A rare manifestation of sarcoidosis with sensomotoric neuropathy of the ulnar nerve as the only symptom

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SUMMARY

A 79-year-old woman was admitted complaining of progressive weakness and numbness of the right hand. The patient was otherwise healthy. The patient's history was unremarkable. Clinical and electrophysiological examination revealed a compression of the ulnar nerve in the ulnar sulcus and in Guyon's canal. Ultrasound evaluation showed a suspicious tumour proximal to the elbow close to the ulnar nerve. The ulnar sulcus was then released and an epineural and perineural lesion 3–4 cm proximal to the sulcus was excised under microscope. The histopathology confirmed the lesion as non-caseating sarcoid granulomas. The patient showed no other signs of systemic sarcoidosis, as neuropathy was the only symptom and the condition improved postoperatively. Sensory deficits and paraesthesia resolved fully. The extension of the minor finger remained slightly inferior compared with the not affected side. Sarcoid neuropathy is a rare neurological complication of sarcoidosis and has to be included in differential diagnosis of nerve conduction impairments.

Criteria upon which clinical diagnosis of neurosarcoidosis is made have not been firmly established. Positive nervous system histology is defined by the presence of sarcoid type granulomas with epithelioid cells and macrophages in the centre of non-caseating lesions surrounded by lymphocytes, plasma cells and mast cells and defines the diagnosis.¹

Peripheral neuropathy occurs in 4–20% of patients with neurosarcoidosis.⁸ The ulnar and peroneal nerves were most commonly affected.¹¹ Patients can present with mononeuritis or mononeuritis multiplex, sensorimotor distal polyneuropathy and even a Guillain-Barre syndrome.^{12–14} Pathologically, the neuropathy has been attributed to epineural and perineural granulomas with an associated granulomatous vasculitis, producing axonal degeneration and demyelination.¹⁵

The outcome of peripheral neuropathy is much more favourable than sarcoidosis of the central nervous system. Systemic sarcoidosis has often been responsive to systemic corticosteroid treatment. Surgery is indicated in expanding mass lesions with progressive worsening of the neurological deficits.

BACKGROUND

Sarcoidosis is a multisystemic granulomatous disease of unknown aetiology, which has a propensity for the lungs and relatively rarely the nervous system.¹ Genetic susceptibility in some individuals exposed to certain unknown environmental factors has been proposed as a potential aetiological factor for sarcoidosis.²

Prevalence rates for sarcoidosis vary widely from greater than 50 per 100 000 in Afro-Americans to under 10 per 100 000.^{3–5} That the disease is frequently asymptomatic is suggested by a Scandinavian study.⁶ Only about 5% of sarcoid patients develop symptoms of the nervous system.⁷

Neurosarcoidosis has variable manifestations and can overshadow many other diseases⁸ as it can affect any part of the neuraxis. It can involve a combination of intracranial structures, cranial nerves, spinal cord and its coverings as well as peripheral nerves and muscles.⁸ Depending on the location of the granulomas in the neuraxis, the symptomatology reflects the neuroanatomical structures compromised. The facial nerves are most commonly involved and multiple nerves are often affected.⁹

The frequency of peripheral nerve involvement in sarcoidosis is uncertain but there seem to be many asymptomatic cases.¹⁰ Zajicek¹ proposed diagnostic criteria with levels of certainty and these criteria are commonly used.

CASE PRESENTATION

A 79-year-old woman was referred to our centre with a progressive loss of grip strength for 4 months of the right hand with numbness of the fourth and fifth finger. On examination, she had asymmetric weakness of the upper extremity. Muscle strength of the abductor digiti minimi and interossei muscles was graded as 3/5. There was a moderate decrease in touch and vibration sensitivity. The patient was otherwise healthy and had no signs of a systemic disease. Neurological examination and patient's history were unremarkable. The electrophysiological evaluation revealed a compression of the ulnar nerve in the ulnar sulcus as well as in Guyon's canal. Therefore, the indication for a release on both localisations was given. Preoperatively, an ultrasound evaluation of the nerve was performed and revealed a tumorous lesion 3–4 cm proximal to the elbow. The operation was performed under plexus anaesthesia. An opening of Guyon's canal was performed, but revealed no signs of entrapment. The ulnar sulcus was then released but showed macroscopically no signs of entrapment, but the nerve had a tumorous lesion, which was epineural and perineural (figure 1). The lesion was excised under magnification with microscope and the tissue was sent for histopathological evaluation (figure 2). The histopathological study confirmed the lesion as

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Figure 1 Tumorous lesion approximately 3 cm proximal to the ulnar sulcus attached to the nerve.

noncaseating sarcoid granuloma (figures 3 and 4). Chest x-ray showed no features of hilar lymphadenopathy or pulmonary infiltrates. The patient's condition improved continuously within 4 weeks postoperatively. Sensitive sensations resolved fully. The extension of the fifth finger remained slightly inferior compared with the not affected side. A corticoid therapy was not initiated because of remarkable postoperative improvement without systemic symptoms.

INVESTIGATIONS

An electrophysiological evaluation was performed that revealed a conduction impairment of the right ulnar nerve in Guyon's canal and the ulnar sulcus. Electrophysiological studies showed lack of excitability of ulnar nerve and reduction in amplitude of the muscle potential and spontaneous fibrillations of hypothenar and flexor carpi ulnaris muscle.

Preoperative ultrasound of the nerve showed a tumorous lesion proximal to the ulnar sulcus. Intraoperatively, the nerve showed a mass directly connected to the nerve, which was compressing the nerve. The lesion was excised under microscope magnification and the tissue was histopathologically evaluated. A sarcoid granuloma was confirmed. Special stains such as Ziehl-Neelsen, Gracott and PAS revealed no specific bacterial or fungal causes.

