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Cerebral vasculitis as a clinical manifestation of neurosarcoidosis: A scoping review

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ABSTRACT

The occurrence of cerebral vasculitis in individuals with neurosarcoidosis (NS) is considered to be rare. Although the number of relevant publications has increased in recent years, evidence is mostly limited to case reports. To obtain a better understanding of this rare and severe manifestation of disease, we carried out a scoping review on cerebral vasculitis in patients diagnosed with NS. The results of the review indicate that the diagnosis of cerebral vasculitis in patients with NS is made especially in patients with systemic sarcoidosis. However, recurrent strokes in patients with NS remains the main indicator of cerebral vasculitis. A tissue biopsy is considered the gold standard to confirm the diagnosis despite occasional false-negative results. Glucocorticoids and steroid-sparing agents are the most successful current treatments. Favorable outcomes were observed with strategies targeting TNFα and B cells. The goal of this review is to summarize the current literature and treatment options for cerebral vasculitis in patients with NS.

1. Introduction

Sarcoidosis is a rare, idiopathic, inflammatory and multisystemic disease characterized by the presence of epithelioid granuloma, mainly occurring in the lungs. Extrapulmonary manifestations have been estimated in approximately 30% of patients suffering from sarcoidosis [3,4,16]. These manifestations vary widely based on gender, age and ethnicity. Most commonly, extrapulmonary manifestations involve the skin, the reticuloendothelial as well as the musculosceletal systems and the eyes. In addition to organ-specific symptomatology, nonspecific symptoms such as fatigue and general weakness may also occur. These symptoms are related to the high levels of cytokines that are produced by granuloma formation. Epidemiologically, the highest incidence of sarcoidosis is observed in African Americans as well as in Northern European countries [21].

1.1. The involvement of central nervous system (CNS) and cerebrovascular manifestations of sarcoidosis

The results from many studies indicate that central nervous system (CNS) involvement is estimated to occur in 5–10% of patients with sarcoidosis [8]. Approximately 50% of patients suffering from sarcoidosis initially present with neurological deficits. The most common neurological manifestation in patients with sarcoidosis is cranial mononeuropathy such as peripheral facial nerve palsy, which affects approximately 25–50% of the patients [22,35,40,42]. Many other possible manifestations such as aseptic meningitis, hydrocephalus, psychiatric symptoms, small-fiber neuropathy, dementia, encephalopathy, intraparenchymal inflammatory lesions and myopathy, have also been reported. Isolated NS (without systemic involvement) has been estimated in 10–17% of patients with sarcoidosis [42]. Pathological imaging findings in patients with systemic sarcoidosis have been

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estimated to be observed in around 10% [3,6].

Cerebrovascular manifestations as a clinical feature of sarcoidosis are relatively rare. The exact mechanisms behind the cerebrovascular involvement in NS patients are still not fully understood. Many studies demonstrate vascular epithelioid cell granulomas as well as other inflammatory infiltrates leading to vasculopathy and resulting in cerebrovascular events. However, in the case of NS related vasculitis, ischemic stroke is a common complication.

The perforating arteries are among the most frequently affected vessels, resulting in involvement of the basal ganglia, brainstem and thalamus [4]. Clinically, the majority of infarcts are silent. It is still unclear whether the silent infarcts are due to the small size of the affected arteries or to the minor stroke symptoms being overshadowed by other, more prominent neurological clinical manifestations of NS. Cerebral infarcts in NS-related vasculitis are often multiple and recurrent. In contrast to the characteristics of common strokes patients, NS patients with ischemic strokes are younger and often present with extracranial manifestations of sarcoidosis. Hemorrhagic strokes have also been reported in patients with NS; however, these occur only in the minority of patients with NS (0.6%) and are mostly supratentorial [33]. In addition, Moyamoya-like vasculopathy patterns have also been reported [25].

Recently, there has been an increasing number of studies indicating that cerebral vasculitis occurs in patients with NS. Such studies are rare and mainly represent data from case reports. Therefore, within this review we aim to summarize the current knowledge of vasculitis in patients with NS and the pathophysiological factors involved in the association between NS and vasculitis.

