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Sarcoidosis of the pineal gland: an unusual presentation of neurosarcoidosis

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Abstract

Introduction—Sarcoidosis is an inflammatory disease characterized by noncaseating granulomas that is rarely found as primary CNS pathology. We report an unusual case of sarcoidosis involving the pineal gland with radiographic, histopathology, and clinical data.

Case report—A 45-year-old man without evidence of systemic sarcoidosis presented with a history of gradual onset of blurry vision and diplopia that progressed over 3 months. MR imaging demonstrated an enhancing mass in the pineal region. A suboccipital craniotomy was performed with resection of the mass through a supra-cerebellar infratentorial approach. Histopathologic

analysis did not reveal a pineoblastoma but instead revealed noncaseating granulomas within the pineal gland. Extensive hematologic laboratory examinations, cerebral spinal fluid studies, and cultures for infection were all negative. This mass lesion was diagnosed as solitary neurosarcoidosis of the pineal gland, without dissemination. The patient was treated with steroids and at 4-year follow-up is asymptomatic with an unremarkable MRI scan.

Conclusion—This is an unusual case of pineal sarcoidosis mimicking a tumor with associated MRI, CT and histopathologic findings reported together. Although rare, sarcoidosis of the pineal gland should not be excluded from a comprehensive differential diagnosis of an enhancing pineal region mass.

Keywords

Pineal gland; Sarcoid; Granulomatous; Inflammation; Pineoblastoma

Introduction

Sarcoidosis is an inflammatory disease of unknown etiology characterized by noncaseating granulomas, typically affecting multiple organ systems [1–4]. Neurosarcoidosis with central nervous system involvement is a rare condition with a poorly defined natural history, occurring in only 5–15% of sarcoidosis cases [1–12]. Diagnosis is difficult due to the clinical heterogeneity of the disease, particularly when systemic symptoms are not manifested [4, 5, 13].

Pineal gland tumors account for only 0.5–1% of all intracranial neoplasms in adults [14]. Most patients with a pineal region mass present with Parinaud's syndrome, other symptoms of obstructive hydrocephalus, or cranial nerve palsies [1, 15–18]. Although magnetic resonance imaging (MRI) can give initial information on the nature of the disease, a conclusive preoperative diagnosis is not possible due to the wide diversity of pineal region tumors, and hence tissue histology is critical for diagnosis of a pineal region tumor. Improvements in neuroradiology, microsurgical techniques, and neuroanesthesia have diminished the morbidity and mortality of surgical tumor removal in the pineal region [14].

Neurosarcoidosis involving the pineal gland is very rare, having only been reported three times in the literature [1, 6, 19]. Comprehensive imaging studies with CT and MRI demonstrations and concomitant associated microscopic histopathology and immunohistochemistry have not been described together in the published literature. Here we present a rare entity of neurosarcoidosis with MRI, CT and affiliated histopathologic immunohistochemistry of pineal sarcoidosis mimicking a pineoblastoma on imaging studies and review the management of neurosarcoidosis.

Case report

A 45-year-old man sought medical attention for gradual onset of blurry vision and diplopia that progressed over 3 months. These symptoms were associated with nausea, coordination difficulties, and intermittent headaches. There was no significant past medical history, no history of tumors or any previous radiation exposure. Physical exam revealed no mental

status, motor, or sensory impairments, and without findings consistent with systemic sarcoidosis. The patient complained of subjective diplopia when looking down and to the right; however, extraocular movements were full with no signs of Parinaud's syndrome and ophthalmologic exam revealed no papilledema.

Non-contrast CT imaging revealed an approximately 1 cm pineal region mass that was mildly hypodense. This lesion was embedded with apparent pineal calcifications, but heterogeneous portions of this mass were not calcified (Fig. 1). Imaging with MRI demonstrated a $1.4 \times 1.8 \times 1.0 \text{ cm}^3$ mass in the pineal region. This lesion exhibited heterogeneous hypointensity on T1-weighted and prolongation on T2-weighted images, and heterogeneous contrast enhancement with gadolinium administration, without hydrocephalus (Fig. 1).

Cerebral spinal fluid (CSF) analysis, bone marrow biopsy, and hematologic studies were negative for lymphoma and other inflammatory diseases. His work up did not indicate an immunocompromised state and he was HIV negative. Of note, his CSF angiotensin converting enzyme (ACE) was measured to be 3 U/l and serum ACE was 12 U/l neither one was elevated (UCSF reference range is 9–67 U/l). Chest, abdomen, and pelvis CT imaging revealed no other mass lesions.

