Indian Journal of Medical Case Reports ISSN: 2319–3832
Online, International Journal, Available at http://www.cibtech.org/jcr.htm
2024 Vol.13, pp. 18-24/Muhammed et al.
Case Report (Open Access)

NEUROSARCOIDOSIS WITH ATYPICAL RADIOLOGICAL FEATURES MASQUERADING AS METASTATIC THYROID NEOPLASM

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ABSTRACT
Sarcoidosis is a chronic inflammatory condition characterized by the formation of multiple non-caseating granulomas. It can affect any organ system, including the nervous system, but the lungs and intra-thoracic lymph nodes are the most common organs involved. Rarely, patients may present solely with nervous system involvement. Neurosarcoidosis most commonly presents with unilateral or bilateral seventh nerve palsies. The involvement of other common organs (the lung and skin) helps guide the diagnosis. It often manifests with focal neurological deficits, seizures, or cranial neuropathies, resembling neoplastic or infectious etiologies. We present a case of a 42-year-old male with focal seizures, initially suggestive of a neoplastic process due to atypical radiological findings. However, thorough investigation revealed neurosarcoidosis, highlighting the importance of meticulous evaluation and histopathological confirmation. The case demonstrates the diverse manifestations of neurosarcoidosis, including extensive brain edema with meningeal contrast enhancement. His brain magnetic resonance imaging showed extensive white matter edema, mild focal cortical thickening, and enhancing lesions that were predominantly along the leptomeninges and pachymeninges in the bilateral frontal region. Detailed investigations, including the whole-body PET scan and lymph node biopsy, helped in the diagnosis of neurosarcoidosis. Rapid symptom and radiological resolution post-steroid treatment underscored the effectiveness of steroids in managing neurosarcoidosis. This case emphasizes the need for a systematic approach to diagnosis and the crucial role of histopathology in resolving diagnostic challenges.

Keywords: *Leptomeninges, Pachymeninges, Sarcoidosis, Seizure*

INTRODUCTION
Sarcoidosis is a chronic inflammatory disorder with the pathological hallmark of non-caseating granulomas, which can affect any organ system, especially the lungs, liver, and lymph nodes (Costabel *et al.,* 2008). Five-20 percent of patients can have involvement of either the central or peripheral nervous systems (Ungprasert *et al.,* 2019). Neurological manifestations are the presenting symptom in more than 50 percent of these patients. When a well-defined neurological syndrome or manifestation is tied to histopathological features, the diagnosis of neuro-sarcoidosis is established (Patel *et al.,* 2009). When histological confirmation is not possible, the neuroimaging findings and clinical response to steroids are taken as empirical evidence, but only after excluding a host of differentials. Neurological involvement is also associated with increased mortality (Caruana *et al.,* 2019).

CASE
A 42-year-old male with a chief complaint of sudden fall (Immediate or within 3 months) visited the neurology outpatient department. He had a previous medical history of left Frontal lobe hyperintensity, history of transient slurring of speech - 2 episodes over 1 year, dyslipidemia and post covid-19 infection- 1 year back.
He did not have any known comorbidities and presented with two episodes of slurred speech lasting a few seconds, separated by a period of one hour. The second episode was associated with eyelid blinking and

forced and sustained deviation of eyes and face towards the left side with relatively preserved awareness lasting for three minutes. He did not have any preceding fever, constitutional symptoms, headache, vomiting, photophobia, limb weakness, or paraesthesias. He also did not report any systemic symptoms during the present illness or in the past. He was fully conscious and alert, with normal language and lobe functions. His detailed neurological assessment was unremarkable, with no cranial nerve palsy or focal deficit. The systemic examination was also unremarkable. A clinical diagnosis of focal seizures without impaired awareness was made. A gadolinium-enhanced three-Tesla magnetic resonance imaging (MRI) of the brain showed extensive white matter edema and mild focal cortical thickening (Figure 1A) and contrast enhancement predominantly along the leptomeninges and pachymeninges in the right frontal region (Figure 1B). Gadolinium enhancement was also seen in the left frontal and left parietal, as well as along the interhemispheric fissure associated with focal white matter edema.