2. Methods

In the preparation of this scoping review, we followed a predefined protocol, approved methodology for scoping reviews [2,27], and recognized reporting guidelines [43]. According to its definition, scoping review addresses a broad research question, describes research gaps and future research priorities instead of focusing at a concrete, specific question, such as, for example, effectiveness of an intervention or reliability of a diagnostic test [11].

An extensive search was performed in three databases (MEDLINE, CINAHL and Embase) specialized resources, and trial registers. Our multidisciplinary research team included neurologists, neuroimmunologists, stroke experts and an information specialist to assist and supervise the peer-review search [30]. We also interacted intensively with stakeholders (patients with CNS vasculitis due to sarcoidosis (n = 4), their caregivers, family doctors and other clinicians treating these patients). Two reviewers (a specialist in neuroimmunology and a stroke specialist) independently screened all abstracts and full texts identified in terms of our search. Data were extracted using predefined forms and included study design, demographics and clinical parameters of patients, details on diagnostics and treatment, and clinical outcome [20]. In studies with mixed populations of patients, data specific to cerebrovascular manifestations of sarcoidosis was extracted.

The following search terms were applied: „cerebral vasculitis“ AND „neurosarcoidosis“; „cerebral vasculitis“ AND „sarcoidosis“; “stroke” AND “neurosarcoidosis”; “stroke” AND “sarcoidosis”; “intracerebral hemorrhage” AND “neurosarcoidosis”; “intracerebral hemorrhage” AND “sarcoidosis” for the time period between May 1953 and May 2023. We did not apply any language or date limitations and included all age groups and geographical regions. Our search revealed 515 records, which matched the search criteria (Fig. 1). After excluding articles, which did not match our subject criteria (e.g. reporting on vasculitis but not related to NS, or reporting on NS but without vasculitis), 10 articles were selected and included in this review. Among them, there were eight case reports and two original articles that reported about cerebral vasculitis in patients with NS. The diagnosis of sarcoidosis or NS was based on histologic and radiological features that were accompanied by

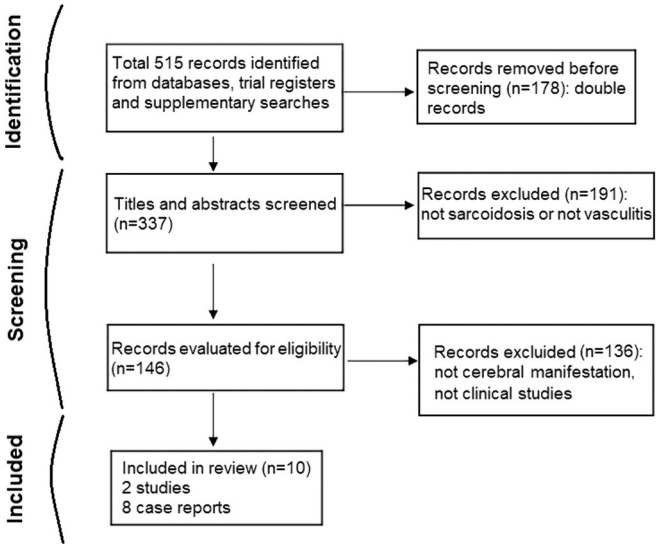

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for identification of literature in scoping review, Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

clinical manifestations. Similarly, the diagnosis of vasculitis was established according to either histological evidence or based on radiological findings that were consistent with cerebral vasculitis. The review data are available from the corresponding author upon reasonable request. This review was no registered in PROSPERO because it's methodology as a scoping review does not permit the registration. The registration was performed at the Open Science Framework.

2.1. Included studies

The literature was presented mainly by case reports (8/10, 80%). No interventional studies were available. One study was devoted to diagnostics and reported on vessel wall imaging in NS. [4] Another study (n = 16) was a descriptive clinical study on patients with different causes of cerebral vasculitis including NS. [26] Below we discuss the current evidence available from the identified studies and case reports.

