptoms is usually gradual, although in some cases, neurosarcoidosis may manifest as an acute neurological emergency, with seizures or stroke-like symptoms [4].

2. Case Presentation

We present the case of a 52-year-old female, teacher, never treated for tuberculosis, with a medical history including gastric ulcer due to H. pylori infection 2 years ago, and vitiligo diagnosed in 2008.

She was admitted for the investigation of episodes of transient ischemic attacks. The episodes (at least 4) consisted of hemiparesis and weakness, sometimes also with dysarthria. The patient had come from another hospital, where brain computed tomography (CT) scan had been normal and acetylsalicylic acid 160 mg/day had been prescribed.

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She had also been suffering for a year from chronic dyspnea and a dry cough with polyarthralgia of inflammatory appearance in the context of feverish sensations and involuntary weight loss .His recent past history included a syndrome of intracranial hypertension: headaches, vision changes and vomiting**.**

Clinical examination of the pleura and lungs revealed bilateral basithoracic crackles. Chest X-ray showed a bilateral mediastinopulmonary opacities associated with diffuse micronodular infiltration (Figure 1)). The thoracic computed tomography (CT) scan showed dense pulmonary micronodules with well-defined borders, distributed in a peri-lymphatic pattern, creating the galaxy sign. Pulmonary micronodules arranged along the right major fissure, creating the appearance of a string of beads. Dense pulmonary nodules with well-defined and regular borders visible in the right upper lobe. Diffuse thickening of septal and non-septal lines and peri-bronchovascular regions (Figure 2). Brain MRI showed SEP-like lesions associated with microischemia and hemorrhage with leptomeningeal involvement in favor of cerebral granulomatous disease. (Figure 3)

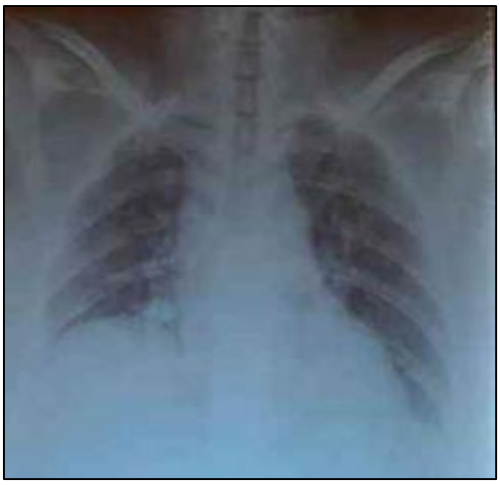

Figure 1 Chest X-ray showing bilateral mediastino-pulmonary opacities associated with a diffuse micronodular infiltration associated with a diffuse micronodular infiltration

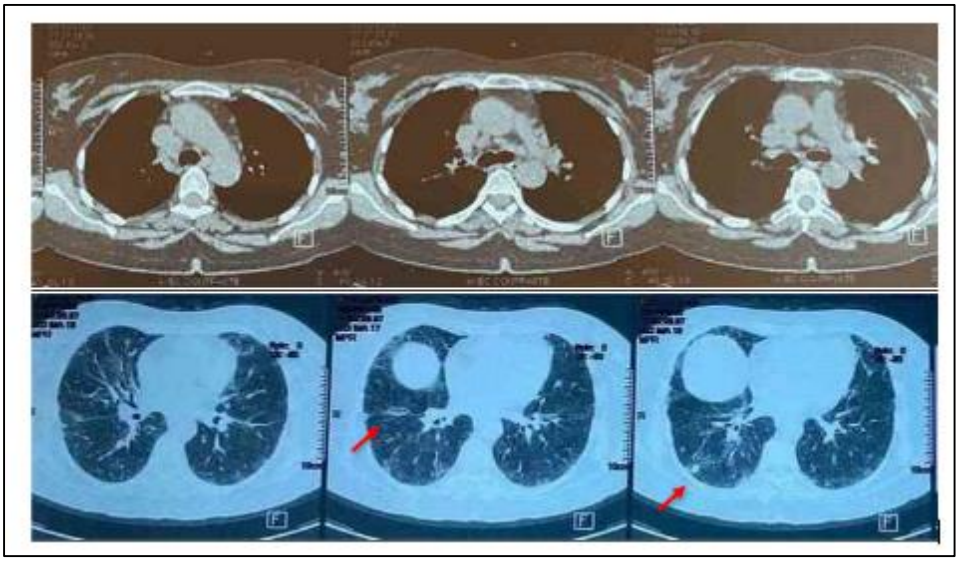

Figure 2 Chest CT axial section (medial and parenchymal window) showing diffuse interstitial involvement associated with mediastinal adenopathies that may be consistent with sarcoidosis type II : Pulmonary micronodules with well-defined borders, distributed in a peri-lymphatic pattern, creating the galaxy sign. Pulmonary micronodules arranged along the right major fissure, creating the appearance of a string of beads. Mediastinal adenopathies in the pre-vascular, subcarinal, Barety, and precarinal regions

