

Neurosarcoidosis Manifesting as Cerebral Metastasis-Like Lesion

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Abstract

Introduction: Sarcoidosis is a systemic granulomatous disease that is still of undetermined aetiology. Neurosarcoidosis (NS) is an uncommon but potentially serious manifestation of sarcoidosis.

Case Report: We describe a case of neurosarcoidosis with initial presentation as confusion. The results of his imaging studies favoured the diagnosis of lung cancer with cerebral metastasis. Tran bronchial lung biopsies provided systemic disease histologic confirmation of sarcoidosis. He was started on steroids with subsequent clinical and radiological improvement.

Discussion and Conclusion: There are a wide variety of clinical presentations of neurosarcoidosis. Both clinically and radiographically, NS can be difficult to diagnose. We want to highlight the importance of histological contribution in redressing the diagnosis of NS and improving the prognosis as NS could be a treatable disease.

Keywords: Neurosarcoidosis, Confusion, Metastasis-like, Biopsy, Corticosteroid

Introduction:

Sarcoidosis is a systemic granulomatous disease that is still of undetermined aetiology^{1,2}. Neurosarcoidosis (NS) is an uncommon but potentially serious manifestation of sarcoidosis. The clinical manifestations of NS are seen only in about 5–10% of cases, even though the neurological localizations of sarcoidosis are seen in up to 50% of patients in autopsic studies^{3,4}. NS tends to occur in patients who have systemic features and active disease. Pseudotumoral forms are rare, making its diagnosis difficult and usually one of exclusion in the absence of histological evidence^{5,6}. Here we describe a case of neurosarcoidosis with cerebral pseudotumoral presentation.

Case Report:

A 54-year-old right-handed male presented to the emergency department with a history of two episodes of altered mental status of 6 hours apart. During the episodes, the patient was confused about where he was. He had long pauses during speech with slurring words. The patient returned to his normal baseline mental status after 20 minutes. He was not able to recall the details of the episodes.

His medical history was remarkable for hypertension, diabetes, dyslipidemia and recurrent renal lithiasis. He smoked 1 pack of cigarettes per day and used no other drugs.

Pertinent physical findings showed a well-nourished man in no acute distress and included a blood pressure of 150/60 mmHg. He was oriented to person and place and the Glasgow Coma Scale score was of 15/15. He had no facial or limb weakness. Reflexes were present and symmetric. Plantar responses were flexor. He had normal sensation in his upper and lower extremities. There was no dysmetria on finger-to-nose and heel-to-shin test. Cranial Nerves were intact.

Initial workup including full blood test, Glycaemia, calcemia, kidney and liver function tests, was unremarkable. A Computed Tomography (CT) scan of the head showed a hypodensity interpreted as acute anterior circulation stroke [figure 1].

