Isolated neurosarcoidosis presenting as granulomatous hypophysitis complicated by arginine vasopressin deficiency

Sirs,

Neurosarcoidosis is a rare manifestation of sarcoidosis, affecting approximately 5–15% of cases and occasionally presenting without systemic involvement (1). It arises from immune dysregulation, where activated T-cells and macrophages form non-caseating granulomas, disrupting central nervous system (CNS) function (2). When the hypothalamic-pituitary axis is involved, granulomatous hypophysitis can lead to arginine vasopressin deficiency (AVP-D), formerly known as central diabetes insipidus, which manifests with polyuria and polydipsia (3). We present a case of isolated neurosarcoidosis presenting with AVP-D and granulomatous hypophysitis.

A 26-year-old female with vitiligo and chondromalacia patellae presented with sudden-onset polydipsia, polyuria, nocturia, and a bilateral frontal headache radiating to the right eye. Ophthalmologic examination revealed peripheral vision loss resembling bitemporal hemianopsia. Laboratory findings showed hypernatraemia and a urine osmolality of 202 mOsmol/kg, and a water deprivation test confirmed AVP-D, which was significantly improved with desmopressin administration. Brain MRI revealed hypophyseal enlargement (Fig. 1), prompting transsphenoidal surgery. Histopathology of the resected tissue demonstrated granulomatous hypophysitis. Infectious work-up for tuberculosis and fungal organisms was essentially negative, and serum ACE levels, chest x-ray, and pulmonary function tests were normal. Postoperatively, the patient developed hand arthralgias, while vision improved. The diagnosis of neurosarcoidosis, and treatment with oral prednisolone and methotrexate was initiated, with continued desmopressin. However, polyuria and polydipsia persisted post-operatively unless desmopressin was taken.

Neurosarcoidosis (NS) frequently affects the cranial nerves, meninges, hypothalamus, and pituitary gland (4). Some sources estimate that fewer than 1% of sarcoidosis cases present as isolated neurosarcoidosis, while others report that 10–20% of NS cases lack systemic involvement (1, 2, 5). This variation underscores the diagnostic challenges posed by its non-specific imaging findings and overlap with other neurological disorders. In the absence of classic systemic signs like pulmonary hilar lymphadenopathy, diagnosis depends on imaging, histopathology, and ruling out infectious or neoplastic causes.

MRI with gadolinium enhancement is the preferred imaging modality, detecting leptomeningeal or dural enhancement, intraparenchymal lesions, and hypothalamic-pituitary abnormalities (6). Findings include pituitary enlargement, stalk thickening, or loss of the posterior pituitary's hyperintense signal (7). However, imaging may be normal, especially post-treatment. In such cases, 18F-FDG PET can identify metabolically active granulomas, aiding diagnosis and monitoring response to therapy (8). CT can serve as an alternative in patients with contraindications to MRI, despite its lower sensitivity in detecting hypothalamic involvement. CSF analysis, laboratory markers, and histopathology further support diagnosis when imaging is inconclusive.

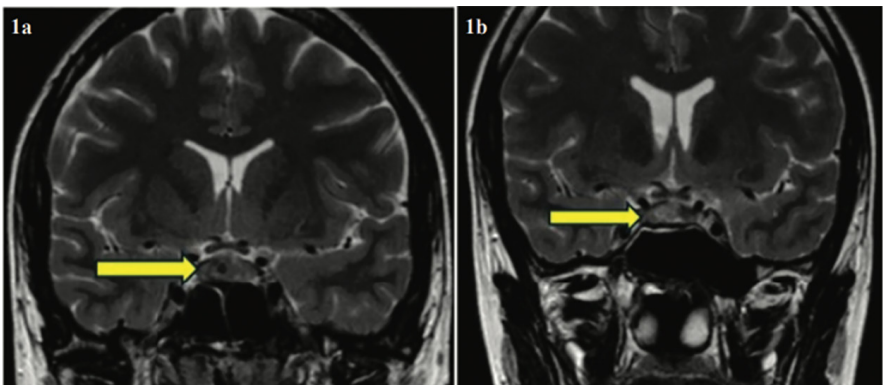

Fig. 1 a. MRI conducted pre-operatively. The arrow is pointing at a macroadenoma of the pituitary gland measuring 17 x 11 x 12 mm in large diameter with slight T2 hyperintensity, comprising a non-vascularised central zone of T1 and T2 hyposignal measuring 3 mm.
b. MRI conducted one year post-operatively. The arrow is pointing at a pituitary gland moderately increased in volume, slightly protruding into the suprasellar cistern.