3. Discussion

Our review scope the breadth of clinical manifestations, available diagnostics and therapies on cerebral vasculitis in NS. We identified 10 repots, including two studies and eight case reports. Data on diagnostics is available from small ($n < 20$) observational studies and no studies on therapeutic interventions have been performed. The evidence for the therapy exists on the level of case reports.

3.1. Vasculitis as a clinical manifestation of neurosarcoidosis

Vasculitis is an unusual clinical manifestation of sarcoidosis, especially as an initial neurological manifestation. [14] In recent years, there have been an increase in the number of studies describing an association between vasculitis and NS in individuals. These publications were mainly case or retrospective studies. In two different studies involving patients with NS, one having 13 patients and the other having 16 patients, one individual in each study was found to have cerebral vasculitis, which was attributed to NS. [4,26] Studies indicate that vasculitis may present as a systemic or as an isolated cerebral vasculitis. [14,28]

Most perforating cerebral arteries eventually lead to lacunar strokes, which are more common in patients with NS [4,6]. However, it was demonstrated that vasculitis in NS may affect different-sized vessels

including small- to large-caliber vessels [15]. Of six patients in the study, three were diagnosed with large vessel vasculitis. Vasculitis involving the intracranial internal carotid artery was observed in a number of patients with NS [1,28]. Using MR-angiography, a complete occlusion of the right internal carotid artery was found in one 35-year old, female patient.

The exact mechanisms of vasculitis in NS patients are still unknown. It has been reported that sarcoid granulomata originally situated in the parenchyma appear to spread into the vascular space of perforating vessels [19]. An inflammatory response in small- and medium-sized arteries due to an invasion by epithelioid cells could also be responsible for these observations. This results in damage to the internal lamina as well as fibrosis and leads to stenosis and occlusion of the lumen of these vessels. Furthermore, infiltration and necrosis have been found in cerebral vessels, which causes inflammation of the vessel wall of small- and medium-sized vessels resulting in thrombosis and occlusions [10,12,24,37]. Less is known of the pathological process in large-sized arteries; however, it appears that inflammation leads to the destruction of the large vessels resulting in a progressive fibrotic stenosis or ectasia [24]. Many arteries from the same or different regional cerebral vessels may be affected by vasculitis in NS patients as has been shown in a 41-year-old African American patient with sarcoidosis who also presented with aphasia and right-sided weakness [9]. Magnetic resonance angiography (MRA) of this patient demonstrated severe stenosis of both M1 and A1 segments, which were successfully treated with angioplasty and led to a remarkable improvement of the initial symptoms (Table 1, [9]). In a study of 54 patients with NS, one 38-year-old male patient developed cerebral vasculitis which manifested as multiple brainstem, thalamic infarctions and seizures [35].

In addition to previously described symptoms of vasculitis in NS

Table 1
Cases of cerebral vasculitis in neurosarcoidosis in the literature.