The sarcoid lesion is characterised by the well-defined appearance of a rounded collection of large epithelioid cells with pale

Figure 2 Ulnaris nerve after excision of epineural and perineural mass with fusiform swelling.

Figure 3 Non-caseating granuloma (H&E stain, magnification $\times 50$).

staining nuclei by a scarcity of lymphocytes located mainly in the periphery and by the absence of caseation or necrosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for ulnar neuropathy includes entrapment in Guyon's canal and ulnar sulcus.

Preoperative radiographical x-ray or ultrasound evaluation is recommended to find out external compression reasons.

A diagnosis of neurosarcoidosis is often difficult. The nervous system is a relatively uncommon site for the disease to manifest and as a consequence, investigation to establish a diagnosis has centred on searching for histological confirmation in other organs. In order to fulfil conditions for definite disease the patient must have an appropriate clinical syndrome with positive nervous system histology in the absence of any other cause.¹

Clinical features similar to those of neurosarcoidosis are Lyme disease, Wegener granulomatosis, tuberculosis and lymphomatosis.

TREATMENT

As the neurological deficit was progressive and the ultrasound evaluation revealed a mass proximal to the ulnar sulcus, the indication of surgical exploration was given to release the nerve. We did not suspect a sarcoid at indication of surgery, as the

Figure 4 Non-caseating granuloma with epithelioid cells and macrophages in the centre surrounded by lymphocytes, plasma cells and macrophages (H&E stain, magnification $\times 100$).

patient had no systemic disease. The mass was epineural and perineural and histopathology of the excised lesion confirmed the diagnosis of a sarcoid with typical histological features. As the patient improved after surgery and had no systemic signs of sarcoidosis steroid therapy was not initiated. The sensory function resolved fully. Motoric function of the fifth finger was impaired possibly due to the long time between initiation of symptoms and operation.

Most patients are treated with systemic corticosteroids, which often carry significant side effects, as dosages tend to be high and prolonged. They should eventually be treated with the lowest dose required to maintain benefit.

OUTCOME AND FOLLOW-UP

The patient's condition improved continuously within 4 weeks postoperatively. Sensitive impairment resolved fully. The extension of the fifth finger remained slightly inferior compared with the not affected side. A rehabilitation therapy was started although the patient was satisfied with the function of the hand. A full flexion of the fourth and fifth finger was possible and grip strength was equal to the not affected side. A corticoid therapy was not initiated because of postoperative improvement without systemic symptoms. In case of additional symptoms or remitting symptoms a systemic corticoid therapy will be initialised.

DISCUSSION

Infiltration of peripheral nerves due to sarcoidosis is usually difficult to demonstrate and its clinical picture depends upon the site of involvement. The neuropathic symptoms involving peripheral nerves can also be transient and the diagnosis therefore can be missed or delayed.

In our patient, epineural and perineural sarcoid granulomas caused direct compression and distortion of nerve fibres morphologically. Nerve compression can induce focal demyelination that presents as conduction block as well as causes axonal degeneration.

Fusiform swellings of the median, radial and ulnar nerve are described at autopsy.¹⁶ Oh¹⁵ described another non-caseating granuloma according to sarcoidosis in sural nerve causing polyneuropathy of the lower limb.

Direct infiltration of sarcoid granuloma thus appears to be the pathological basis for sarcoid neuropathy. Oh¹⁵ stated that axonal degeneration is the secondary result of panangitis and periangitis as well as a compression by perineural sarcoid granuloma.

The mechanism of neuropathy is often uncertain but could be due to compression by granulomas and immune factors with either axonal loss or demyelination.

As we perform preoperative ultrasound evaluation routinely in patients with nerve conduction impairments, the tumorous lesion proximal to the cubital tunnel was detected preoperatively. Therefore, an open approach to the cubital tunnel was chosen. A suspected tumour precludes endoscopic cubital tunnel release. A trial of conservative treatment like elbow splinting in rapidly developing tumorous lesions is contraindicated.

We believe that sarcoidosis has caused ulnar neuropathy as the initial symptom in our patient.

Most patients with neurosarcoidosis are those with previously diagnosed systemic sarcoidosis who develop signs of neurological involvement in the course of their illness. Rarely is neurological involvement the initial sign.

The response to steroids is usually good and they are the most frequently used therapy. They should be reserved for symptomatic stages as there are possible side reactions. Since the patient's condition improved postoperatively, a steroid therapy was not initiated.

This is an example of sarcoid neuropathy that showed histological non-caseating granulomas and was mimicking ulnar nerve entrapment in the ulnar sulcus.

Awareness of this disease in patients with nerve conduction impairment is important.

Learning points

- ▶ Neurosarcoidosis has variable manifestations and can overshadow many other diseases⁸ as it can affect any part of the neuraxis.
- ▶ Histological examination defines the diagnosis in neurosarcoidosis which can be difficult to achieve.
- ▶ Peripheral nerves can be affected in 4–20% of patients with neurosarcoidosis⁸ but can be asymptomatic in many cases.
- ▶ The outcome of peripheral neuropathy is much more favourable than sarcoidosis of the central nervous system. Systemic sarcoidosis has often been responsive to systemic corticosteroid treatment.
- ▶ Surgery is indicated in expanding mass lesions with progressive worsening of the neurological deficits.
- ▶ Preoperative ultrasound evaluation or MRI in case of entrapment syndromes can reveal tumorous lesions or mechanical reasons for nerve conduction impairment. Preoperative planning has to be adapted to these findings.

Competing interests None.

Patient consent Obtained.

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