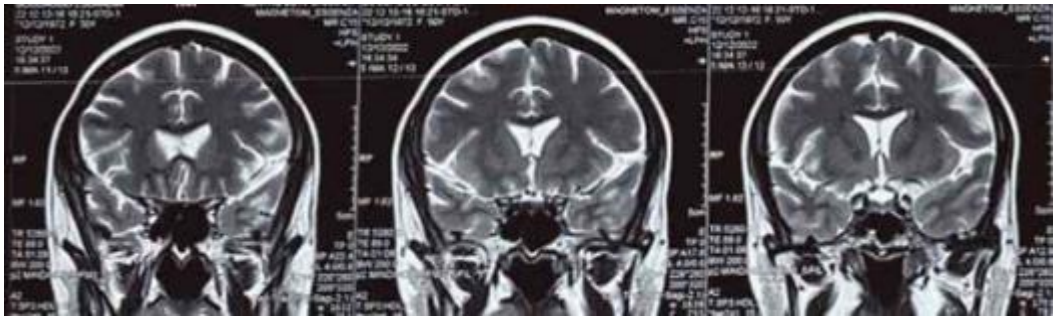

Figure 3 Brain MRI showed SEP-like lesions associated with microischemia and hemorrhage with leptomeningeal involvement in favor of cerebral granulomatous disease

The flexible bronchoscopy performed found diffuse 1st degree inflammation with anthracosic spots, staged bronchial biopsies showed bronchial mucosa reworked by a non-specific chronic inflammatory lesion (Figure 3). The search for an acid-alcoholresistant bacillus in the bronchial aspirates was negative, and the bronchoalveolar lavage (BAL) showed a macrophagic (80%) predominance.

The angiotensin-converting enzyme assay showed a serum activity of 59 IU/L. The phosphocalcic, urinary and serological tests were normal. An immunological workup was negative. The biopsy of the salivary glands showed a discrete and non-specific interstitial sialadenitis of degree 1 of Chisholm and Mason. During the diagnostic process, Plethysmography was performed found a moderate restrictive ventilatory disorder with a forced vital capacity (FVC) of 71%, total lung capacity of 67%, and diffusing capacity of the lungs for carbon monoxide of 52%. Cardiac ultrasound was normal, with arterial blood gas revealing compensated metabolic acidosis secondary to vomiting.

Six-Minute Walk Test Findings : the patient covered a distance of 585 meters, which is 91% of the theoretical distance. Diagnosis is based on the patient's medical history, physical examination, and radiological lesions. A diagnosis of neurosarcoidosis with pulmonary involvement was made. Corticosteroid therapy was started but during the tapering process, the patient experienced symptom exacerbation along with side effects. Cyclophosphamide was instituted 1g/month for 6 months, The patient received 6 boluses of cyclophosphamide, followed by a switch to azathioprine 50mg/day, the maximum dose tolerated by the patient.

Over the ensuing many months, the patient showed improvement in her symptoms the patient’s transient neurologic episodes had fully disappeared) ,regression of radiological lesions (Figure 4,5) and improved values of FVC from 71% to 97% with an increase in DLCO (diffusing capacity of the lungs for carbon monoxide) to 65% of the predicted value (Table 1), PET-CT Examination revealed:Moderately hypermetabolic right lateral cervical and bilateral mediastinal-hilar lymph nodes, associated with a bilateral nodular pulmonary infiltrate, also moderately hypermetabolic, likely related to known active sarcoidosis..Heterogeneous uptake in the left ventricle, warranting further dedicated investigation in this context..No suspicious hypermetabolism in the rest of the explored volume, notably in the subdiaphragmatic lymph nodes, bones, and the rest of the explored volume.