A suboccipital craniotomy with a supra cerebellar infratentorial approach was performed. In the context of a patient with progressive diplopia and no diagnosis, the tissue histology is critical for diagnosis of a pineal region tumor. Intra-operatively, biopsies of the superior posterior aspect of the pineal gland were taken for frozen and permanent pathology samples. Histopathology demonstrated granulomatous inflammation with numerous well-developed compact noncaseating granulomas without associated necrosis and characteristic sarcoid morphology. Immunohistochemistry with synaptophysin, CD68, CD3, and CD20 were performed to confirm the histologic diagnosis (Fig. 2). The synaptophysin was positive in the background, indicating pineal gland tissue (Fig. 2c). No evidence of a neoplasia was identified. Thus, the histologic diagnosis was sarcoidosis of the pineal gland with typical granulomatous proliferation. Post operatively the patient underwent a short course of corticosteroids for treatment. Four years later, the patient was asymptomatic without recurrence on follow up MRI.

Discussion

Approximately 5% of all sarcoidosis cases involve the central nervous system [1–4, 6–11]. Although the meninges, cranial nerves and hypothalamus are frequently involved in neurosarcoidosis [1, 3, 4], pineal gland involvement is extremely rare, having been reported only three times in the peer-reviewed literature [1, 6, 19]. This is the first reported patient with illustrative MRI, CT, and histopathologic immunohistochemistry of pineal gland sarcoidosis with invasive characteristic on imaging mimicking a pineoblastoma.

Formation of granulomas in the central nervous system is the hallmark of neurosarcoidosis, but this characteristic is a rare finding in pineal pathology. The pathophysiology of isolated pineal sarcoidosis may be due to an autoimmune response to the unique milieu of the pineal

gland. The antigens of the pineal gland may represent a unique target for the exaggerated autoimmune response resulting in pineal neurosarcoidosis. The specific etiology of sarcoidosis is unknown.

The CT imaging characteristics of neurosarcoidosis involving the pineal gland are indistinguishable from those of pineal germinomas, as sarcoids are also isodense with homogenous enhancement on CT [1, 6, 20–22]. On CT imaging pineal germinomas appear isodense or mildly hyperdense with uniform contrast enhancement, typically with no calcifications other than normal pineal calcifications [1, 6, 20, 23]. Pineocytomas are typically well defined and non invasive, but our reported lesion mimicked a pineoblastoma with features of pineal tissue invasion [1, 23, 24]. The imaging characteristics of our reported pineal tumor suggested an infiltrative process suggestive of a pineoblastoma.

On MRI, neurosarcoidosis granulomas have been reported as heterogeneous masses (slightly decreased signal compared to adjacent cortical tissue on T1 weighted images) with modest gadolinium enhancement, and with hyperintense signal on T2-weighted images [1, 25, 26]. These usually consist of high intensity signals on T2 weighted images also demonstrating enhancing granulomas, meningeal involvement, paraventricular lesions, and lacunar lesions near corticomedullary junctions [22, 25–30]. The difficulties in diagnosing pineal region neurosarcoidosis with MRI are confounded by the myriad of imaging characteristics associated with neurosarcoidosis [31]. An intra-axial solitary mass lesion (as reported here) is infrequent, seen in only 9% of neurosarcoidosis cases [31–33]. Sarcoidosis of the pineal gland may also be interpreted with imaging characteristics similar to those of pineoblastomas as reported here in these MRI imaging findings. Neurosarcoidosis of the pineal gland is a challenging diagnosis using either CT or MR imaging.

Patients with neurosarcoidosis should be treated with corticosteroids as the mainstay of therapy [4, 34, 35]. Other anti-inflammatory agents can be used if steroids are not tolerated or contra-indicated [4, 36]. Prognosis and clinical course are best determined by clinical presentations [37, 38]. Patients exhibiting mild cranial neuropathies, aseptic meningitis, and solitary mass lesions were noted to have the best outcomes [25, 37, 38].

Our report illustrates that neurosarcoidosis should be considered in the comprehensive differential diagnosis for pineal region lesions, even if the patient has no evidence of systemic sarcoidosis. This rare presentation of sarcoidosis is amenable to steroid treatment with the expectation of good outcomes after diagnosis.

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Fig. 1.

(a) Non-contrast head CT revealing a 1.4-cm pineal region mass with embedded pineal calcifications. (b) MRI imaging revealing a $1.0 \times 1.4 \text{ cm}^2$ T1 hypodense lesion with heterogenous gadolinium contrast and T2 prolongation

Fig. 2.

(a) Hematoxylin and eosin staining demonstrating areas of well circumscribed, compact granulomas (100×) with (b) No necrosis within pineal gland (200×). (c) Immunohistochemistry for synaptophysin demonstrating negative granulomas within synaptophysin positive pineal gland (100×). (d) Immunohistochemistry for CD68 demonstrating well-circumscribed, non-necrotic CD68 positive granulomas within pineal gland (100×)