A Rare Case of Isolated Cerebral Sarcoidosis Presenting as Suprasellar Mass Lesion with Salt-Wasting Hypopituitarism

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Abstract

Background Sarcoidosis is a systemic disorder of unknown origin characterized by noncaseating granulomas. Clinical symptoms due to central nervous system (CNS) involvement occur in 5 to 7% of all cases; subclinical involvement is more frequent. Sole CNS involvement is very rare.

Case Report A 25-year-old man presented with increasing polyuria and polydipsia over 8 weeks. Magnetic resonance imaging (MRI) revealed a supra- and infra-chiasmatic prethalmic mass lesion 1.0 × 1.4 × 1.4cm in diameter. Microsurgical biopsy verified a necrotizing noncaseating epithelioid cell tumor indicative for neurosarcoidosis. All symptoms dissolved within 3 months under stringent corticoid therapy.

Conclusion Intracranial mass lesions as the primary and only manifestation of neuronal sarcoidosis are rare. Because conservative treatment is safe and effective, surgery is limited to biopsy and the alleviation of pressure-related symptoms to preserve neurologic function.

Keywords
► neurosarcoidosis
► intracranial mass lesion
► salt-wasting hypopituitarism
► diabetes insipidus

Introduction

Sarcoidosis is a systemic granulomatous disease whose etiology is still unknown. The incidence is estimated to be as high as 20 per 100,000.¹ Only a few patients develop a neurologic involvement throughout the course of their disease. A manifestation limited to the central nervous system (CNS) is rare. Due to the absence of any specific criteria, the diagnosis is often difficult and delayed. We present a quintessential case of isolated intracranial sarcoidosis mimicking a suprasellar mass lesion causing hypophyseal insufficiency.

Case Report

History
A 25-year-old white man presented with increasing polyuria and polydipsia over 8 weeks. Daily fluid intake reached 12 L per day. In addition, the patient complained about sweating, fatigue, and impaired heat tolerance. He denied fever or current infections. Medical history revealed a chronic thyroxin-dependent hypothyroidism. Social anamnesis and family history were normal.

Physical Examination
His body weight was 85 kg and his height was 174 cm (body mass index: 28.1). On inspection the skin was pale and sweaty. Pitting edemas were palpable on both lower limbs. Body temperature was 37.2°C. Blood pressure was 130/80. Normal heart sounds were heard on auscultation. Peripheral pulses were all palpable, strong, and regular at a heart rate of 80 bpm; no jugular venous pressure (JVP) elevation was visible. No enlarged lymph nodes were palpable. The abdomen was soft with no masses. On neurologic examination the patient was oriented. His muscle tone was normal; no paresis.
was present or sensory deficits. All joints were painless with a normal range of motion. There were no signs of nuchal rigidity. Tendon reflexes were normal. No deficits of eyesight or visual field were found on ophthalmologic examination.

**Laboratory Work-up**

Blood tests showed a hyponatremia of 127 mmol/L (136–146 mmol/L). As a marker for sarcoidosis, angiotensin-converting enzyme (ACE) was slightly decreased at 18 U/L (20–70 U/L). The soluble interleukin-R receptor was elevated at 868 U/L (158–623 U/L). Prolactin levels were within normal range at 4.5 µg/L (4–15 µg/L). Diagnostic lumbar puncture revealed no abnormalities. Urine specific gravity was lowered to 1.010 (1.020–1.025).

**Imaging**

A chest X-ray performed on admission showed no abnormalities.

**MRI Imaging**

T2-weighted cranial magnetic resonance imaging (MRI) images revealed a supra- and infra-chiasmatic pre-thalamic mass lesion 1.2 cm in diameter, extending from the lamina terminalis into the third ventricle. The lesion appeared solid, fuzzy, and T2-hyperintens. No leptomeningeal involvement was noted. The inhomogeneous wall stretched filamentous to the surrounding tissue. After administration of intravenous gadolinium contrast, a strong signal enhancement was noted (►Fig. 1).

**Differential Diagnosis**

Possible pathologic conditions causing suprasellar mass lesions encompass entities such as pituitary adenomas and carcinomas, pituitary pseudotumors, vascular lesions, craniopharyngiomas, meningiomas, germ cell tumors, hypothalamic and optic gliomas, lymphoma, metastasis, epidermoid cysts, tuberculosis, and cysticercosis as well as inflammatory diseases such as sarcoidosis or lymphocytic adenohypophysitis.

