A pragmatic approach to diagnosing and treating neurosarcoidosis in the 21st century

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Purpose of review

Neurosarcoidosis may be a serious complication of sarcoidosis. As the presentation of neurosarcoidosis is manifold, solitary nervous system sarcoidosis without systemic activity remains a difficult diagnosis. Appropriate treatment may be a dilemma.

Recent findings

Most neurosarcoidosis patients present with neurological symptoms as the first manifestation. Whole-body fluorodeoxyglucose positron emission tomography has been found useful in neurological patients suspected of sarcoidosis. Small-fiber neuropathy is commonly associated with sarcoidosis and can cause significant morbidity to afflicted patients. New drugs such as antitumor necrosis factor α have been proven valuable in the treatment of neurosarcoidosis in different locations. Progressive multifocal leucencephalopathy should be considered in neurosarcoid patients, especially when treatment fails.

Summary

In this paper an update on clinical manifestations of neurosarcoidosis, diagnostic dilemmas, and therapeutic options is provided.

Keywords

diagnosis, neurosarcoidosis, therapy

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Introduction

Sarcoidosis is an inflammatory multisystem disorder of unknown origin. Neurosarcoidosis can involve any part of the nervous system. The incidence in a sarcoidosis population is estimated at approximately 5–15%.

Evidence of neurosarcoidosis or the exclusion of it remains difficult, especially as previous studies reported that in the majority of patients the first manifestations of neurosarcoidosis are neurological symptoms [1••,2,3••].

Prospective studies on neurosarcoidosis are scarce. Neurosarcoidosis is rare; most papers report small numbers of patients or case reports. Consequently, multicenter studies are needed to gain more insight into this manifold disease. In this paper we propose a pragmatic diagnostic and therapeutic approach based on personal opinion and the present available data.

Neurological manifestations of sarcoidosis and its differential diagnostic considerations

The presentation of neurosarcoidosis is manifold, including any part of the nervous system.

Cranial neuropathy

Cranial neuropathy appears as the most frequent neurological complication of sarcoidosis. The facial and optic nerve are the most commonly affected cranial nerves. Facial nerve palsy may occur bilaterally. In cases initially presenting with bilateral facial nerve palsy neurosarcoidosis as well as Lyme disease will considered early in the differential diagnosis. In the differential diagnosis evidence of Borrelia in the cerebrospinal fluid (CSF) will be helpful.

Sarcoidosis of the optic nerve may occur without systemic involvement [4]. In these cases differentiation from multiple sclerosis is difficult (Table 1). CSF analysis may help to differentiate: a dysfunction of the blood–brain barrier, high CSF–angiotensin converting enzyme (ACE) and intrathecal production of not only IgG but also isolated IgA are uncommon in multiple sclerosis (MS) and should initiate the search for another underlying disease [5]. Finally, in an atypical progressive course, one should keep neurosarcoidosis in mind. Optic nerve biopsy may be considered. Optic nerve involvement in sarcoidosis is associated with poor prognosis for visual recovery [6], especially the chronic-type and bilateral lesions. The acute type responds better to prednisone

Table 1 Different features in inflammatory diseases of the central nervous system

Features	Neurosarcoidosis	MS	Sjögren's syndrome	Lupus erythematodes	Behçet's disease	infections
Hypercalcemia	Present <15%	Absent	Absent	Absent	Absent	May be present
Uveitis	Present 25%	Absent	May occur	May occur	May occur	May be present
Genitooral aphthae	Absent	Absent	Absent	Absent	97%	Absent
Facial nerve involvement	May occur	May occur	Rare	Rare	Absent	Absent
Meningitis	May occur	May occur	May occur	May occur	May occur	May occur
CSF–ACE	Present	Absent	Absent	Absent	Absent	Absent
CSF lysozyme	Present	Absent	Absent	Absent	Absent	Present
CSF cell count	May be >50/μl	Normal 50/μl	Normal 50/μl	Rarely >50/μl	Normal 50/μl	Usually >50/μl
CSF glucose quotient	May be decreased	Normal	Normal	Normal	Normal	May be decreased
CSF oligoclonal IgG	Frequently present; suppressed during corticosteroid therapy and diminish during course of disease	Frequently present; stable during corticosteroid therapy	Frequently present; suppressed during corticosteroid therapy and diminish during course of disease	Frequently present; suppressed during corticosteroid therapy and diminish during course of disease	Frequently present; suppressed during corticosteroid therapy and diminish during course of disease	May be present
Serum	Elevation of soluble interleukin-2 receptor	Normal	ENA SS-A or SS-B antibodies	ANA, ds-DNA-Ab, ACLA	Often HLA-B51 positive; CRP and BSG mostly elevated	CRP and BSG may be elevated