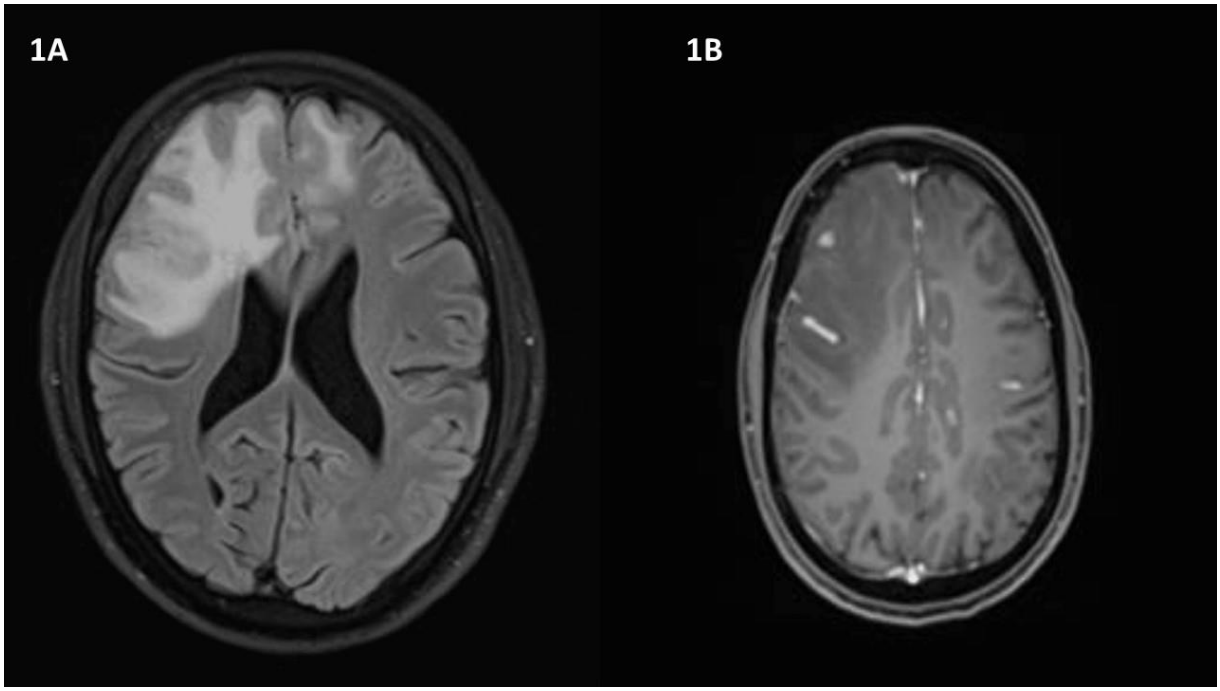

Figure1 A: Magnetic resonance imaging T2 FLAIR (fluid-attenuated inversion recovery)- axial sequence showing bifrontal white matter edema (right >left) and mild focal cortical thickening.
Figure1B: Magnetic resonance imaging T1 post-contrast image.

His EEG showed a mild degree of electrophysiological dysfunction. There were no epileptiform discharges. Based on these imaging findings, the differential diagnosis of meningeal metastasis, lymphoma, IGG4-related pachymeningitis, fungal or tuberculous infection, primary or secondary vasculitis, and sarcoidosis was considered. His routine blood investigations were normal, and his chest X-ray did not reveal any pulmonary infiltrates or mediastinal widening. A cerebrospinal fluid (CSF) study showed mild elevations of protein (65.9 milligrams per deciliter, or mg/dL), glucose (60 mg/dL), and 12 cells, all of which were lymphocytes. CSF gram stain, culture, adenosine deaminase, tuberculosis DNA PCR, an extended meningoencephalitis panel, and malignant cytology all returned negative. Serum angiotensin-converting enzyme (ACE) levels, calcium, phosphorus, and IgG4 levels were normal; the anti-nuclear antibody profile, antiphospholipid panel, complement levels, anti-neutrophil cytoplasmic antibody (ANCA) panel, and viral markers (HBV, HCV, and HIV 1 and 2) were negative. His ultrasound (USG) abdomen showed grade I fatty liver and grade I prostatomegaly (Figure 2). The ultrasound scan of the neck showed an isoechoic nodule on

the left lobe and bilaterally enlarged supraclavicular lymph nodes, larger on the left side with preserved fatty hilum and morphology (Figure 3).

