Neurosarcoidosis is characterized by abnormal inflammation in any part of the nervous system. It is estimated to occur in approximately 5%-15% of patients with sarcoidosis. When the hypothalamus or pituitary gland is involved patients may present with neuroendocrine dysfunction. Without prompt identification and treatment, this can be fatal.

2 | CASE PRESENTATION

A 56-year-old African-American man with past medical history of pulmonary sarcoidosis and neurosarcoidosis diagnosed at age 21 by craniotomy with biopsy presented to the hospital for generalized weakness and slurred speech. On arrival he was hypotensive (81/50 mm Hg), hypothermic (30.8°C), hypoglycemic (40 mg/dL), and bradycardic (42 bpm). He reported poor follow-up for his Sarcoidosis and was not currently on any medications at home. Physical examination revealed an alert and oriented male. His pupils were reactive to light and accommodation. Cardiac exam revealed bradycardic rate (Figure 1), regular rhythm, distinct S1/S2 without murmurs, rubs, or gallops. His lungs were clear to auscultation bilaterally. Extremities had non-pitting edema bilaterally. On neurologic exam, his cranial nerves II-XII were intact. Strength was 5/5 in bilateral upper and lower extremities, sensation was intact throughout all extremities, and Babinski reflex was down going. He was slow to answer questions, which appeared to be secondary to his acute illness and generalized weakness; however, his answers to questions were appropriate. His judgment and fund of knowledge were intact. This neurologic exam was consistent with his prior exams that were documented during previous office visits and hospitalizations. Broad spectrum antibiotics and warm fluids were initiated; however, the patient failed to improve after several days of treatment. Infectious workup was negative, leading to further evaluation for an endocrine cause. Laboratories showed normal thyroid-stimulating hormone (TSH) (0.724 mIU/L), which initially misled to believe that thyroid function was uninvolved in presentation. Further investigation showed a low free thyroxine (FT4, 0.7 ng/dL), suggestive of central hypothyroidism. The patient initially failed a cosyntropin stimulation test but repeated stimulation test with 16-hour infusion produced a positive increase in the cortisol, suggestive of a secondary adrenal insufficiency. LH (<0.1 mIU/mL), FSH (1.0 mIU/mL), free testosterone levels (<0.2 pg/mL), and growth hormone (0.2 ng/mL) were also severely low. Angiotensin-converting enzyme (ACE) level was within normal limits (31 U/L). MRI brain (Figure 2) revealed a 3.0 × 2.1 × 0.7 cm lesion extending into the anterior hypothalamus.
sella turcica (Figure 3). This was significantly larger than the lesion present on the previous MRI performed 8 years prior. This finding was consistent with progression of his neurosarcoïdosis. Treatment was initiated with IV corticosteroids, IV levothyroxine, and testosterone patch. The patient clinically improved and was able to be transitioned to oral corticosteroids, oral thyroid supplementation, and testosterone patch on discharge.

3 | DIFFERENTIAL DIAGNOSIS

The differential diagnosis of neurosarcoïdosis is broad due to the variable nature of its symptoms. Symptoms depend on which anatomic structure sarcoïd lesions involve. Many clinical findings have been reported, for example, it has been shown to manifest as hemorrhagic stroke and as seizures.\(^1\)

A review of approximately 1000 patients with sarcoïdosis revealed a mere 5% went on to have neurologic involvement. In these patients, only one out of every four had a definitive diagnosis made.\(^3\) Different authors have constructed diagnostic criteria; however, only those described by Judson do not require histologic confirmation of neurologic involvement.\(^4\) This set of criteria requires presence of granulomatous inflammation in another organ and having ruled out other alternative causes.\(^5\) Our patient had a known history of neurosarcoïdosis and after testing demonstrated panhypopituitarism was found to have an enlarging mass of the anterior sella turcica. The differential diagnosis can be separated into different categories including neoplastic causes (primary or metastatic tumors), brain damage (traumatic brain injury), congenital (pituitary hormone deficiencies), vascular (cerebral hemorrhage or aneurysm), and infiltrative processes such as amyloidosis or granulomatosis with polyangiitis. Infectious etiologies such as human immunodeficiency virus, neurosyphilis, and tuberculosis should also be considered.\(^6\) A history of pulmonary sarcoïdosis or cutaneous sarcoïd lesions proven by skin biopsy can assist in narrowing the
differential diagnosis. Abnormal endocrine laboratories can lead toward obtaining diagnosis, as well as support the need for brain imaging. However, to obtain definitive diagnosis of neurosarcoidosis, brain biopsy is essential.

4 | TREATMENT AND OUTCOME

Intravenous corticosteroids and hormone supplementation were initiated while the patient was admitted to the hospital, and he dramatically improved. Electrocardiogram changes which previously had shown bradycardia, prolonged QTc, and Osborn waves resolved (Figure 4). He was discharged from the hospital to a physical therapy rehabilitation center to gain strength after being inpatient for over 3 weeks. At 1-month follow-up, the patient continued to do well on therapy. He was still on the regimen and he was discharged on. This included 40 mg prednisone daily, 200 mcg levothyroxine daily, and testosterone patch (2 mg/d). He continues to follow up outpatient with his primary care physician, pulmonologist, neurologist and endocrinologist.

5 | DISCUSSION

Neurosarcoidosis involving the pituitary gland may manifest as panhypopituitarism. Symptoms such as hypoglycemia, hypotension, and weakness can be nonspecific. This makes the diagnosis less recognizable without a high
index of suspicion. Interestingly, our patient also presented with hypothermia which is a rarer manifestation of neurosarcoïdosis. This is suggestive of neurosarcoïdosis causing insult to the hypothalamus and subsequently causing thermodyssregulation. A review of the literature between the years of 2002 and 2014 revealed 64 reported cases of neurosarcoïdosis affecting the hypothalamic-pituitary axis, and of these cases, only 1 case was reported to have caused thermodyssregulation. However, it is possible that simultaneous pituitary and hypothalamic involvement is underreported. Decreased ability for thermoregulation and hypoglycemic response are suggestive of involvement of the median preoptic nucleus and ventromedial nucleus of the hypothalamus. Whereas manifestations of panhypopituitarism could suggest sarcoïdosis in the pituitary gland or in the regions of the hypothalamus that regulate it. When pituitary involvement is suspected endocrine studies and brain imaging are essential; however, biopsy of lesions will give the definitive diagnosis. Histology of the lesions will consist of noncaseating, non-necrotizing epithelioid cell granuloma. Of note, FT4 must be measured if pituitary involvement is suspected, as TSH may be normal in these patients. If panhypopituitarism is suspected, it is imperative to start corticosteroids and hormone replacement to prevent long-term sequelae. Second-line therapy includes immunosuppressive agents.

6 | CONCLUSION

Panhypopituitarism secondary to neurosarcoïdosis is a rare manifestation. However, the inclusion of this condition in the differential diagnosis must be considered in patients with sarcoïdosis or symptoms consistent with neuroendocrine dysfunction. Treatment with corticosteroids and hormone replacement can be lifesaving.

CONFLICT OF INTEREST

None Declared.

AUTHOR CONTRIBUTIONS

MO and PR: conceived the idea for the case report. MO; wrote the first draft of the manuscript. All authors: involved in patient care, provided input, reviewed, and approved the final version of the manuscript.

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