ACE, angiotensin converting enzyme; ACLA, anti-cardiolipin antibodies; ANA, anti-nuclear antibody; BSG, bovine serum globulin; CRP, C-reactive protein; CSF, cerebrospinal fluid; ds-DNA-Ab, double-stranded DNA antibody; ENA, extractable nuclear antigen; HLA, human leukocyte antigen.

therapy. Newer drugs such as anti-tumor necrosis factor alpha (anti-TNF-α) therapy may be considered early in chronic and refractory sarcoidosis as good results have been published [7].

Other cranial nerves may be affected as well. The prognosis of lower cranial nerves appears good.

Aseptic meningitis

Meningeal symptoms may be acute or chronic. The chronic type is more difficult to recognize. CSF glucose levels may be low in about one-fifth of the patients. The basal meninges may be affected, resulting in cranial neuropathy. Chronic meningitis is often recurrent and requires long-term therapy, whereas acute meningitis responds favorably to corticosteroids.

Hydrocephalus

Hydrocephalus is rare and may occur due to impaired absorption or obstruction. Altered brain tissue compliance with impairment of normal pulsatile augmentation of aquaduct CSF flow may also cause obstructive hydrocephalus in sarcoid patients with hydrocephalus in which no mass lesion or abnormal enhancement can be found [8]. Therefore, in case of idiopathic communicating hydrocephalus neurosarcoidosis should be considered.

Cerebral sarcoid lesions

Granulomas may remain small [9] or form large intracranial tumors [10] and may be single or multiple. They can occupy extradural, subdural, and parenchymatous locations. Occasionally, periventricular white matter lesions are observed. The latter may resemble multiple sclerosis or vascular changes. Whether these lesions are related to sarcoidosis may frequently be questioned. Shah and co-workers [3••] found that nonenhancing parenchymal lesions often did not correlate with symptoms and that these lesions did not improve or worsen after follow-up. Thus, asymptomatic periventricular white matter lesions without meningeal enhancement in sarcoidosis patients more than 50 years of age are most likely not due to sarcoidosis and can often be regarded as age-related small-vessel disease.

The clinical features of mass lesions are similar to any space-occupying intracranial mass. Granulomatous lesions are relatively frequently found in the hypothalamus and/or pituitary gland. This may cause endocrine manifestations, such as diabetes insipidus, adenopituitary failure, amenorrhea–galactorrhea syndrome, isolated or in various combinations.

Granulomatous cerebral angiitis also occurs in sarcoidosis [11]. Ophthalmologic screening may be helpful in uncovering angiitis. Diffuse cerebral vasculopathy may

produce psychosis, dementia, and epileptic seizures. Stroke-like episodes may also occur.

Seizures

Seizure as a result of cerebral lesions may be the first manifestation of neurosarcoidosis; any type of seizure may occur. The presence of seizures is often thought to reflect serious brain pathology and poor prognosis. The latter was, however, not supported in a recent study in 30 new cases [1••].

Psychiatric symptoms

Granulomatous infiltration of the CNS may produce a wide variety of mental symptoms. In a patient with multisystem sarcoidosis and unexplained mental deterioration evaluation of the CNS is indicated. A subset of sarcoidosis patients report memory problems, without objective deterioration or neurological deficit. This is also the case in other inflammatory diseases such as multiple sclerosis. These types of amnestic problems might be related to fatigue and concentration problems more than cerebral lesions.