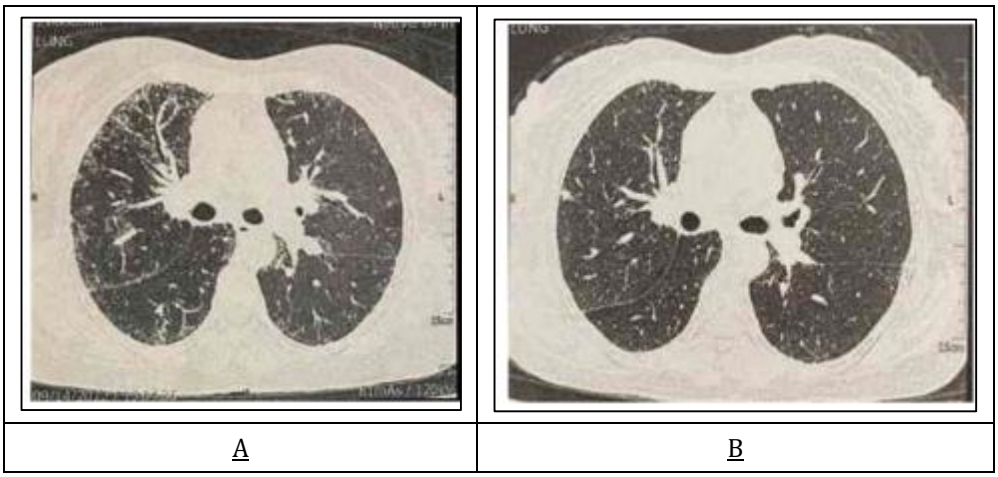

Figure 4: Scannographic follow up assessment showed a quasi-stable scannographic appearance of the disease The thoracic computed tomography (CT) Before treatment (A) and 1 year after (B)

Figure 5 Brain MRI 1 year after treatment showed a stable appearance of supratentorial and infratentorial signal abnormalities

Table 1 Plethysmography follow-up assessment

	Before treatment	**6 months**	**1 year**
DLCO %	52%	58 %	64 %
FVC	71%	84 %	97 %
DLCO: Carbon Monoxide Diffusing Capacity FVC: Forced Vital Capacity			

3. Discussion

Sarcoidosis is a systemic illness characterized by a diverse range of clinical manifestations. A definitive diagnosis relies on the presence of noncaseating granulomas, which should align with the characteristic clinical and radiological profile [5]. It is crucial to exclude alternative causes of granulomatous formation, including tuberculosis, fungal infections, foreign body reactions, autoimmune conditions, and drug allergies [6] and cultures must be negative, as happened in our case.

The most commonly affected organs in sarcoidosis are the lungs and intrathoracic lymph nodes (over 90% of patients) and ocular sarcoidosis, following skin involvement, is the second most common extrathoracic manifestation of this disease [6].

Neurosarcoidosis has a diverse clinical spectrum, ranging from cranial neuropathies to myelopathies. Our patient presented with a combination of symptoms including headache, transient visual changes; His headache could be explained by leptomeningeal involvement.

Stroke is an apparently very rare complication of sarcoidosis. Our literature review found only 9 cases of sarcoidosis with stroke or TIA episodes. Stroke was the presenting clinical manifestation of sarcoidosis in only 2 of these 9 patients, but both of those cases also had meningeal involvement with hydrocephalus, the remaining 7 patients with sarcoidosis and stroke/TIA either had other typical manifestations of neurosarcoidosis or clear systemic and laboratory findings associated with the disease. [7].Our patient had pulmonary and neurological involvement.

The treatment of multisystemic sarcoidosis necessitates a multifaceted approach comprising pharmacotherapy and adjunctive supportive interventions. The therapeutic objective entails mitigating inflammation, managing symptoms, and preempting potential complications and enduring organ impairments. [8].

Traditionally, high-dose corticosteroids have been the standard of care for treatment of neurosarcoidosis. Unfortunately, a significant percentage of patients with neurosarcoidosis have disease refractory to corticosteroids or are unable to tolerate the high doses that are often required for effective treatment. Other immunosuppressive medications, such as methotrexate, azathioprine, or mycophenolate mofetil, may also be used [9]. In more severe cases of neurosarcoidosis, such as those involving compression of the spinal cord or brain stem, surgical intervention may be necessary.

The positive outcome observed in our patient, treated with cyclophosphamide followed by azathioprine is in line with current recommendations for the management of severe SNC neurosarcoidosis. After one year follow-up, there was a clear clinical, radiological and functional improvement. Pulmonary function tests showed improved volumes and thoracic-brain imaging confirmed effective control of the disease.

4. Conclusions

Sarcoidosis remains a diagnosis of exclusion based on supportive clinical, radiological, and histological findings. The varied ways the disease presents and the lack of specificity in diagnostic tests often lead to uncertainty in diagnosis. Neurological involvement in sarcoidosis is relatively rare, with an unpredictable clinical progression and prognosis. In summary, the significant improvement seen after therapy highlights the importance of awareness toward this clinical entity in order to start treatment as early as possible.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

All authors have confirmed that this study involved human participants or tissue.

Statement of informed consent

Consent was obtained or waived by all participants in this study.

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