CASE REPORT

A rare comorbidity: neurosarcoidosis and cutaneous sarcoidosis

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SUMMARY

We present a case of a neurosarcoidosis patient with skin lesions. A 50-year-old woman was admitted with a 1-year history of violaceous, smooth and shiny plaques on her face and right arm. These lesions were biopsied and the histological examination indicated sarcoidosis. The patient had a history of headache and syncope that lasted for about 1 h. Brain CT showed masses measuring 37×20 mm in both frontal lobes. Thoracic and abdominal CT showed many pathologically enlarged lymph nodes. The patient was diagnosed with cutaneous, lung and neuronal sarcoidosis, and treated with 20 mg/day methylprednisolone, 15 mg/week methotrexate, 10 mg/week folic acid, 400 mg/day hydroxychloroquine and 800 mg/day carbamazepine. One month later, the patient's neurological symptoms had improved and her skin lesions had decreased. At 6-month follow-up, the size of the cranial masses had markedly regressed.

BACKGROUND

Sarcoidosis is a granulomatous multisystemic disease that involves the lungs, lymph nodes, skin and nervous system (figure 1). Its cause is unknown. Sarcoidosis shows different local and racial spread patterns. Its diagnosis requires a histopathological finding of non-necrotising granulomas in one or more organ, in the presence of clinical and radiological findings, after excluding other causes of granuloma. Of these cases, 25% present with skin involvement, while 5–15% have nervous system involvement. Neurosarcoidosis is rare; however, it may be life-threatening if it is diagnosed late. It is often difficult to diagnose because patients have non-specific symptoms.

We report a case of a patient who presented with skin findings and non-specific neurological symptoms, and who was diagnosed with neurosarcoidosis based on intracranial MRI.

CASE PRESENTATION

A 50-year-old woman was admitted with a 1 year history of violaceous, smooth and shiny plaques on

her face and right arm. The laboratory results were: erythrocyte sedimentation rate 41 mm/h (normal 0–20), C reactive protein normal (0–3.5 mg/L) and calcium 10.5 mg/dL (8.6–10). The lesions on the patient's face and right arm were biopsied and showed granulomatous structures made up of epithelioid histiocytes, with no central necrosis and no lymphocytes under the epithelium or in the shallow or deep dermis. The granulomas were considered to be sarcoidosis because they were non-necrotising and exposed (figure 2). The patient had a history of headache and syncope that lasted for about 1 h. Her neurological examination was normal. Brain CT showed subcortical oedema in both frontal lobes on supratentorial cuts and massive hypodense oedema in the deep white substance.

Masses with a widest axial diameter of 37×20 mm were seen in both frontal lobes anteriorly and inferiorly. Brain MRI showed a T1-weighted hypointense lesion that reached 12 mm at the thickest place frontally bilaterally and hyperintense leptomeningeal involvement on T2-weighted parasagittal images. The dural and leptomeningeal masses were markedly enhanced after administering a contrast agent. Images consistent with oedema secondary to a pressure effect were observed (figure 3). EEG showed a mildly active epileptiform anomaly in the frontal areas. Thoracic CT showed many axillary and mediastinal lymph nodes, the biggest measuring 19 mm; millimetric nodular pleural thickening was observed at the level of the right apical posterior panacinar infiltration and left superior basal segment (figure 4).

Figure 1 Violaceous, smooth and shiny plaques on the nose and the left cheek.

Figure 2 Granulomatous structures made up of epithelioid histiocytes, with no central necrosis and no lymphocytes under the epithelium or in the shallow or deep dermis (×200 magnification, H&E stain).

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Figure 3 Leptomeningeal and dural sarcoidosis of the brain in a 50-year-old woman. (A) T2-weighted axial image showing bilateral frontal dural masses to be low-signal intensity (arrows), with some high signal of adjacent brain parenchyma, most likely vasogenic oedema (arrowhead). (B) Contrast-enhanced T1-weighted axial image showing extra-axial-enhancing masses of bilateral frontal dura (arrows), and enhancement involving frontal cortical sulci (arrowhead). (C, D) T2-weighted and contrast-enhanced T1-weighted axial images obtained after therapy showing marked decrease in the size of bilateral frontal dural masses (arrows). Vasogenic oedema and enhancement involving frontal cortical sulci disappeared.

It was considered to be sarcoidosis with lung involvement. Abdominal CT showed that the liver was 160 mm long vertically and revealed many pathological-appearing lymph nodes, the largest measuring 18×14 mm in the left external iliac group and 26×13 mm in the right external iliac group.

DIFFERENTIAL DIAGNOSIS

The violaceous plaques on both cheeks and the nose, along with neurological symptoms, suggested a collagen tissue disease, such as systemic lupus erythematosus (SLE), which has both skin and central nervous system (CNS) involvement. The patient's

Figure 4 (A) Transverse CT image of the chest with mediastinal window setting showing bilateral hilar lymphadenopathy (arrows). (B,C) Transverse CT images of the chest showing micronodules along bronchovascular bundle (arrow), reticular density (arrow). (D) Transverse CT image obtained after therapy showing marked decrease in the size of reticular density (arrow).

advanced age made a diagnosis of SLE less likely, although late-onset SLE is possible. A diagnosis of SLE was not considered, because our patient lacked other clinical findings of SLE or laboratory findings such as leucopaenia, lymphopaenia, proteinuria and haemolytic anaemia, and was negative for SLE autoantibodies. Skin and CNS involvement can be seen in sarcoidosis. A lupus pernio appearance is typical of sarcoidosis, especially on the face. The skin lesion on our patient's face matched that of lupus pernio.