Spinal sarcoidosis

Spinal sarcoidosis encompasses a spectrum of intraspinal diseases, including arachnoiditis, extradural and intradural extramedullary lesions, and intramedullary lesions. Granulomas involving the spinal cord are often clinically and radiologically indistinguishable from a malignant tumor.

Peripheral neuropathy

The clinical and pathological spectrum of sarcoid neuropathy is wide and includes multiple mononeuropathies, polyradiculopathy, Guillain–Barré syndrome, and symmetric distal polyneuropathy [12]. Epineural and perineural granulomas and granulomatous vasculitis can cause ischemic axonal degeneration and demyelination due to local pressure. Nerve biopsy may be helpful in diagnosing problems. In most patients the clinical course of sarcoid neuropathy is subacute, and according to the literature many patients seem to respond to corticosteroid therapy. In our experience weakness due to large fiber involvement indeed frequently improves after corticosteroid treatment, but symptoms of small fiber neuropathy appear resistant to corticosteroids.

Small fiber neuropathy

Recently, small fiber neuropathy was demonstrated in sarcoidosis [13,14••] and appeared to be relatively frequent [15]. However, as standard nerve conduction tests evaluate only large nerve fiber function and quantitative techniques for the assessment of small nerve fibers are not routinely applied, the diagnosis of small fiber neuropathy can easily be missed. If not recognized, the following symptoms suggestive of small fiber neuropathy may be an enigma to both patient and doctor:

(1) Sensory symptoms
  (a) Pain
  (b) Paresthesias
  (c) Sheet intolerance
  (d) Restless legs syndrome
(2) Symptoms of autonomic dysfunction
  (a) Hypo- or hyperhidrosis
  (b) Diarrhea or constipation
  (c) Urinary incontinence or retention
  (d) Gastroparesis
  (e) Sicca syndrome
  (f) Blurred vision
  (g) Facial flushes
  (h) Orthostatic intolerance
  (i) Sexual dysfunction

Diagnosis

Virtually every neurological problem could in fact be due to neurosarcoidosis, and the list of differential diagnosis of neurosarcoidosis is long:

(1) Infectious diseases
  (a) Leprosy
  (b) Tuberculosis
  (c) Whipple's disease
  (d) Toxoplasmosis
  (e) Mycosis
  (f) Helminthic infections
  (g) Treponemal infections
  (h) Lyme disease
  (i) Human polyoma virus (JC-Virus) [progressive multifocal leucencephalopathy (PML)]
(2) Granulomatous diseases
  (a) Wegener's granulomatosis
  (b) Churg–Strauss syndrome
  (c) Lymphomatoid granulomatosis
(3) Tumors
  (a) Neurolymphomas
  (b) Gliomas
  (c) Meningeomas
  (d) (Leptomeningeal) metastases
(4) Vasculopathies
  (a) Vasculitis
  (b) Behçet's disease
(5) Systemic diseases
  (a) Amyloidosis
(6) Chronic subdural hematoma
(7) Neurological diseases
  (a) Multiple sclerosis
  (b) Acute demyelinating encephalomyelitis

Table 2 Diagnostic criteria for neurosarcoidosis according to Zajicek *et al.* [2] and Marangoni *et al.* [16]

	Zajicek criteria	Marangoni-modified criteria
'Certain NS'	Positive nervous system histology	Positive nervous system histology
'Probable NS'	Signs of inflammation in the central nervous system, positive histology for a systemic lesion, or a positive Kveim–Silzbach test and/or positive results for at least two of the following tests: Ga scan, serum ACE level and chest radiology	Signs of inflammation in the central nervous system, positive histology for a systemic lesion, and/or positive results for at least two of the following tests: Ga scan, chest HRCT, BAL with a CD4 : CD8 ratio >3.5 and a CD4 : CD8 ratio >5 in the CSF
'Possible NS'	Absence of histological confirmation and ruling out other inflammatory pathologies	Absence of histological confirmation and ruling out other inflammatory pathologies

ACE, angiotensin converting enzyme; BAL, bronchoalveolar lavage; HRCT, high resolution computer tomography; NS, neurosarcoidosis.