Authors/ Year	Age/ Sex	Image morphology	Symptoms and clinical findings	Diagnostic work-up	Treatment	Outcome
Brisman et al., 2006 [9]	41 yo Female	watershed infarcts in the left MCA and ACA territories, left M1- and A1-stenosis, leptomenin-geal enhancement	Aphasia and right-sided weakness	CSF: lymphocytic pleocytosis, ↑ proteins + Biopsy: mediastinal lymph node + DSA: consistent with vasculitis	High-dose corticosteroids	The hemiparesis was completely regredient, aphasia improved
Pegat et al. 2015 [36]	48 yo Female	Recurrence of episodes by NS under long-term corticosteroid therapy. The last episode was with spinal cord hemorrhage	Rash gait difficulties, urinary retention, sensible deficits in the lower extre-mities	MRI: high-intensity periventricular lesions, and a low-intensity left frontoparietal lesion, suggestive of hemosiderin deposits + CSF: pleocytosis (40 leukocytes/ mm3), protein ↑, oligoclonal bands were positive. Interventional observation of enlarged blood vessels on	Long-term corticosteroid Therapy + neurosurgical evacuation	Paraparesis and gait difficulties, however no relapses
Macêdo et al., 2017 [28]	62 yo Male	MRI: stenosis in ICA links and vertebral artery links	Initial: Fever, skin lesions (petechiae), headache Later: mental confusion	CSF: ACE ↑, protein ↑ Brain angiography: multiple distal irregularities over all vascular territories, which were suggestive of cerebral vasculitis	Corticosteroids, cyclophosphamide, immunoglobulin (IV)	The patient died after one month
Kidd et al. 2018 [24]	47 yo Male	MRI: thickening and enhancement of the left internal carotid artery, and enhancing intrinsic lesion of the left temporal lobe with meningeal enhancement extending back to the midbrain	Recurrent left sided amaurosis fugax later: headache, diplopia, upper quadrantinopia right, a partial left third nerve palsy	Biopsy of cerebral temporal lesion revealed granuloma-tous inflammation CT thorax and abd.: mediastinal and axillary lymphadenopathy + Parotid glands, the mediastinal and axillary nodes and liver	Oral cortico-steroids, methotrexate	Symptom-free
Arif et al. 2020 [1]	35 yo Female	Complete occlusion of right ICA, bilateral stenosis in MCA and ACA and vasculitis of small vessels of brain. Multiple foci in bilateral frontoparietal regions and centrum semiovale	Progredient headache and Lupus Pernio	Biopsy of the lesion, CSF: ↑ proteins (no pleocytosis) ↑ ACE Angiography: bilateral stenosis of MCA and ACA	Corticosteroids, Plasmapheresis, cyclophospha-mide (6 months). Long-term immuno-suppression with azathioprine	Symptom-free after 12 months
Maekawa et al. 2021 [29]	71 yo Female	MRI: Progredeint lesion in the parietal lobe	Headache, nausea, left-hand numbness, left homonymous hemianopia	CSF: pleocytosis (160 leukocytes/ mm^3) ↑ proteins Brain biopsy	Corticosteroids	Clinical and radiological improvement
Mehta, et al. 2022 [32]	49 yo Male	Multiple bilateral supratentorial IPHs, multifocal micro-hemorrhages	Bilateral weakness, hear loss (leftsides), urinary urge incontinence, and gait instability. Generalized seizures,	Abnormal angiographic findings, brain biopsy, elevated antiproteinase3 (PR-3) antibodies	Methotrexate, low dose prednisone taper, infliximab	Improvement clinically and image morpho-logically
Gakosso et al. 2023 [17]	51 yo Female	Bilateral subcortical hemispheric white matter lesions, some of them with restriction in diffusion-weighted imaging and petechial hemorrhagic foci along with a micronodular menin-geal thickening and intracranial vascular wall enhancement	Sudden-onset mental confusion, fever, sweating, fatigue, moderate-intensity headaches	CSF: pleocytosis (47 leukocytes/ mm^3) ↑ proteins Thoraco-abdomino-pelvic CT scan revealed multiple hilar and lower cervical mediastinal lymphadenopathies at the thoracic level. An ultrasound-guided biopsy showed giant cell epithelioid granu-loma without caseous necrosis suggestive of sarcoidosis	Methylprednisolone pulse therapy	Complete recovery

Abbreviations: A1, 1st segment of anterior cerebral artery; ACE, angiotensin converting enzyme; CSF, cerebrospinal fluid; DSA, digital subtraction angiography; ICA, internal carotid artery; IPH, intraparenchymal hemorrhage; M1, 1st segment of middle cerebral artery; MRI, magnetic resonance imaging; NS, neurosarcoidosis.

patients, which manifest clinically, vasculitis may present with mild symptoms such as headache or progredient confusion. Previous reports described cases of cerebral vasculitis, in the context of CNS sarcoidosis, presenting with headache [1,4].