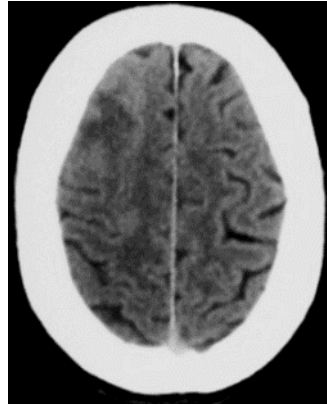
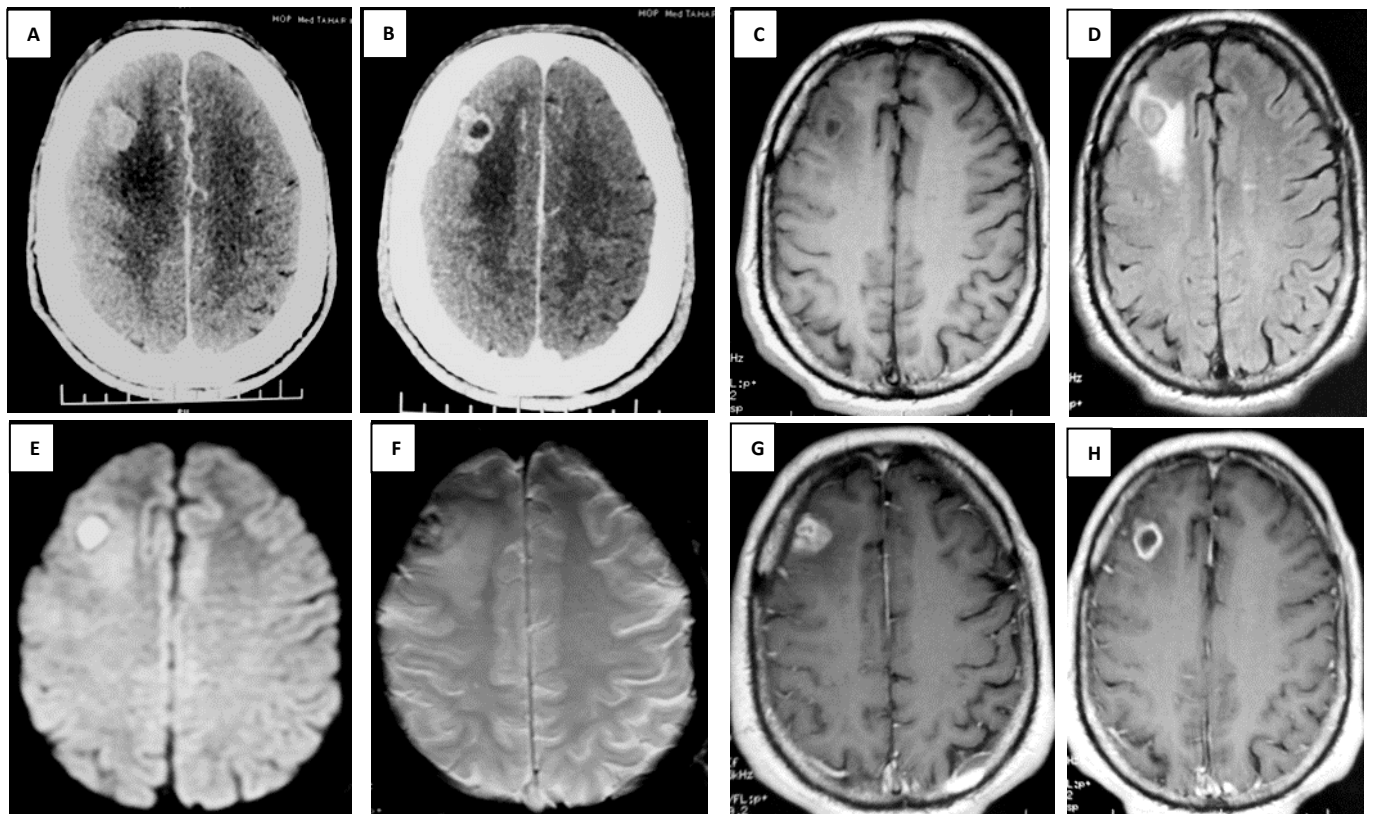


Figure 1: Computed Tomography scan showing hypodensity in the right frontal lobe.

One month later, he re-presented to the emergency department for secondary generalization of focal-onset seizure. A right frontal lobe mass lesion was seen on CT scan with a hypodense area which enhanced after contrast injection (ring enhancement) [figure 2A]. On cerebral magnetic resonance imaging (MRI) the lesion presented a hypointensity with T1 weighting and a hypersignal with T2-FLAIR weighting with ring enhancement on T1-weighted MRI [figure 2B].

On further investigation, screening tests for infectious and inflammatory diseases were unremarkable, but Chest X-ray (CXR) and Computed tomography angiography (CTA) chest showed two heterogeneous consolidations in the upper and the lower right lobes [figure 3]. Given the age, the gender, the smoking history as well as the investigation results, the diagnosis of lung cancer with cerebral metastases was suspected. According to the Union of International Cancer Control (UICC) 8th edition, it would be classified as clinical T4 N0 M1b. As the lesions were not accessible for trans-bronchial lung biopsies, CT-guided biopsy was discussed but finally we opted for per-operative biopsies. Non-necrotizing granulomas were revealed in the pathological specimen with fibrosis and inflammatory reaction, most of which were associated with multinucleated giant cells and macrophages. Tuberculosis-deoxyribonucleic acid test and special stains for acid-fast bacilli and fungi were negative. No histological signs of malignancy had been identified. As part of the granulomatosis assessment, the level of angiotensin-converting enzyme (ACE) blood level was ordered and was high at this time. The diagnosis was finally made as probable neurosarcoidosis according to the modified Zajicek criteria⁷. Then the patient was treated with long-term, high-dose corticosteroid (CS) therapy, and serial imaging examination 4 months later revealed that the lesions extremely decreased [Figure 4].