**Biopsy**

Based on clinical and imaging findings, microsurgery was initiated to establish the diagnosis based on histopathology and perform a tumor resection if feasible. Surgery was performed using a subfrontal approach. After a subdural cisternostomy, the optic nerve and chiasm were exposed. The arachnoid layer covering the lamina terminalis was carefully dissected, freeing a curly flower-like exophytic lesion. The lesion was excavated toward the third ventricle. Multiple specimens were sent for intrasurgical frozen section. Immediate pathology suggested a necrotizing epithelioid cell tumor indicative of chronic inflammation. Thus the surgical exploration was confined at this stage (►Fig. 2).

Further intra- and postoperative course was uneventful. No new neurologic deficits were detected. Postoperative MRI showed no signs of ischemia or bleeding.

**Histopathology**

Definite histology proved epithelioid cell granulomas and multinucleated giant cells with surrounding lymphocytes. Occasional central necroses without caseation were noted. Granulomas were rich in fibrous tissue and reticulin. PAS and Ziehl-Neelsen staining were negative. The polymerase chain reaction remained negative for mycobacteria (►Fig. 3).

**Treatment**

After histopathologic confirmation, a glucocorticoid therapy using dexamethasone 8 mg three times a day was initiated. Subsequently the fluid uptake attenuated to normal amounts. After 8 weeks it had decreased to 4 L per day with consecutive normouria. The hyponatremia normalized to 4.5 mmol/L. The patient developed signs of Cushing disease and complained about painfully swollen joints. All symptoms vanished after reduction of the corticosteroid treatment.

In MRI scans 3 months after admission the preexisting mass lesion had regressed completely. Only the pituitary stalk showed a residual, limited focal contrast enhancement in T1-weighted images after gadolinium administration (►Fig. 4).

**Discussion**

Sarcoidosis, also known as Boeck or Schaumann disease, is a systemic disorder defined by the presence of noncaseating granulomas that compromise the integrity and function of any tissue where they occur. Chronic as well as self-limiting forms are described. Sarcoi- didosis is histopathologic characterized by the presence of noncaseating epithelioid-cell granulomas in several

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**Fig. 1** Preoperative magnetic resonance imaging. (A) T2-weighted image depicts a 1.8 × 1.2 cm hypointense filamentous spreading suprasellar mass lesion above the optic chiasm. (B and C) T1-weighted imaging after intravenous gadolinium: inhomogeneous contrast enhancement with contact of the lesion to the pituitary stalk.
affected organs. Involvement of only one organ or compartment is less common and only reported sporadically. The multiple lesions do not contain tuberculosis-like necrotizing areas or mycobacterium tuberculosis. Some may develop fibrinoid or paramyeloid necrosis. Epithelioid or multinucleated cell formation occurs in differing frequency. These cells contain nonspecific asteroid or radiating inclusion bodies, so-called Schaumann bodies. Granuloma progression either leads to resolution or conversion into hyaline connective tissue.

The first CNS form was described as early as 1905 when Jörgen Schaumann recognized the systemic nature and genetical equity of Boeck sarcoid and lupus pernio. Later osseous forms were described. Due to its highly variable clinical appearance, the incidence of sarcoidosis can only be estimated from mass screenings and is assumed to be as high as 20 per 100,000. Sarcoidosis is most frequent in young adults with a female predominance. Only 16% of all cases develop clinical symptoms. Neurologic symptoms due to CNS involvement are found in 5 to 7% of all patients with systemic sarcoidosis. The number of silent neural signs detected solely by autopsy is even higher. Rarely sarcoidosis is strictly confined to CNS manifestations with an estimated incidence < 0.2 per 100,000 within the white population. Lesions found in CNS tissue are no different from those found in other organs. Spreading occurs leptomeningeally, alongside the Virchow-Robin spaces and entering the cortical and subcortical layers following penetrating blood vessels. Thus the hypothalamus, third ventricle, pituitary gland, optic nerve, and chiasm are most frequently involved. There is a broad variety of clinical variants with intra- or extraaxial diffusely disseminated or more localized leptomeningeal or parenchymal plaques reported. In 1947, Everts et al described the first tumorlike CNS lesion caused by nonsystemic sarcoidosis. Clinical symptoms depend on location of the lesion and encompass seizures, sensor and motor deficits, pituitary dysfunction, neuropsychological deficits, and cranial nerve palsies as well as hydrocephalus and unspecific headaches.