A 31-year-old man with a history of headaches, forgetfulness, apathy and psychomotor slowing, with NS, showed an involvement of the septum pellucidum and intracranial vessels. In this case, a brain biopsy from the septum pellucidum revealed noncaseating epithelioid granulomas [14].

3.2. Suggested diagnostic pathways

Due to low specificity and sensitivity of magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) findings, establishing a diagnosis of vasculitis in NS can be both difficult and challenging. Clinical manifestations may be widely variable and include unusual deficits in cranial nerve functions (e.g., bilateral facial neuropathy), cognitive dysfunction, ataxia, stroke-like symptoms and seizures, particularly when a history of unclear headaches is present. Therefore, when neurological symptoms in patients with sarcoidosis develop, NS should be considered as a factor. NS patients presenting with CNS vasculitis as an initial symptom is relatively infrequent and rarely reported.

Obtaining a patient's detailed history in combination with the clinical findings is essential. Patients presenting with multi-focal neurological deficits accompanied by psychiatric/cognitive symptoms, headaches and signs of systemic inflammatory disorder should undergo further diagnostic testing to exclude cerebral vasculitis, particularly in patients with recurrent strokes and without previously known cardiovascular risk factors. An elevation of acute phase proteins such as high erythrocyte sedimentation rate (ESR), hypochromic anemia (and low complement) are typical serum findings in systemic vasculitis.

The typical CSF-finding of vasculitis is a mild, lymphocytic pleocytosis with an elevated protein level [42]. However, it is important to note that an analysis of the CSF can often be nonspecific, as shown in Table 1.

An analysis of immunoglobulins in the CSF by the detection of oligoclonal bands may be of importance, but in some cases, bands may only be detected temporarily. Zajicek et al. reported that positive oligoclonal bands were only observed in 55% of patients with NS indicating that this is not specific [46].

MRI is also considered to be a basic diagnostic tool in order to evaluate possible vascular abnormalities in NS patients. Leptomeningeal involvement is a common MRI feature found in patients with NS (Table 1, [5]). Multiple stenoses and vascular irregularity should always raise the suspicion of an ongoing inflammatory process (Table 1).

If clinical or radiological results indicate vasculitis, digital subtraction angiography (DSA) should be performed. It is important to note that both MRI and cerebral angiography could indicate cerebral vasculitis. However, neither test system is sufficient to confirm such a diagnosis. Sensitivity of DSA in diagnosing vasculitis has previously been estimated to be approximately 60% [45]. Moreover, visualizing the inflammation of vessels with positron emission tomography (PET) imaging should be considered when other findings are not conclusive.

Tissue biopsy remains the “gold standard” to confirm the diagnosis of cerebral vasculitis, especially in small-vessel vasculitis, which is usually associated with a negative cerebral angiography. A systemic review on primary CNS vasculitis (PCNSV) gathered data of 701 patients with PCNSV. Pathological brain biopsies were found in 99 of those patients with normal cerebral angiography [31].

A `definite` NS diagnosis requires a biopsy of the CNS tissue; however, false negative brain biopsies can be observed due to segmental involvement of vessels [13,46]. Therefore, diagnosis of NS should be based on clinical manifestations in combination with other clinical and diagnostic findings, especially in cases where a brain biopsy is not done.

An elevation of angiotensin converting enzyme (ACEs) in the CSF has been observed in 33% of NS patients and is produced by granulomas [46].

3.3. Treatment and prognosis of cerebral vasculitis in patients with NS

To date, there are no clear guidelines for treating patients with vasculitis due to NS. This could be due to the lack of controlled trials, which evaluate the management of vasculitis in NS patients. Most treatment strategies in NS patients are mainly based on previous studies evaluating therapeutic efficiency in systemic sarcoidosis. Table 2 summarizes the treatments that have been used in patients with vasculitis with NS.