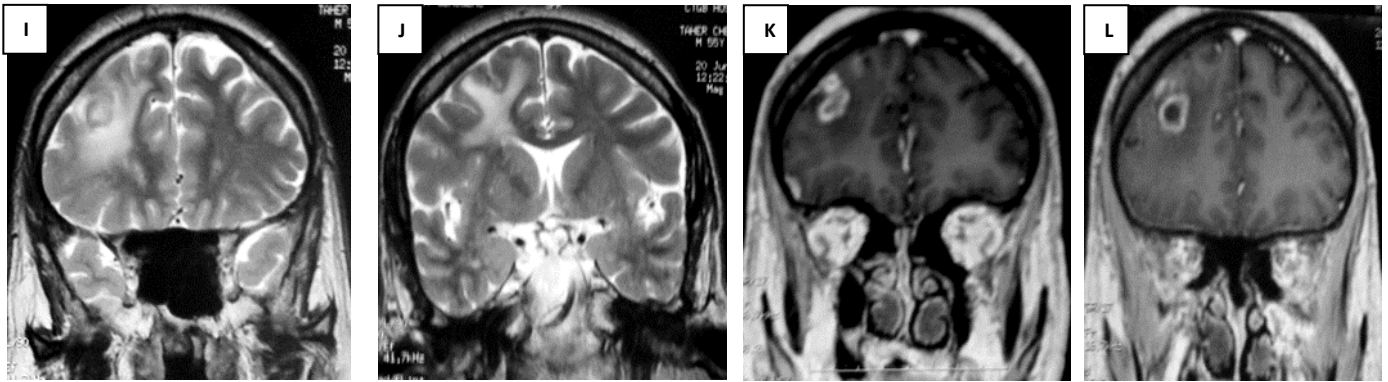


Figure 2A (a, b): Contrast-enhanced CT (CECT) showing a ring enhancing hypodense lesion in the right frontal lobe.

Figure 2B (c, d, e, f, g, h, i, j, k, l): On Magnetic Resonance Imaging (MRI), the lesion presented a hyposignal with T1 weighting (*c*) and a hypersignal with T2- FLAIR weighting (*d, i, j*) with surrounding hypointensity (*d*). The post-contrast T1-weighted MRI demonstrated ring enhancement (*g, h, k, l*), and FLAIR confirmed vasogenic oedema (*d, i, j*). DWI demonstrated restricted diffusion centrally (*e*) and the T2 star showed no haemorrhage (*f*). No mass effect has been demonstrated (*j*).

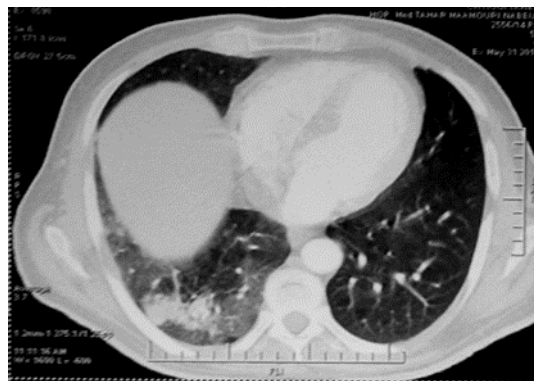
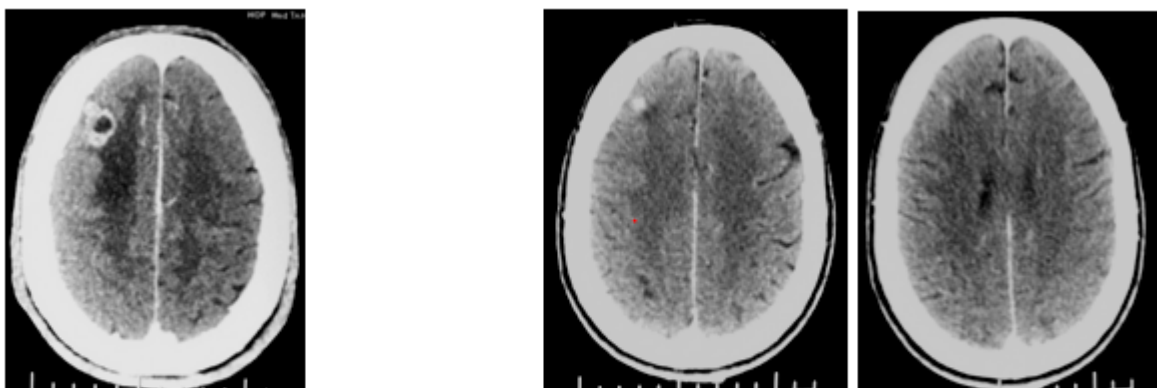


Figure 3: Chest CT at the level of the right lower lobe at lung window: Focal area of heterogeneous consolidation surrounded by a “halo” of ground glass.