TREATMENT

The patient was diagnosed with cutaneous, lung and neuronal sarcoidosis, and treated with 20 mg/day methylprednisolone, 15 mg/week methotrexate, 10 mg/week folic acid, 400 mg/day hydroxychloroquine and 800 mg/day carbamazepine.

OUTCOME AND FOLLOW-UP

One month later, the patient's neurological symptoms had improved, as had the lesions on her arms, while the lupus pernio appearance of the face remained, although it had decreased. At 6-month follow-up, the cranial masses had markedly regressed (figure 3). The patient is still under treatment.

DISCUSSION

Sarcoidosis is a multisystem disease. It has a bimodal peak incidence at 25–35 and 45–55 years of age, and it is more common in women.¹ Skin involvement is seen in 25% of cases.² The skin lesions of cutaneous sarcoidosis are non-specific and specific lesions such as maculopapular, nodular, plaques, infiltrated scars, lupus pernio and erythroderma, which are more common in chronic diseases, often indicate a poor prognosis.³ Our patient reported violaceous, smooth and shiny plaques that started on her forehead 1 year earlier, and then appeared on both cheeks, the nose and right arm in the last 5 months. The lesions on the face were considered to be lupus pernio. Clinical involvement of the nervous system is seen in 5–15% of cases.⁴ The most common clinical symptoms in these patients are cranial neuropathies, especially of the seventh cranial nerve (50–75%). Other findings include facial paralysis, aseptic meningitis, hydrocephaly, endocrinopathy, encephalopathy, intracranial mass and myopathy. There are few reports of cases with sarcoidosis and an intracranial mass. Ortega *et al*⁵ reported four cases of neurosarcoidosis with intracranial involvement: a lesion involving the hypothalamus, a mass in the brain parenchyma, leptomeningeal involvement and a focal white matter lesion. Our patient had a contrast-enhancing mass in both frontal lobes with dural and leptomeningeal involvement (figure 3). In cutaneous sarcoidosis, cases of lupus pernio tend to be resistant to treatment. Other forms of cutaneous sarcoidosis are quite varied and demonstrate a fair to good response to therapy, depending on morphology, extent and location. Although topical steroids are used for local lesions, they do not have good tissue penetration. Multiple and progressive lesions require systemic treatments, such as steroids, methotrexate and hydroxychloroquine.

Patients with neurosarcoidosis can have a monophasic illness (approximately two-thirds of patients), a relapsing-remitting course, or progressive disease punctuated by episodic deteriorations.^{6–8} Monophasic disease can be treated with short-term steroids. If the disease continues and enters a chronic period, a disease activation evaluation should be made again after low-dose steroid treatment. If there is persistent disease and relapsing-remitting processes, treatment should be continued with oral steroid dosage adjustment. However, during persistent disease and progressive processes, other immunosuppressive

treatment methods, intravenous steroid and, if needed, surgical treatment options, should be taken into account. In the case of a lack of response to pharmacological treatment or a contraindication to surgical procedure, cerebral radiotherapy is recommended.⁹ Steroid doses in neurosarcoidosis are higher than those advised for the treatment of other localisations of sarcoidosis. In general, the initial recommended dose is 40 mg daily, whereas in neurosarcoidosis, an initial dose of 1 mg/kg/day is typically recommended. In severe cases, high doses of intravenous methylprednisolone may be used for a few days to obtain a high initial loading dose. Some may use bolus pulsed methylprednisolone once a week, eventually along with daily low doses of oral prednisone, or alternate day treatment; to avoid the side effects associated with long-term, high-dose oral treatment, dose and duration of therapy should be dictated by disease severity and response to therapy.¹⁰ Our patient was reporting of skin lesions on hospital admission. She did not have a severe disease manifestation except for headache and one h syncope history as neurological status. Because of this, we preferred low-dose steroid treatment instead of intravenous or pulse steroid treatment. In the follow-up, as skin lesions partially declined and neurological symptoms did not repeat, methotrexate and hydroxychloroquine were added, and the treatment was continued. Tumour necrosis factor is released at high concentrations by alveolar macrophages from patients with active sarcoidosis, and the concentrations go down with corticosteroid or methotrexate therapy.¹¹ Infliximab has been shown to be effective in a few cases with refractory sarcoidosis. In refractory neurosarcoidosis, it may also be effective.¹²

Combined neurosarcoidosis observed as a mass in the brain and cutaneous sarcoidosis is rare. Our patient was admitted with typical skin lesions. The lymphadenopathy seen on thoracic and abdominal CT, nodular pleural thickening and elevated calcium in serum aided the diagnosis, and the definitive diagnosis was made with a skin biopsy. Neurosarcoidosis was diagnosed after a mass was found in the cranial images taken because of neurological symptoms; these images complied with the cranial involvement of sarcoidosis. Without a dural biopsy, it is not possible to make a definitive diagnosis of neurosarcoidosis; however, as there was no other logical reason to explain the mass, it was accepted as neurosarcoidosis. If the patient had been admitted with a cranial mass only, regardless of the systemic findings, a biopsy would have been required for a diagnosis.

Learning points

- ▶ Not all intracranial masses are associated with malignancy; they can include a neurosarcoidosis intracranial mass.
- ▶ Lupus pernio is a skin lesion seen in sarcoidosis, and finding non-calcified granulomatous areas in a biopsy is important for the diagnosis.
- ▶ Sarcoidosis is a multisystem disease and assessment is very important in patients with non-specific neurological symptoms.
- ▶ Neurosarcoidosis can be treated successfully with methotrexate, hydroxychloroquine and low-dose steroids.

Competing interests None declared.

Patient consent Obtained.

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