Glucocorticoids remain the first-line of therapy in patients with NS and vasculitis. A number of studies have shown positive responses in NS patients who were treated with corticosteroids [42]. Furthermore, favorable outcomes were reported in many vasculitis cases with NS (Table 1). Depending on symptom severity as well as the disease process, pulse-dose of intravenous (IV) methylprednisolone (usually 1 g/d for 3–5 days) may be required. This is usually followed by prolonged oral corticosteroids (weight adapted). In patients with less severe disease, oral glucocorticoid therapy (0.5–1 mg/kg/d) could be effective and sufficient. Other reports, nevertheless, revealed refractory cases and relapses when using glucocorticoids [35,38].

Steroid-sparing agents are usually used as a long-term therapy in patients with NS in order to avoid the numerous side effects that occur with glucocorticoids. A meta-analysis, published in 2016, classified the following immunosuppressive treatments of NS as a second-line therapy: methotrexate, azathioprine, mycophenolate mofetil, cyclosporine A, or (hydroxyl) chloroquine. Treatment with cyclophosphamide or immunomodulatory medication was indicated as a third-line therapy [16].

Currently, there are no clear guidelines recommending one of the steroid-sparing agents over the others. In one retrospective study that included 40 patients with NS, methotrexate was shown to have better effects compared to mycophenolate mofetil [7]. In another retrospective study with 234 patients with NS, a lower risk of relapse was observed when using methotrexate, cyclophosphamide and infliximab [23]. Relapse risk was, however, increased in patients treated with mycophenolate mofetil. In summary, most studies demonstrated a favorable outcome in NS patients with vasculitis, who were treated with methotrexate, azathioprine and cyclophosphamide (Table 1).

Other favorable outcomes were reported in NS patients given TNFα inhibitors (e.g. infliximab) [16,18,44], B cell depleting antibodies (e.g. rituximab) [47] and IV immunoglobulin [34,39]. However, there is still no clear evidence of the efficacy of these compounds in patients with NS and CNS vasculitis (Table 3).

Many case studies described responses to therapy and good outcomes in NS patients with CNS vasculitis. In some cases, however, patients developed unfavorable conditions despite treatment. A 62-year-old patient rapidly developed grave complications and died after one month despite initial treatment with corticosteroids, cyclophosphamide and IV immunoglobulins [28]. It is important to note that various factors such as age and a previous history of hypertension in this patient may have

Table 2
Common treatments of cerebral vasculitis by neurosarcoidosis.

Medication	Dose	References
Glucocorticoids (Prednisone/ Methylprednisolone)	Prednisone: 0.25–1 mg/kg/d oral Methylprednisolone: 1000 mg/d x 3–5 days IV	[16,35,38]
Methotrexate	10–25 mg weekly oral or SC	[23,24,32]
Azathioprine	Up to 2–2.5 mg/kg oral daily	[1,23]
Cyclophosphamide	The dose may vary depending on the type of vasculitis and the severity 15 mg/kg body weight IV (max. 1200 mg), at weeks 0, 2, 4, 7, 10, 13	[1,28]

Abbreviations: AE, adverse events; IV, intravenous; NS, neurosarkoidosis; SC, subcutaneous; TPMT, thiopurine *S*-methyltransferase.

Table 3
Potential treatments of CNS-Vasculitis by neurosarcoidosis.

Medication	Dose	Comments	References
Mycophenolate mofetil	500–3000 mg/d oral, BID	Effectiveness was shown in NS and systemic vasculitis as well as antibody-associated vasculitis It is classified as a second-line-agent in treating sarcoidosis	[7,16]
Infliximab	3-7 mg/kg IV at weeks 0, 2, and 6, then 3–7 mg/kg IV every 4–8 weeks	A retrospective study showed improvement/remission in 70% of patients with NS. It is classified as a third-line-agent in treating sarcoidosis	[16,32]
Rituximab	375 mg/m^2 IV at days 0, 7, 14, 21	Favorable outcomes were observed in ANCA-associated vasculitis as well as patients with refractory NS	[41,47]

Abbreviations: AE, adverse events; BID, bidaily; IV, intravenous; NS, neurosarkoidosis.

played a role in worsening the prognosis when compared with other case reports of patients of younger age and with fewer comorbidities.