A: CT scan before corticosteroid therapy

B: CT scans after corticosteroid therapy

Figure 4: Serial CT scans showing a decrease of the lesion size.

Discussion

Sarcoidosis is a multisystemic granulomatous disorder of unknown cause. It is characterized by the formation of non-caseating granulomas, typically in the lungs and lymphatics, but can also affect other organs including the skin, eyes, heart, kidneys, and nervous system⁸. Approximately 5% to 10% of patients with sarcoidosis often develop neurosarcoidosis within 2 years of systemic disease onset^{3,4,7}.

Patients with NS may present with various symptoms depending on which part of the neurologic axis is affected. The most common presentation is cranial neuropathy especially facial nerve palsy, followed by basal meningitis and hypothalamic-pituitary dysfunction⁷. Encephalopathy, seen in our patient, as the first manifestation of NS is rare: Confusion has been described in only 3 to 4 % of cases in some studies^{9,10} and seizures was seen in 17% of patients with NS^{9,11}.

Radiological findings in neurosarcoidosis are sub-divided into four groups⁵.

- White matter lesions, particularly in the periventricular region which could be confused with multiple sclerosis lesions.
- Leptomeningeal contrast enhancement which is a classic manifestation.
- Hypothalamic and hypophyseal abnormalities with a thickening of the pituitary stalk extending towards the optic chiasma on MRI.
- Pseudotumoral form: Rarely does sarcoidosis occur as a mass in the central nervous system, especially when the involvement of neuroparenchyma proper manifests as solitary supra/intra-tentorial lesion (10% vs 35% for the multiple lesions)^{12,13}. Intraparenchymal involvement is probably due to progression of the pathological process along the Virchow-Robin spaces which are expansions of the subarachnoid spaces along the perforating arteries⁵. This could explain the localisation of the lesion revealed in the case reported here. Smaller parenchymal granulomas may be seen only after intravenous contrast medium administration¹⁴. Unlike the lesion described in our patient, large masses are often iso-intense on T1-weighted images (T1WI)¹⁴. The lesion has either hyper or hypointense signals on T2 weighted sequences¹⁴. The hypointense signal on T2 weighted sequences probably corresponds to the fibrous component⁵ as in this case. Necrosis and calcification are rare^{13,15}. Contrast-enhanced images often reveal diffuse or rim enhancement, although non-enhancing lesions may rarely occur^{12,16}. Oedema is rarely found around the lesion⁵ reason for which our case was misdiagnosed with cerebral metastasis.

Clinically, the diagnosis of NS relies on the modified Zajicek criteria⁷ where in the diagnosis is considered definite if there is biopsy confirmation from neural tissue, probable if there is evidence of neurological inflammation on MRI or CSF (elevated protein, cells, immunoglobulin G indices, or presence of oligoclonal bands) compatible with neurosarcoidosis; and evidence of systemic sarcoidosis with histologic confirmation and/or at least two of the following indirect indicators: fluorodeoxyglucose positron emission tomography (FDG-PET), gallium scan, chest imaging, serum angiotensin-converting enzyme (ACE) and possible if above criteria are not met. Given the fact that in most cases patients with NS are ultimately found to have sarcoid lesions elsewhere in the body¹⁷, as it is the case for our patient, and depending on the location of lesions, skin biopsy, trans-bronchial lung biopsies and CT- guided biopsies have the best yield and lowest morbidity for diagnosis¹⁸.

In our patient, pseudotumoral MRI lesions suggestive of sarcoidosis, pulmonary sarcoidosis with histologic confirmation along with high serum ACE level, favoured the diagnosis of probable neurosarcoidosis.

Neurosarcoidosis is a treatable disease and its management in a correct and timely way can avoid patients having severe residual neurological impairments¹⁹. Corticosteroids are the cornerstone of treatment for NS leading to both clinical and radiological improvement, as seen for our patient. But previous experiences, pointed out that prolonged high doses are often needed. A good initial response often being followed by relapse or deterioration on dose reduction^{19,20}. Immuno-suppressive agents such as Methotrexate, mycophenolate mofetil and azathioprine, are essential not only as steroid-sparing but as disease modifiers reducing relapses risk²¹. It has been proved recently the effectiveness of the biological agent infliximab, which blocks TNF α receptors in severe forms of the disease, particularly invasive leptomeningeal disease and treatment-resistant pachymeningeal disease, and may over time remove the disease entirely^{19,22,23}.