Only few combinations of features are clinically suggestive of neurosarcoidosis (Table 1). The diagnostic procedure should always aim to locate a site of disease that is accessible to biopsy. In our opinion diagnostic evaluation should include neuro-imaging, CSF examination including CD4 : CD8 ratio, and chest HRCT. If no suitable site for biopsy can be found, ophthalmological assessment (conjunctival biopsy) may be considered, and fluorodeoxyglucose positron emission tomography (FDG-PET) scanning to search for occult inflammation. Zajicek and colleagues [2] formulated a series of diagnostic criteria for neurosarcoidosis, which were later modified by Marangoni and colleagues [16] (Table 2).

Diagnostics in the search for 'sarcoid activity': neuro-imaging

MRI is the most sensitive diagnostic tool in detecting and localizing central nervous system lesions. These tests, however, are not specific as radiological expressions are highly variable. Differential diagnosis with malignancies such as lymphoma and glioma may be difficult [10,17]. Furthermore, the occurrence of PML in sarcoid patients is reported, often regarded as neurosarcoidosis at first [18,19•]. The occurrence of PML in patients without immunosuppressive treatment may be caused by impaired cell-mediated immunity in sarcoid patients (sarcoid patients show an absolute decrease in T-lymphocytes, by increased CD4 : CD8 ratio and B-cell activity). Whether the occurrence of PML in sarcoidosis will increase with the use of new immunosuppressants such as anti-TNF therapy is as yet unknown.

In a recent study by Shah *et al.* [3••] different MR imaging findings were assessed. A relatively typical imaging feature proved to be thickening and enhancement of the basilar leptomeninges of the brain and dural involvement. In contrast, nonenhancing white matter lesions were unlikely to correlate with symptoms. From the clinical point of view, patients presenting with dysphagia, hearing loss, movement disorder and memory loss did not have correlating imaging lesions.

Chest imaging

Marangoni *et al.* [16] described seven neurosarcoidosis patients. In all chest radiography was performed and normal, whereas in six of them high resolution computer tomography (HRCT) was performed and four of these six were compatible with sarcoidosis. Therefore, on the basis of this small group of patients, chest radiography appears to have very low sensitivity to reveal pulmonary involvement in a group of neurosarcoidosis patients whereas HRCT appears a better tool. On the other hand, chest CT may be normal but a fluorodeoxyglucose positron emission tomography (FDG-PET) scan does reveal lymph node inflammation [20••].

Whole-body Gallium scanning and FDG-PET scanning

Whole-body Gallium (Ga) scanning or FDG-PET scanning can be utilized to search the whole body for occult inflammation or neoplasia and therefore find suitable sites for biopsy. It is important to remember that whole-body Gallium scanning is insensitive for detection of CNS involvement: it shows uptake in fewer than 5% of CNS lesions, but may detect other systemic disease in 45% of patients with CNS involvement [2]. The use of such scanning is limited by poor specificity, as intravenously injected Ga-67 is taken up not only by sites of active sarcoidosis but also by other inflammatory and neoplastic processes [21]. Recent studies have demonstrated FDG-PET scan as a promising alternative due to greater sensitivity than Gallium-67 scintigraphy for detection of systemic sarcoid lesions, especially lymph node inflammation [20••]. Other advantages of FDG-PET are higher spatial resolution and faster uptake of the radiopharmaceutical that enables images within 2 h, whereas Gallium-67 scanning has to be performed approximately 8–72 h after injection [22]. In spite of these advantages, the finding of lymphoid hypermetabolism by FDG-PET imaging is not specific and still shows limitations, especially regarding differentiation between sarcoidosis and lymphoma [20••].

Conjunctival biopsy

Conjunctival biopsy, a technically simple, inexpensive, and safe method, may also be used for diagnosis. Given that as many as 54.1% of patients with sarcoidosis will have ocular abnormality, it is worthwhile to refer suspected cases for opthalmological assessment and to consider conjunctival biopsy as a method of tissue diagnosis [23].

