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Systemic Sarcoidosis with Neurosarcoidosis Revealed by Central Diabetes Insipidus

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Abstract:

Neurological involvement in sarcoidosis is rare, often indicative of the disease, and may be the only involvement. It can affect the central or peripheral nervous system or the cranial nerves.

This is a 28-year-old female patient with no particular medical history who consulted for bilateral rhinorrhea and intermittent nasal obstruction that had been developing for 8 months, associated with stage 1 mMRC dyspnea and spaniomenorrhea, developing in a context of apyrexia and preservation of general condition.

Clinical examination revealed cervical lymphadenopathy associated with a subcutaneous nodule on the left arm, with chest CT showing bilateral mediastinal and hilar lymphadenopathy. Staged bronchial, labial, nasopharyngeal, and skin biopsies were consistent with tuberculoid granuloma without caseous necrosis.

Pituitary MRI showed typical neurosarcoidosis involvement revealed by central diabetes insipidus, and a diagnosis of neurosarcoidosis was made.

Keywords: Systemic sarcoidosis, Neurosarcoidosis, Central diabetes insipidus, Spaniomenorrhea, Hypothalamic-pituitary axis, Immunosuppressants.

INTRODUCTION:

Sarcoidosis is a multisystemic granulomatosis of unknown cause characterized by the presence of epithelioid and giant cell granulomas without caseous necrosis. Neurological involvement is rare and can affect any part of the central or peripheral nervous system. It is often indicative of the disease and may be the only site of involvement.

It is marked by its clinical and radiological polymorphism. It therefore poses a real diagnostic and therapeutic challenge.

Case report:

We report the case of a 28-year-old female patient with no particular medical history who has had bilateral crusty rhinorrhea with intermittent nasal obstruction for 8 months, associated with stage I mMRC dyspnea and spaniomenorrhea, developing in a context of apyrexia and preserved general condition.

Clinical examination of the lymph node areas revealed the presence of submandibular, supraclavicular, retroauricular, and left jugulocervical lymphadenopathy measuring 1 cm, firm, painful, and fixed in the

deep plane. examination of the skin and mucous membranes revealed a subcutaneous nodule measuring 1 cm in the middle third of the posterior aspect of the left arm, which was hard, painful, fixed in the deep plane, and without signs of inflammation. The rest of the
physical examination was unremarkable.

The frontal chest X-ray showed chest distension, a large right hilum, a convex mid-cardiac arch, and a straight left cardiac border (Figure 1).

The chest CT scan showed multiple mediastinal lymph nodes (stations 2R + 2L+ 4R+ 4R + 3A + 6) and bilateral hilar lymph nodes (Figure 2).

Histological examination of staged bronchial, accessory salivary gland, and skin biopsies revealed a tuberculoid granuloma without caseous necrosis.

She presented with polyuro-polydipsic syndrome (diuresis at 9350 ml) with a negative diabetes mellitus assessment and hypotonic polyuria with urinary osmolarity at 60 mosm/l becoming > 750 mosm/l after Minirin testing, confirming the diagnosis of central diabetes insipidus.

Pituitary MRI showed typical neurosarcoidosis involvement (Figures 3, 4, 5, 6, 7).

Abdominal and pelvic ultrasound was normal.

To investigate the various disorders of the hypothalamic-pituitary axis and in view of the spaniomenorrhea, the estradiol, FSH, and LH levels were normal. The patient showed no signs of somatotropic insufficiency, thyrotropic insufficiency, corticotropic insufficiency, or hypothyroidism. She had no signs of hypothalamic damage, memory problems, sleep disorders, or appetite problems.

The levels of proteinorachia, prealbumin, alpha 2 and B globulins, IgG, IgG index, and soluble interleukin 2 receptors in the cerebrospinal fluid were normal.

According to the criteria established by Stern and his team, neurosarcoidosis is likely.

Rhinoscopy revealed an inflamed pituitary mucosa with polypoid middle and lower turbinates with crusting, and sinus CT showed a 14 mm cystic lesion in the midline of the nasopharynx, which biopsy confirmed as a tuberculoid granulomatous lesion without caseous necrosis.

The diagnosis reached after a collegial decision: sarcoidosis affecting the chest, nasopharynx, salivary glands, and skin, with probable neurosarcoidosis revealed by diabetes insipidus and spaniomenorrhea.

The patient was placed on oral corticosteroid therapy (prednisone) at a dose of 1 mg/kg/day, or 60 mg/day, with adjuvant therapy, combined with replacement therapy with a desmopressin antagonist at a dose of 60 µg/day. Diuresis reached 3200 ml/day after 15 days of treatment.

The follow-up brain MRI performed after 3 months of corticosteroid therapy did not reveal any abnormalities in the hypothalamic-pituitary axis.

When signs of corticosteroid impregnation appeared (weight gain, facial swelling, excessive hirsutism, acne), the patient was placed on immunosuppressants (azathioprine) as corticosteroid-sparing therapy with tapering corticosteroid treatment.