The whole body fluorodeoxyglucose-positron emission tomography (FDG-PET) scan discovered FDG-avid bilateral supraclavicular, a few abdominal and sub-centimetric retroperitoneal lymph nodes, as well as a thyroid nodule (Figure 4). A left supraclavicular lymph node excision biopsy was performed, which was later identified as thyroid tissue in one nodule and reactive changes only in the second nodule.

Ultrasound-guided fine needle aspiration cytology (FNAC) of the thyroid revealed Bethesda four-suspicious of follicular neoplasm. His thyroid functions were normal, but his serum thyroglobulin level was elevated (126.70 nanograms per milliliter with a normal reference value of 1-50).

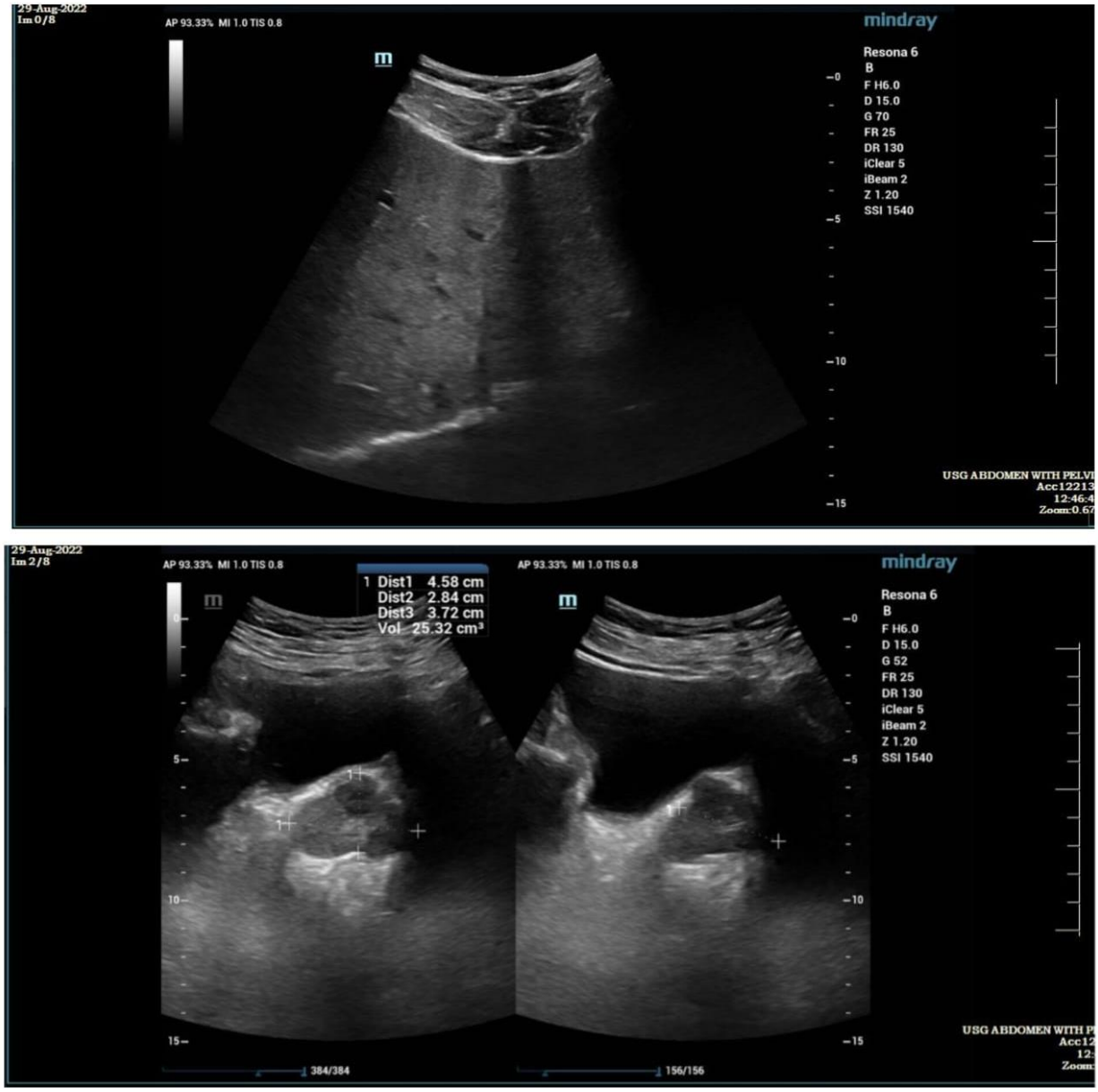

Figure 2: USG abdomen showing grade I fatty liver and grade I prostatomegaly

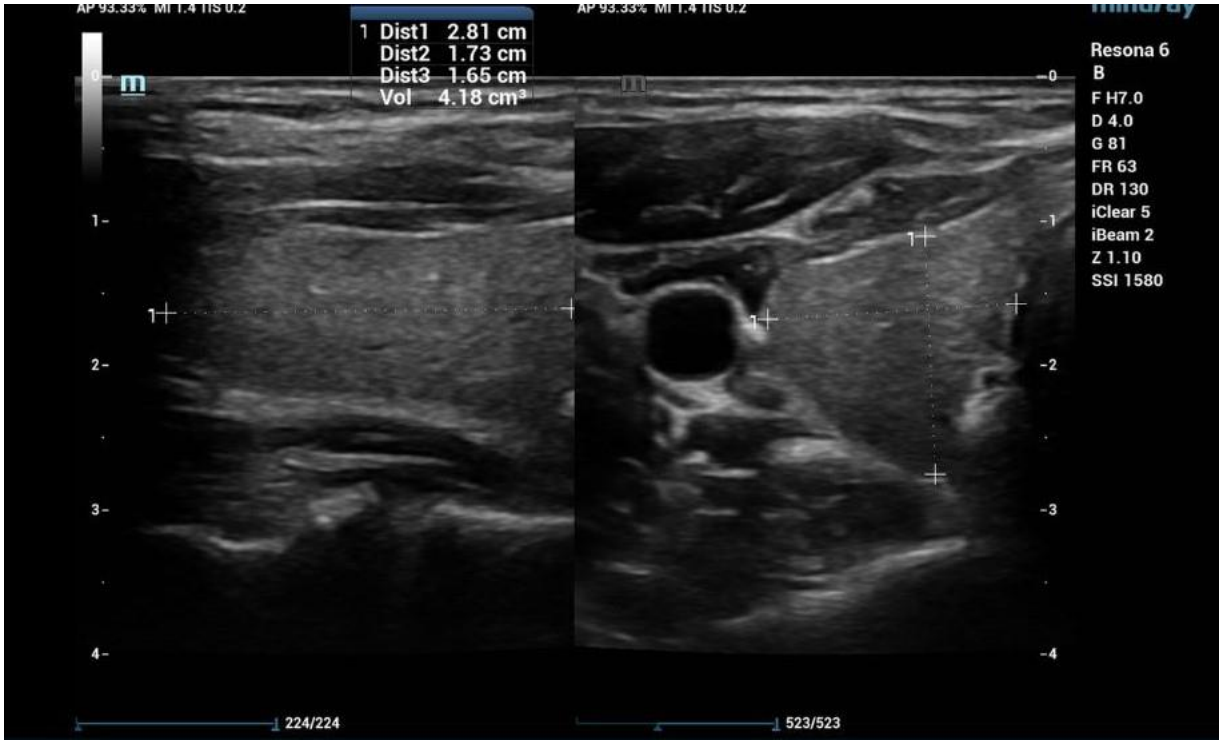

Figure 3: The ultrasound scan of the neck showing isoechoic nodule on the left lobe and bilaterally enlarged supraclavicular lymph nodes, larger on the left side with preserved fatty hilum and morphology.