Serum angiotensin converting enzyme

Serum levels of ACE are not specific for detecting neurosarcoidosis as they can be elevated in a number of disorders, including diabetes, silicosis, and cirrhosis [21]. Again, this test is not very sensitive. Patients with neurosarcoidosis have been reported to have elevated serum ACE in 5–50% of the cases [21,24].

Serum IL2R

Interleukin-2 receptor (IL2R) is a measure of T-cell activation and may be increased in sarcoidosis. However, also in case of lymphoma and MS IL2R may be increased. Serum IL2R is better in monitoring disease activity than the more commonly used serum ACE [25,26]. The value of CSF-IL2R has yet to be established.

Cerebrospinal fluid

Routine CSF abnormalities are usually nonspecific inflammatory and include mild pleocytosis, increased protein content and sometimes mildly decreased glucose levels. Furthermore, elevations of ACE, IgG-index, oligoclonal bands, CD4:CD8 lymphocyte ratios, lysosyme, and β2-microglobulin levels in CSF have been reported. About one-third of the patients with neurosarcoidosis have normal CSF examinations [27]. Moreover, in conditions such as MS, Sjögren's syndrome, Behçet's disease, and systemic lupus erythematosus (SLE) similar CSF abnormalities may be found. One common finding is a chronic inflammatory syndrome in CSF with intrathecally produced immunoglobulins (Ig), commonly in an oligoclonal pattern and a mild pleocytosis [5]. In Table 2 differences between these inflammatory conditions are listed. The literature has to be taken with caution as studies are based on small sample sizes and so-called 'typical' abnormalities have to be interpreted cautiously.

Determination of CSF–ACE is not specific for neurosarcoidosis but seems to be especially useful in monitoring disease activity and treatment response.

Less frequently used is CSF-CD4:CD8 ratio. This may be important when it exceeds 5. CSF-CD4:CD8 ratio was found abnormal in a minority of patients in previous studies [16,28].

Prognosis

Long-term clinical outcome of neurosarcoidosis has not been thoroughly evaluated. The low prevalence of the disease makes large, long-term follow-up studies difficult. The course seems to depend on the type of nervous tissue involved: patients with dural lesions, peripheral neuropathy, cranial nerve lesions, and nonenhancing brain lesions seem to fare better than patients with leptomeningeal, enhancing brain parenchymal, and spinal lesions [3••,29]. Most relapses occur while tapering prednisone to 10–20 mg or less. In case of increasing deterioration after immunosuppressive treatment further diagnostic testing is indicated, including JCV-DNA analysis by PCR [18].

Table 3 Medical treatment in neurosarcoidosis

Medication	Starting dose	Side-effects[a]	Remarks
Corticosteroids			
Prednisone	1 mg/kg/day orally	Osteoporosis, Cushing syndrome, hypertension, diabetes mellitus, ulcus pepticum, pseudotumor cerebri, glaucoma, cataract, euphoria, psychosis	
Methylprednisolone	1000 mg/day i.v. for 3 days	Very rare within 3 days	
Cytotoxic agents[b]			
Methotrexate	10–25 mg/once weekly orally or subcutaneously	Anemia, neutropenia, hepatic dysfunction, pneumonitis	Should be combined with folic acid (1 mg/day orally)
Cyclosporine	5 mg/kg/day, divided in 2 doses orally	Renal insufficiency, hypertension	Expensive
Azathioprine	50 mg three times daily orally	Anemia, neutropenia, hepatic dysfunction	Cheap
Cyclophosphamide	50–200 mg daily orally 500 mg i.v. once every 2–3 weeks	Cystitis, neutropenia	Urinanalysis monthly to monitor for microscopic hematuria
Immunomodulators[b]			
Hydroxychloroquine	200 mg/day orally	Retinopathy, ototoxic, myopathy, cardiomyopathy, neuropathy, neuropsychiatric	Routine eye examinations every 3–6 months
Infliximab	5 mg/kg i.v. once in week 1, week 2 and than once every 4 weeks	Fever, headache, dizziness, flushes, nausea, abdominal pain, dyspepsia, fatigue, myalgia, arthralgia, polyneuropathy	Tuberculosis screening is mandatory before treatment is started Contra-indicated in patients with heart failure Should be combined with low-dose methotrexate

[a] All can cause infection due immunosuppression.
[b] These drugs are generally used as adjuncts to low-dose steroids, or as steroid-sparing agents when long-term treatment is necessary. In refractory patients they may be used in combination with high-dose steroids.