The outcome after 7 months of corticosteroid therapy with tapering (5 mg/day) and 4 months of immunosuppressant therapy (100 mg/day), with a desmopressin antagonist (60 µg/day), was marked by the disappearance of subcutaneous nodules and peripheral lymphadenopathy, normalization of her urine output with the resumption of a regular menstrual cycle, and the pleuropulmonary examination was essentially normal.

Discussion:

Sarcoidosis is a systemic granulomatous disease of unknown etiology. It is characterized by a wide range of clinical and radiological manifestations associated with multiorgan involvement. Neurological involvement varies between 5% and 40% depending on the series. It can affect the central or peripheral nervous system or the cranial nerves(1)..

Meningeal involvement appears to be symptomatic in only 10% of cases (2). Other patients may go unnoticed, and there is no indication in current guidelines to screen them systematically in the absence of warning signs. Leptomeningitis is associated with an increased risk of hydrocephalus due to obstruction of the ventricles by inflammatory granulomas or infiltration of the meningeal spaces (2).

The pituitary region is rarely affected, and complications include endocrine disorders due to hypopituitarism, most commonly hypogonadism, central hypothyroidism, diabetes insipidus, or isolated hyperprolactinemia.

Optic nerve involvement clinically manifests as a decrease in visual acuity of varying severity, visual field abnormalities, and color vision abnormalities. The visual prognosis is quickly compromised.

Bitemporal hemianopsia due to optic chiasm involvement accounts for approximately 10% of neuro-ophthalmic locations of neurosarcoidosis (2).

These clinical symptoms are non-specific, suggesting neurosarcoidosis with all its differential diagnoses, hence the importance of paraclinical tests, with MRI being the gold standard for confirming the diagnosis. It may show hypersignals in the white matter at the level of the floor of the V4, brainstem, cerebellar peduncles , optic nerves, and hypothalamic-pituitary axis; typically micronodular leptomeningeal enhancement; or complications such as hydrocephalus(3).

Positron emission tomography with 18FDG allows the localization of inflammatory sites, visualization of metabolic activity, and targeting of histological sampling(4).

The CSF study may show lymphocytic meningitis (200 cells/mm3) and hypoglycorrhachia with hyperproteinorrachia greater than 1 g/L. ECA testing has a specificity of 65 to 95% and a sensitivity of 66%; the immunoglobulin G index may be elevated(5).

An electroencephalogram may reveal signs of encephalopathy or percritical encephalopathy. ENMG may reveal signs of large fiber neuropathy or muscle damage (5).

Anatomopathological confirmation, although necessary, is technically challenging to perform and interpret, with a risk of false negatives showing axonal degeneration (6).

To overcome the problems of diagnosing neurosarcoidosis, several proposals have been made since 1999 based on the combination of clinical and paraclinical signs. In 2018, recommendations proposed confirming a diagnosis of neurosarcoidosis based on clinical and paraclinical findings (MRI results, CSF analysis, and/or ENMG) typical of granulomatous inflammation of the nervous system, with neurological histological confirmation of granulomatosis and after exclusion of differential diagnoses(7).

There are currently no randomized trials available on the treatment of neurological sarcoidosis. Several are currently underway. Corticosteroids are the cornerstone of treatment for neurosarcoidosis, often in combination with immunosuppressants.

Neurological manifestations of sarcoidosis are serious: two-thirds of patients are left with motor, sensory, sphincter, or cognitive sequelae. Hormonal deficits caused by involvement of the hypothalamic-pituitary axis are often irreversible, which can be explained by irreversible cellular damage(8).

Conclusion

Neurosarcoidosis remains a rare condition but poses numerous diagnostic problems in the absence of obvious extra-neurological locations. Corticosteroid therapy is the first-line treatment, which may be combined with other immunosuppressants in the event of failure or worsening.

Figure 1: Frontal chest X-ray: Left hilar enlargement with a convex left middle arch and chest distension