Corticosteroids remain the mainstay of treatment, with prednisone (1 mg/kg/day) or IV methylprednisolone (1 g/day for severe cases) (9). Relapses during tapering are common, necessitating steroid-sparing agents like methotrexate, azathioprine, and mycophenolate mofetil (9).

Regarding prognosis, corticosteroid therapy can improve radiologic abnormalities in hypothalamic-pituitary neurosarcoidosis, but hormonal dysfunction is often permanent due to irreversible neuronal damage (8, 10). Even with immunosuppressive treatment, full recovery of endocrine function is rare, necessitating long-term hormone replacement (8, 10). This underscores the need for further research, especially multicentre prospective studies, to determine whether early detection and intervention could prevent these lasting hormonal deficiencies.

In conclusion, isolated neurosarcoidosis is a rare condition that may involve hypophyseal tissue, causing AVP-D. While imaging techniques, such as MRI, might demonstrate hypointense signals in the hypophysis suggestive of the condition, a biopsy is still recommended for tissue examination. Early treatment, including pharmacotherapy and surgery, is vital for a better prognosis. However, complications, especially hormonal deficiency, may persist after treatment.

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References

1. COURTIN E, OUALLET JC, LAZARO E, MARTIN-NEGRIER ML, COHEN-AUBART F, DUFFAU P: Isolated CNS sarcoidosis versus systemic sarcoidosis with CNS involvement: a same disease? *Neurohospitalist* 2022; 12(2): 290-94. https://doi.org/10.1177/19418744211030416
2. BRADSHAW MJ, PAWATE S, KOTH LL, CHO TA, GELFAND JM: Neurosarcoidosis: pathophysiology, diagnosis, and treatment. *Neurol Neuroimmunol Neuroinflamm* 2021; 8(6): e1084. https://doi.org/10.1212/nxi.0000000000001084
3. MURIALDO G, TAMAGNO G: Endocrine aspects of neurosarcoidosis. *J Endocrinol Invest* 2002; 25(7): 650-62. https://doi.org/10.1007/bf03345093
4. STERN BJ, ROYAL W 3RD, GELFAND JM *et al.*: Definition and consensus diagnostic criteria for neurosarcoidosis: from the Neurosarcoidosis Consortium Consensus Group. *JAMA Neurol* 2018; 75(12): 1546-53. https://doi.org/10.1001/jamaneurol.2018.2295
5. SHIMIZU K, YUKI K, SADATOMO T, KURISU K: Isolated neurosarcoidosis presenting with multiple cranial nerve palsies. *Surg Neurol Int* 2016; 7: 44. https://doi.org/10.4103/2152-7806.180765
6. SINHA T, TAHIR S, NAMAL F *et al.*: Neurosarcoidosis: current perspectives on diagnosis, management, and future directions. *Cureus* 2024; 16(9): e69208. https://doi.org/10.7759/cureus.69208
7. KAKEHI E, ADACHI S, FUKUYASU Y *et al.*: Magnetic resonance imaging and symptoms in patients with neurosarcoidosis and central diabetes insipidus. *Endokrynol Pol* 2019; 70(5): 430-37. https://doi.org/10.5603/ep.a2019.0035
8. MARTIN-GRACE J, MURIALDO G, TAMAGNO G: Hypothalamic-pituitary alterations in patients with neurosarcoidosis. *EMJ Neurol* 2015; 3(1): 51-56.
9. SEGAL BM: Neurosarcoidosis: diagnostic approaches and therapeutic strategies. *Curr Opin Neurol* 2013; 26(3): 307-13. https://doi.org/10.1097/wco.0b013e3283608459
10. LANGRAND C, BIHAN H, RAVEROT G *et al.*: Hypothalamo-pituitary sarcoidosis: a multicenter study of 24 patients. *QJM* 2012; 105(10): 981-95. https://doi.org/10.1093/qjmed/hcs121