The prognosis of small fiber neuropathy in sarcoidosis is also not accurately known. In our experience the course of small fiber neuropathy is mostly a chronic, more or less stable condition. Recently, a study in a large series of patients suffering from small fiber neuropathy due to other causes was published. The authors found in 67 small fiber neuropathy patients after a 2-year follow-up that in 46% the clinical picture did not change, in 30% only small fibers remained involved but pain worsened, in 11% spontaneous remission occurred, and in 13% involvement of large fibers occurred [30]. Treatment effects were not mentioned.

Therapy

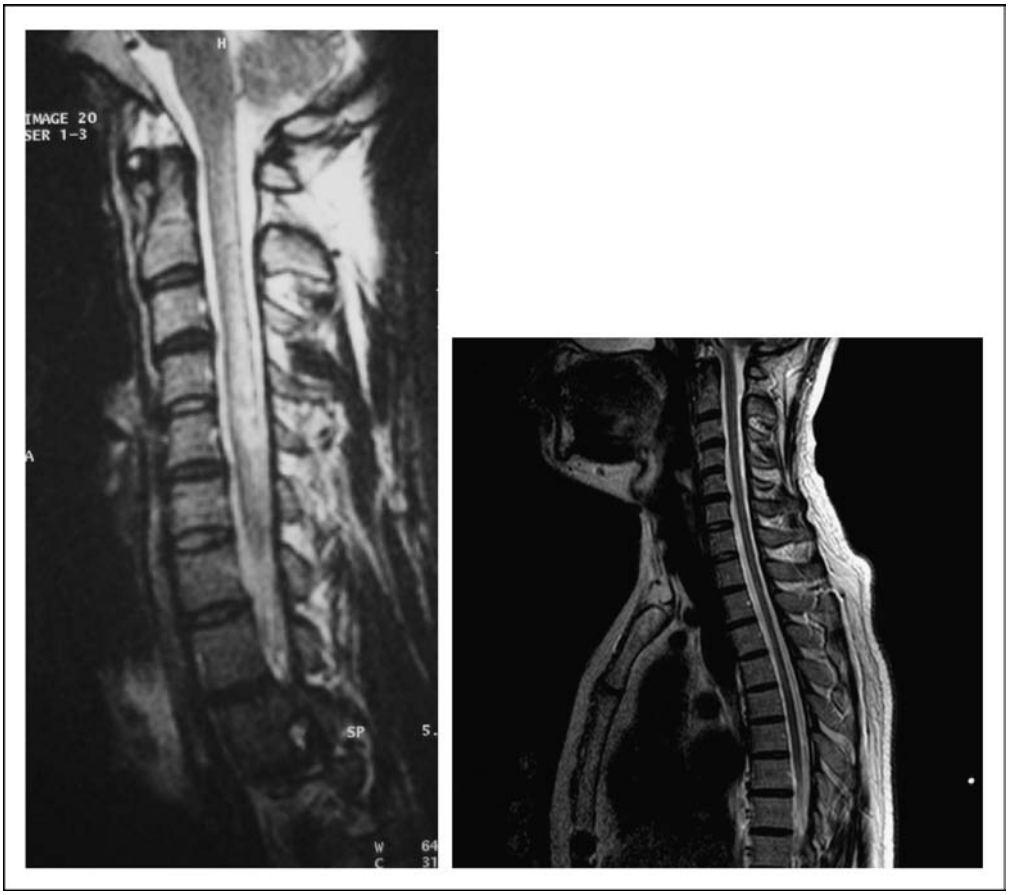
Considering the morbidity and mortality of neurosarcoidosis, most authors recommend early treatment. However, recommendations about treatment are based on experience rather than evidence.