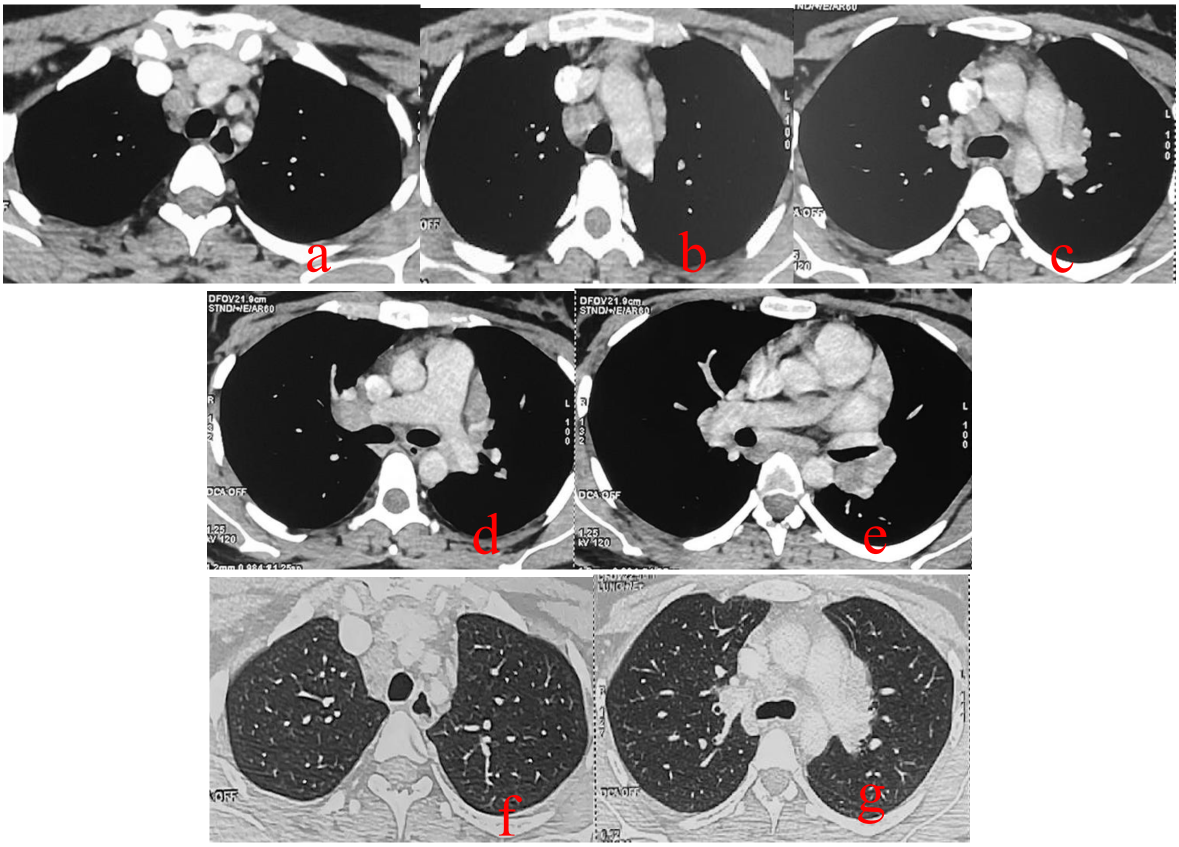

Figure 2: Chest CT scan axial slices of the mediastinal window (a, b, c, d, e): ADP 2R, 4R, 3A, PRECARINARY, BILATERAL HILARY, SYMMETRICAL NON-COMPRESSIVE. Axial slices of the parenchymal window (f, g): No parenchymal involvement

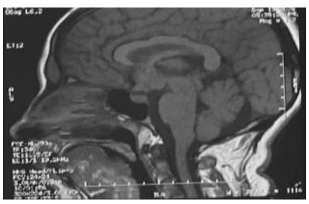

Figure 3: Enlarged anterior pituitary gland with homogeneous signal intensity, intense and homogeneous enhancement after gadolinium injection, loss of T1 hypersignal in the posterior pituitary gland.

Figure 4: Thickening of the pituitary stalk, site of excessive enhancement after gadolinium injection

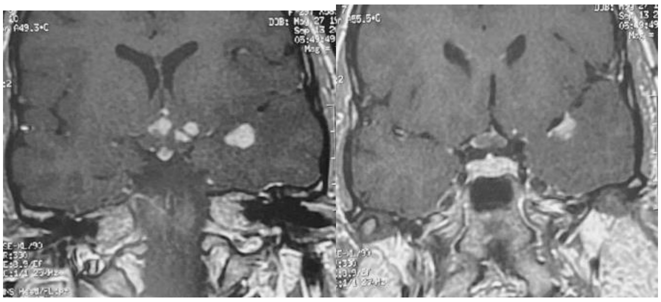

Figure 5: Nodular and patchy infiltration of the hypothalamus, mammillary bodies, optic chiasm, and thalamus with discrete T1 hyposignal and discrete T2 hypersignal, enhanced homogeneously after gadolinium injection

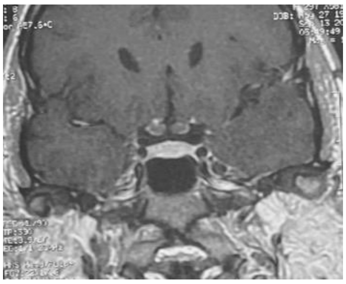

Figure 6: Exaggeration of the elevation of the optic nerves at the prechiasmatic level

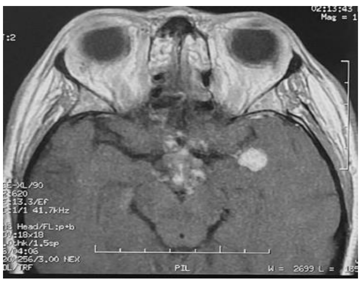

Figure 7: Bilateral frontal temporal leptomeningeal nodular contrast uptake of both peduncles, with iso signal on T1 and T2

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