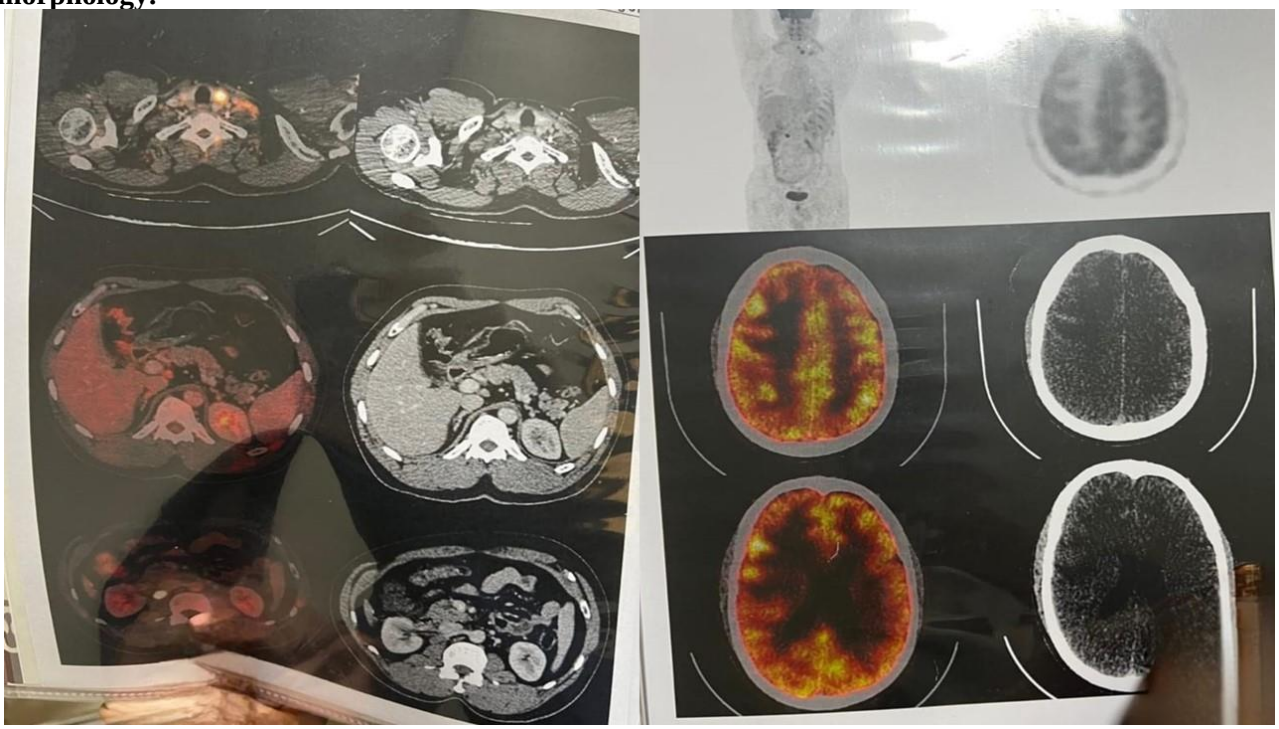

Figure 4: FDG-PET scan showing FDG-avid bilateral supraclavicular, a few abdominal and sub-centimetric retroperitoneal lymph nodes, as well as a thyroid nodule.