Patients with vasculitis and NS are in most of cases relatively young. Due to possible severe complications as a consequence of vasculitis, an early diagnosis and treatment of cerebral NS with involvement of brain supplying arteries is extremely important to improve the functional outcome and prevent serious health consequences or death of affected individuals.

3.4. Gaps in the evidence

As already reported above, the evidence for diagnostics in cerebral vasculitis in NS is at the level of small observational studies. For therapy, it exists only at the level of case reports. Our scoping review underlines the urgent need for randomized controlled trials (RCTs) to improve the level of the evidence in this important disease. Because of the fact that cerebral vasculitis in NS is a rare condition, the possible way to improve the evidence is to either perform RCTs in multicenter designs with involvement of hundreds of recruiting sites or to include patients with cerebral vasculitis in NS in studies with mixed populations of patients with cerebral vasculitis.

4. Conclusions

Vasculitis as a cerebral manifestation in patients with sarcoidosis is increasingly reported. Currently, there is no data describing the incidence or recommended treatment strategies. Further clinical trials are needed to evaluate conditions for an efficient therapy and to establish guidelines for treatment of cerebral vasculitis and NS.

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Ethical standards

The manuscript does not contain clinical studies or patient data.

Declaration of competing interest

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Data availability

Data will be made available on request.

References

[1] Arif S, Arif S, Liaqat J, Slehria AU, Palwa AR. Central nervous system vasculitis secondary to sarcoidosis: a rare case of lupus Pernio with complete occlusion of right internal carotid artery. Cureus 2020;12:e10274.
[2] Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005;8:19–32.
[3] Bagnato F, Stern BJ. Neurosarcoidosis: diagnosis, therapy and biomarkers. Expert Rev Neurother 2015;15:533–48.
[4] Bathla G, Abdel-Wahed L, Agarwal A, Cho TA, Gupta S, Jones KA, et al. Vascular involvement in neurosarcoidosis: early experiences from intracranial vessel wall imaging. Neurol Neuroimmunol Neuroinflamm 2021;8.
[5] Bathla G, Singh AK, Policeni B, Agarwal A, Case B. Imaging of neurosarcoidosis: common, uncommon, and rare. Clin Radiol 2016;71:96–106.
[6] Bathla G, Watal P, Gupta S, Nagpal P, Mohan S, Moritani T. Cerebrovascular manifestations of neurosarcoidosis: an underrecognized aspect of the imaging spectrum. AJNR Am J Neuroradiol 2018;39:1194–200.
[7] Bitoun S, Bouvry D, Borie R, Mahevas M, Sacre K, Haroche J, et al. Treatment of neurosarcoidosis: a comparative study of methotrexate and mycophenolate mofetil. Neurology 2016;87:2517–21.
[8] Bradshaw MJ, Pawate S, Koth LL, Cho TA, Gelfand JM. Neurosarcoidosis: pathophysiology, diagnosis, and treatment. Neurol Neuroimmunol Neuroinflamm 2021;8.
[9] Brisman JL, Hinduja A, McKinney JS, Gerhardstein B. Successful emergent angioplasty of neurosarcoid vasculitis presenting with strokes. Surg Neurol 2006;66:402–4.
[10] Camp WA, Frierson JG. Sarcoidosis of the central nervous system. A case with postmortem studies. Arch Neurol 1962;7:432–41.
[11] Campbell F, Tricco AC, Munn Z, Pollock D, Saran A, Sutton A, et al. Mapping reviews, scoping reviews, and evidence and gap maps (EGMs): the same but different— the "big picture" review family. Syst Rev 2023;12:45.
[12] Caplan L, Corbett J, Goodwin J, Thomas C, Shenker D, Schatz N. Neuro-ophthalmologic signs in the angiitic form of neurosarcoidosis. Neurology 1983;33:1130–5.
[13] Chu CT, Gray L, Goldstein LB, Hulette CM. Diagnosis of intracranial vasculitis: a multi-disciplinary approach. J Neuropathol Exp Neurol 1998;57:30–8.
[14] Degardin A, Devos P, Vermersch P, de Seze J. Cerebrovascular symptomatic involvement in sarcoidosis. Acta Neurol Belg 2010;110:349–52.
[15] Fernandes SR, Singsen BH, Hoffman GS. Sarcoidosis and systemic vasculitis. Semin Arthritis Rheum 2000;30:33–46.
[16] Fritz D, van de Beek D, Brouwer MC. Clinical features, treatment and outcome in neurosarcoidosis: systematic review and meta-analysis. BMC Neurol 2016;16:220.
[17] Gakosso Jr CLG, Badr S, Zouine Y, Hammoune N, Mouhsine A. Cerebral vasculitis revealing systemic sarcoidosis: a case report and review of the literature. Cureus 2023;15:e36968.