In MR tomography, neurosarcoidosis lesions present as nodular or diffusely infiltrating that are mostly attached to the leptomeninges. After intravenous administration of gadolinium-diethylenetriamine pentaacetic acid, a homogeneous or diffuse enhancement has been reported. MRI is the imaging modality of choice. Without systemic spread and symptoms, neurosarcoidosis can mimic almost every other intracranial disease in clinical and imaging appearance. Therefore the diagnostic process is often prolonged and challenging.

In this case report, we presented a patient with isolated cerebral sarcoidosis presenting with isolated diabetes insipidus. The initial MRI scan revealed a T2 hyperintense supra- and infrachiasmatic mass lesion with inhomogeneous enhancement after intravenous gadolinium administration. The imaging results fall in line with the described pattern commonly observed in intracranial neurosarcoidosis. Nevertheless there is a whole
plethora of more commonly seen differential diagnoses presenting with similar tomographic findings. Extensive blood tests and cerebrospinal fluid (CSF) examination revealed no findings indicating the presence of neurosarcoïdosis. ACE can be of diagnostic value because elevation indicates the presence of neurosarcoïdosis. The low sensitivity of ACE elevation in the cerebrospinal fluid (CSF) leads to a high number of false-negative results. Although distinction of neurosarcoïdosis from other tumor entities by CSF examination alone is impossible, elevation of serum ACE occurs in 56 to 85% of all cases of sarcoïdosis. Thus ACE elevation is indicative but may be observed in other inflammatory diseases such as multiple sclerosis, Behçet disease, Guillain-Barré syndrome, and other infections. The ACE level in the presented case was normal in serum and in CSF, illustrating the low sensitivity and specificity for the diagnosis of neurosarcoïdosis. After completion of the diagnostic work-up, an intracranial neoplasia such as a germinoma or craniopharyngioma seemed the most likely diagnosis. Although not overly common in western European countries, cerebral tuberculosi s should always be considered because radiography and histopathology share numerous similarities. To initiate adequate therapy, histopathologic diagnosis is essential. We therefore pursued a microsurgical approach that could be used for radical tumor removal if feasible. Only open microsurgical biopsy was able to establish the diagnosis in the current case.

Over the last decade, several case reports have been published depicting intracranial lesions in patients with known sarcoïdosis. Primary neurosarcoïdosis in the absence of a systemic disease is still diagnostically a headache. Pituitary involvement occurs in 10% of all patients with neurosarcoïdosis. Patients often present with profound endocrinological dysfunction including obesity, psychosis, diabetes insipidus, amenorrhea, and hypoglycemia. Symptoms may be secondary to pituitary or thalamic infiltration and destruction. Diabetes insipidus occurrence is attributed to an infiltration of the pituitary stalk.

Thus the presented case illustrates a rare manifestation of neurosarcoïdosis and demonstrates the diagnostic obstacles and pitfalls of this disease. Several case reports dealing with the diagnostically and therapeutically conundrum have been published over the last decade. Guoth et al describe a young woman with clinical hypopituitarism and systemic sarcoïdosis of the lung, gastrointestinal tract, and a cystic pituitary mass. Isolated CNS involvement mimicking a mass lesion without disseminated disease or prior systemic appearance is even more rare. Grand et al report a pseudotumoral right frontotemporal mass lesion as only sign of the disease.

Another case was presented by Stübgen describing a 22-year-old woman with a clival mass as the only manifestation. Table 1 lists the cases published in the English literature over the last decade. In most cases signs of a systemic disease were apparent at the time of pituitary-hypothalamic symptom development. In these cases a conservative approach with corticosteroid treatment is feasible. Histopathology should be established via bronchial lavage or lymph node biopsy. In cases of primary solitary intracranial mass lesions, a trial corticosteroid treatment should be considered in stationary diseases. In patients presenting with pressure-related symptoms or signs of fast disease progression, microsurgery is indicated.

### Conclusion
Neuronal sarcoïdosis mimicking intracranial mass lesions has been described in several case reports over the past decade. In most of theses cases systemic manifestations preceded or accompanied the neuronal manifestation. Almost all localizations of intracranial lesions have been described including sellar and suprasellar lesions. More than one intracranial lesion is found in most of the patients. A solitary sellar mass lesion due to neurosarcoïdosis has only mentioned twice to our knowledge.