Conclusion:

There is a wide variety of clinical presentations of neurosarcoidosis. Both clinically and radiographically, NS can be difficult to diagnose. Histological proof is necessary in order to rule out other aetiologies, in particular tumours. The prognosis is often favourable with corticosteroid therapy, that represent the cornerstone of treatment, leading to both clinical and radiological improvement.

References

1. Iannuzzi, M. C., Rybicki, B. A. & Teirstein, A. S. Sarcoidosis. *N Engl J Med* 357, 2153–2165 (2007).
2. Newman, L. S., Rose, C. S. & Maier, L. A. Sarcoidosis. *N Engl J Med* 336, 1224–1234 (1997).
3. Nozaki, K. & Judson, M. A. Neurosarcoidosis. *Curr Treat Options Neurol* 15, 492–504 (2013).
4. Lacomis, D. Neurosarcoidosis. *Curr Neuropharmacol* 9, 429–436 (2011).
5. Grand, S. et al. Pseudotumoral brain lesion as the presenting feature of sarcoidosis. *BJR* 69, 272–275 (1996).
6. Gizzi, M. S., Lidov, M. & Rosenbaum, D. Neurosarcoidosis presenting as a tumour of the basal ganglia and brainstem: sequential MRI. *Neurol Res* 15, 93–96 (1993).
7. Tavee, J. O. & Stern, B. J. Neurosarcoidosis. *Continuum (Minneapolis)* 20, 545–559 (2014).
8. Carnero Contentti, E. et al. Application of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorders in a cohort of Latin American patients. *Mult Scler Relat Disord* 20, 109–114 (2018).
9. Joseph, F. G. & Scolding, N. J. Neurosarcoidosis: a study of 30 new cases. *J Neurol Neurosurg Psychiatry* 80, 297–304 (2009).
10. Pawate, S., Moses, H. & Sriram, S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. *QJM* 102, 449–460 (2009).
11. Zajicek, J. P. et al. Central nervous system sarcoidosis--diagnosis and management. *QJM* 92, 103–117 (1999).
12. Nowak, D. A. & Widenka, D. C. Neurosarcoidosis: a review of its intracranial manifestation. *J Neurol* 248, 363–372 (2001).
13. Ginat, D. T., Dhillon, G. & Almast, J. Magnetic Resonance Imaging of Neurosarcoidosis. *J Clin Imaging Sci* 1, (2011).
14. Bathla, G., Singh, A. K., Policeni, B., Agarwal, A. & Case, B. Imaging of neurosarcoidosis: common, uncommon, and rare. *Clin Radiol* 71, 96–106 (2016).
15. Shah, R., Roberson, G. H. & Curé, J. K. Correlation of MR imaging findings and clinical manifestations in neurosarcoidosis. *AJNR Am J Neuroradiol* 30, 953–961 (2009).
16. Lury, K. M., Smith, J. K., Matheus, M. G. & Castillo, M. Neurosarcoidosis--review of imaging findings. *Semin Roentgenol* 39, 495–504 (2004).
17. Pasternak, A. V. & Graziano, F. M. Neurosarcoidosis: Case Report and Brief Literature Review. *J Am Board Fam Pract* 12, 406–408 (1999).
18. Gilman, M. J. & Wang, K. P. Transbronchial lung biopsy in sarcoidosis. An approach to determine the optimal number of biopsies. *Am Rev Respir Dis* 122, 721–724 (1980).
19. Kidd, D. P. Sarcoidosis of the central nervous system: Safety and efficacy of treatment, and experience of biological therapies. *Clin Neurol Neurosurg* 194, 105811 (2020).
20. Kidd, D. P. Neurosarcoidosis: clinical manifestations, investigation and treatment. *Practical Neurology* 20, 199–212 (2020).
21. Joubert, B. et al. Association of Prognostic Factors and Immunosuppressive Treatment with Long-term Outcomes in Neurosarcoidosis. *JAMA Neurol* 74, 1336 (2017).
22. Cohen Aubart, F. et al. Long-term outcomes of refractory neurosarcoidosis treated with infliximab. *J Neurol* 264, 891–897 (2017).

23. Gelfand, J. M. et al. Infliximab for the treatment of CNS sarcoidosis. *Neurology* 89, 2092–2100 (2017).

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