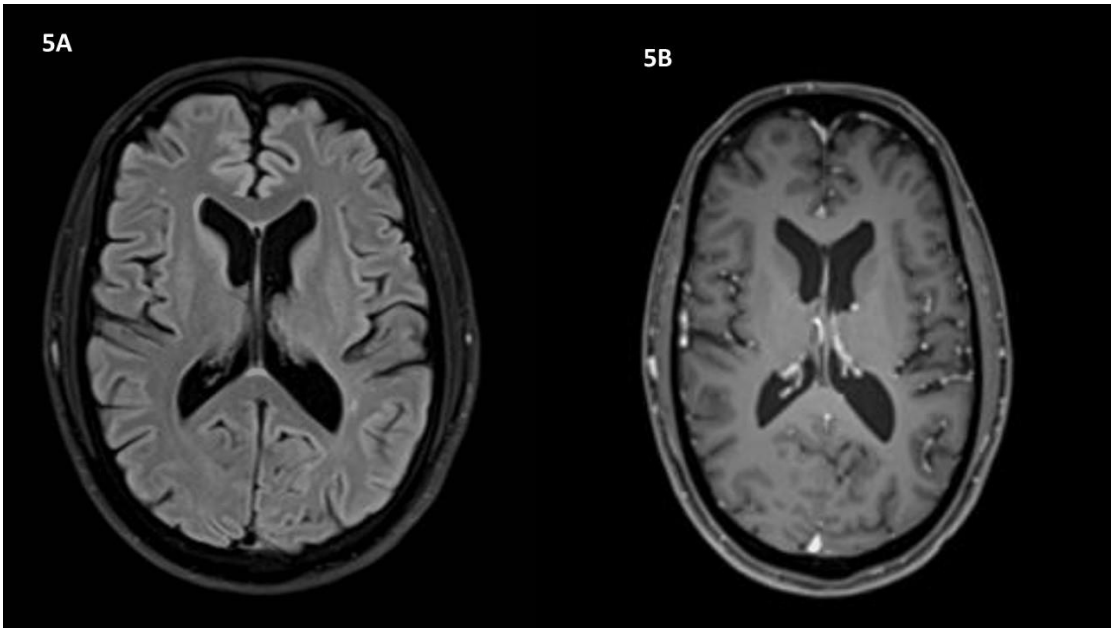

Figure 5A: Magnetic resonance imaging T2 FLAIR axial image. 6 weeks post-steroid treatment showing resolution of white matter edema.
Figure 5B: Magnetic resonance imaging T1 post-contrast -axial image 6 weeks post- steroid treatment showing resolution of meningeal enhancement.

Given his thyroid nodule FNAC finding and MRI brain findings, the possibility of thyroid malignancy with possible meningeal metastasis was considered, and he was referred to the oncology department for further management. The case was discussed at the tumor board. The slide and block review of the left supraclavicular lymph node excision showed the presence of thyroid tissue only (the possibility of metastasis from a well-differentiated thyroid neoplasm could not be excluded). Slide and block review of the left lobe nodule of the thyroid gland (FNAC) showed features of follicular neoplasm (Bethesda category four). Serum carcinoembryonic antigen, beta-human chorionic gonadotropin, alpha-fetoprotein, and lactate dehydrogenase were normal. A computer tomography (CT) -guided FNAC of the retroperitoneal node did not show any atypical cells. A transurethral biopsy of the retroperitoneal node was suggestive of granulomatous inflammation without any necrosis. Because of the patient's presenting symptom (focal seizure), the presence of a thyroid nodule in the ultrasound scan of the neck, and a normal ACE level, the diagnosis of sarcoidosis was kept lower down in the differential diagnosis. Since thyroid malignancy presenting as leptomeningeal metastasis is very unusual (Spiekermann *et al.,* 2017) and non-caseating granuloma in biopsy of the retroperitoneal node, we considered treating this as a case of neuro-sarcoidosis with steroids and watching for a clinical and radiological response. Treatment was initiated with steroids (T-Prednisolone 40 mg once daily for six weeks, then tapered slowly over the next six weeks, and then a maintenance dose of 10 mg on alternate days). Even before steroid treatment, his symptoms resolved completely with antiepileptic medication. (T. LEVIPIL 500mg twice daily for 4 weeks.) He had a near-total radiological resolution within six weeks of steroid treatment (Figure 5A, 5B). For the suspected thyroid neoplasm, it is planned to repeat the FNAC and decide on thyroidectomy on follow-up.