CSF examination with pleocytosis, ACE- and protein-level elevation is indicative but not conclusive for the diagnosis of neurosarcoïdosis. Therefor biopsy taking is still obligatory today. There is no evidence of a superior clinical benefit from surgical resection because neurosarcoïd lesions respond well to steroid therapy. Surgery should therefore be confined to the collection of biopsy material as soon as histopathology is available. In cases of clinically apparent lesions, microsurgery should be considered to alleviate pressure-related symptoms or deficits caused by space occupation alone.
| Study               | No. of patients | SD   | Symptoms                  | HA                        | MRI                          | Treatment                                      | Outcome       |
|---------------------|----------------|------|---------------------------|---------------------------|------------------------------|-----------------------------------------------|---------------|
| Hwang et al<sup>26</sup> | 1              | No   | PU/PD, Ha, EM, WL, HCa    | Yes                       | 8-mm mass lesion             | CT over several years                       | Remission     |
| O’Reilly et al<sup>27</sup> | 1              | Yes  | PU, Ha, WG, lethargy      | Yes                       | Hypothalamic infiltration    | Cervical LN biopsy, anti-TNF-α therapy        | Remission     |
| Tanaka et al<sup>28</sup> | 1              | Yes  | PU/PD, visual field defect| Yes                       | Pituitary gland and stalk enlargement | CT                                            | Partially remission |
| Langrand et al<sup>29</sup> | 24             | No (2)/Yes (22) | PU/PD (12), Ha (1), EM (1), decreased libido (8), impotence (1), galactorrhea (2) | Yes                       | –                             | CT (21)/MTX (9)/AZA (5)/MMF (6)               | Partial improvement (17)/Aggravation (7) |
| Tedford et al<sup>30</sup> | 1              | Yes  | Postpartum galactorrhea   | Yes                       | Pituitary mass               | CT                                            | Remission     |
| Titić et al<sup>31</sup> | 1              | Yes  | Mild cognitive impairment | NA                       | NA                           | NA                                            | NA            |
| Skowasch et al<sup>32</sup> | 1              | Yes  | PU/PD, lethargy           | No                        | Pituitary gland and stalk enlargement | Bronchial lavage, CT/AZA                      | Remission     |
| Alam et al<sup>33</sup> | 1              | Yes  | PU/PD                     | No                        | No intracranial abnormality  | LN biopsy, CT                                | Remission     |
| Kimball et al<sup>23</sup> | 1              | No   | Ha, visual field defect   | No                        | Pituitary mass               | Transsphenoidal decompression and biopsy, CT/MTX | Remission     |
| Jomaa et al<sup>34</sup> | 1              | No   | PU/PD, Ha, visual field defect | Yes                       | Infiltrating lesion of pituitary gland/stalk and hypothalamic region | CT                                            | Remission     |
| Sundaresan et al<sup>35</sup> | 1              | Yes  | PU/PD, weight gain, amenorrhea | No                       | Suprasellar mass and contrast enhancement of optic chiasm, pituitary stalk, and hypothalamus | LN biopsy, CT, Rtx after relapse               | Partial remission |
| Shimaoka et al<sup>36</sup> | 1              | Yes  | PU/PD, decreased libido   | Yes                       | Pituitary mass               | Bronchial lavage, CT                         | Remission     |
| Pillai et al<sup>37</sup> | 1              | No   | Visual field defect       | No                        | Pituitary mass               | Transsphenoidal decompression and biopsy, CT | Stable disease |
| Hasumi et al<sup>37</sup> | 1              | Yes  | Visual field defect       | No                        | Pituitary mass               | CT                                            | Remission     |

Abbreviations: AZA, azathioprine; CT, corticosteroid therapy; EM, emesis; Ha, headache; HA, hormonal alteration; HCa, hypercalcemia; LN, lymph node; MMF, mycophenolate; MRI = magnetic resonance imaging; MTX, methotrexate; NA, not available; PD, polydipsia; PU, polyuria; Rtx, radiation therapy (e.g., Gamma Knife); SD, systemic disease; TNF, tumor necrosis factor; WG, weight gain; WL, weight loss.
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