Medication

Therapeutic medical options for neurosarcoidosis are similar to those for sarcoidosis at other locations, and corticosteroids represent the drugs of first choice (Table 3). In neurosarcoidosis usually an initial dose of 1 mg/kg/day is recommended. In severe cases high doses (500–1000 mg) 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. However, at present there is not enough evidence to recommend this. Although corticosteroids suppress inflammation in many patients, symptoms tend to recur in a subset of patients at doses of prednisone less than 10–25 mg/day or the equivalent in other corticoid types, making cessation of corticoids difficult. Furthermore, the incidence of steroid-related side-effects is extremely high with prolonged treatment.

In patients with refractory disease, cytotoxic agents such as methotrexate, azathioprine, cyclosporine, and cyclophosphamide have been used. The choice for one or the other is more a matter of experience than of double-blind studies. Combination therapy of corticosteroids and alternative immunosuppressive agents immediately at the time of initial diagnosis are recommended in cases

Figure 1 Spinal neurosarcoid patient before and after infliximab treatment



with poor prognosis such as intracranial masses and myelopathy [2,31]. In long-term follow-up of 26 patients initially treated with corticosteroids and alternative immunosuppressive agents, all had favorable outcome with minimal toxic effects [32].

Anti-TNF-α

Immunomodulators known to suppress TNF release have been shown effective in cases with refractory (neuro)sarcoidosis [7,33,34,35••,36•,37••,38••,39]. Figure 1 shows a spinal neurosarcoid patient before and after infliximab treatment, illustrating its potential value in refractory cases.

Recently, Elfferich *et al.* [40] reported that anti-TNF-α therapy (either infliximab or adalimumab) had a positive effect on cognition, fatigue, and other symptoms related to sarcoidosis. After 6 months follow-up, only those patients treated with anti-TNF-α therapy ($n = 42$) demonstrated a significant improvement of the fatigue assessment score and cognitive failure questionnaire score [compared with the untreated patients ($n = 189$) and with patients treated with prednisone, with or without methotrexate ($n = 93$)].

Infusion reactions are important immunologic events induced by the presence of a substantial concentration of antibodies against infliximab in the serum. Antibody formation is associated with loss of response. Concomitant immunosuppressive treatment may optimize response to infliximab by preventing the formation of antibodies. Finally, anti-TNF therapy can be responsible for autoimmune reactions, including SLE. Whether infections such as PML will occur more frequently is unknown so far.

Whether anti-TNF-α therapy is beneficial in small-fiber neuropathy related to sarcoidosis is unknown so far. In our experience a subset of about one-third of sarcoid-related small-fiber neuropathy patients may benefit from anti-TNF-α treatment. Others also reported relief of neuropathic pain in sarcoidosis after treatment with infliximab [37••].

Radiation

There are several reports on radiation therapy in refractory neurosarcoidosis. Although evidence-based recommendation cannot be provided, radiation therapy or stereotactic radiotherapy may be considered in patients who do not respond on medication [41,42]. The latter may be preferred considering late neurotoxic effects after whole-brain radiotherapy (postradiation encephalopathy).

Neurosurgical treatment

Neurosurgical resection of intracranial and spinal granulomas is only indicated in life-threatening situations or when insufficient effect is achieved with medical treatment. However, extramedullary spinal lesions may be amenable to surgical resection with postoperative steroid therapy. Hydrocephalus usually needs ventriculoperitoneal shunting.

Angioplasty

In neurosarcoid large-vessel vasculitis successful treatment with balloon angioplasty has been reported [11].

Conclusion

Neurosarcoidosis is a manifold disease. The diagnosis is based on the combination of clinical and radiological evidence and histological evidence of granuloma formation. High-resolution computerized tomography of the chest, a PET scan and CSF-CD4 : CD8 ratio may be helpful in the diagnostic process. Once the diagnosis has been established, the treatment choices are limited. These include corticosteroids, methotrexate, and azathioprine, but also new drugs such as anti-TNF-α therapy.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 524).

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