DISCUSSION

Neurosarcoidosis ranks high among the disease category of "great masqueraders." Not only does it cause diagnostic confusion with other chronic inflammatory disorders like tuberculosis, but also with neoplastic

conditions like lymphoma, carcinomatous meningitis, and metastatic lesions. The present report highlights this diagnostic dilemma, which was resolved through the meticulous exclusion of alternate etiologies and the relentless pursuit of histopathological evidence. In this case, because of the patient's presenting symptom (focal seizure), the presence of a thyroid nodule in the ultrasound scan of the neck, and a normal ACE level, the diagnosis of sarcoidosis was initially kept lower down in the differential diagnosis. Since thyroid malignancy presenting as leptomeningeal metastasis is very unusual, non-caseating granuloma in biopsy of the retroperitoneal node and rapid resolution brain and meningeal lesions with steroid treatment all favours the diagnosis of sarcoidosis. Another highlight of this report is the atypical radiological finding of extensive edema resembling a parenchymal lesion. The contrast enhancement restricted to the meninges in these regions demonstrates that the pathology is still extra-parenchymal. The meningeal disease is seen in about 40% of cases with an acute, relapsing-remitting, or chronic pattern of presentation (Lacomis, 2011, Smith *et al.*, 2004). CSF examination reveals a lymphocytic pleocytosis with marginally elevated protein in most cases where leptomeninges are involved (Zajicek *et al.*,1999). Cranial neuropathies can be seen as part of meningeal involvement, especially in pachymeningitis. Hydrocephalus and parenchymal infiltration are rare complications. In the latter scenario, the patient may present with seizures, which was the primary and only manifestation in the present case. As opposed to the basal meninges, which is the favored site, we found the frontal and parietal regions to be involved with disproportionately severe brain edema, evoking the suspicion of a neoplastic pathology. A dramatic response to steroids is well known with leptomeningeal disease, and cytotoxic edema also responded equally well in our patient (Fritz D et.al 2016). In steroid-unresponsive cases, other immunosuppressants like the anti-TNF alpha agent infliximab have been used with variable success (Jamilloux *et al.*, 2017).

CONCLUSION

In conclusion, this case highlights the diagnostic challenges of neurosarcoidosis, which can mimic other conditions. Through thorough investigation, the diagnosis was confirmed, underscoring the importance of meticulous evaluation. Atypical radiological findings, with extensive edema but meningeal contrast enhancement, showcased the diverse manifestations of neurosarcoidosis. Although the lesion distribution initially suggested a neoplastic process, rapid symptom and radiological resolution post-steroid treatment supported the neurosarcoidosis diagnosis. This underscores the effectiveness of steroids in managing neurosarcoidosis, with immunosuppressants like infliximab reserved for steroid-resistant cases. This case emphasizes the need for a systematic approach to diagnosis, considering various possibilities, and the crucial role of histopathological confirmation in resolving such diagnostic challenges.

ACKNOWLEDGMENT

I would like to express my heartfelt gratitude to all those who contributed to the success of this case report endeavor. I want to acknowledge the invaluable support from my colleagues, whose collaborative efforts were instrumental in writing the case report. Furthermore, I extend my thanks to Dr Krishnan Puthusseri, Senior consultant radiology, who generously provided their resources and time for this study. This research would not have been possible without your collective support and encouragement.

Declaration of conflict of interest:
The author(s) do NOT have any potential conflicts of interest with respect to this manuscript.
Declaration of funding:
The author(s) received NO financial support for the preparation, research, authorship, and/or publication of this manuscript.
Declaration of informed consent:
The author(s) hereby declare that there is no information (names, initials, hospital identification numbers or photographs) in the submitted manuscript that can be used to identify patients.

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