[18] Gelfand JM, Bradshaw MJ, Stern BJ, Clifford DB, Wang Y, Cho TA, et al. Infliximab for the treatment of CNS sarcoidosis: a multi-institutional series. Neurology 2017; 89:2092–100.
[19] Herring AB, Urich H. Sarcoidosis of the central nervous system. J Neurol Sci 1969; 9:405–22.
[20] Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. Bmj 2014;348:g1687.
[21] Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007;357: 2153–65.
[22] Joseph FG, Scolding NJ. Neurosarcoidosis: a study of 30 new cases. J Neurol Neurosurg Psychiatry 2009;80:297–304.
[23] Joubert B, Chapelon-Abric C, Biard L, Saadoun D, Demeret S, Dormont D, et al. Association of prognostic factors and immunosuppressive treatment with long-term outcomes in neurosarcoidosis. JAMA Neurol 2017;74:1336–44.
[24] Kidd DP, McCabe DJ, Wilhelm T, Galloway M. Carotid arteritis causing amaurosis fugax and ischaemic cerebrovascular events in neurosarcoidosis. Clin Neurol Neurosurg 2018;169:103–6.
[25] Ko JK, Lee SW, Choi CH. Moyamoya-like vasculopathy in neurosarcoidosis. J Korean Neurosurg Soc 2009;45:50–2.
[26] Kraemer M, Berlit P. Systemic, secondary and infectious causes for cerebral vasculitis: clinical experience with 16 new European cases. Rheumatol Int 2010;30: 1471–6.
[27] Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010;5:69.
[28] Macêdo PJ, da Silveira VC, Ramos LT, Nóbrega FR, Vasconcellos LF. Isolated central nervous system vasculitis as a manifestation of neurosarcoidosis. J Stroke Cerebrovasc Dis 2016;25:e89–92.
[29] Maekawa T, Goto Y, Aoki T, Hino A, Oka H, Yokoya S, et al. Acute central nervous system vasculitis as a manifestation of neurosarcoidosis: a case report and literature review. Radiol Case Rep 2021;16:410–4.
[30] McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol 2016;75:40–6.
[31] McVerry F, McCluskey G, McCarron P, Muir KW, McCarron MO. Diagnostic test results in primary CNS vasculitis: a systematic review of published cases. Neurol Clin Pract 2017;7:256–65.
[32] Mehta A, Khan F, Wagner C, Hashemzadeh T, Stemer A, Sloan EA, et al. A Case of Neurosarcoid presenting as multiple Intraparenchymal hemorrhages. Neurohospitalist 2022;12:162–6.
[33] O'Dwyer JP, Al-Moyeed BA, Farrell MA, Pidgeon CN, Collins DR, Fahy A, et al. Neurosarcoidosis-related intracranial haemorrhage: three new cases and a systematic review of the literature. Eur J Neurol 2013;20:71–8.
[34] Parambil JG, Tavee JO, Zhou L, Pearson KS, Culver DA. Efficacy of intravenous immunoglobulin for small fiber neuropathy associated with sarcoidosis. Respir Med 2011;105:101–5.
[35] Pawate S, Moses H, Sriram S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. Qjm 2009;102:449–60.
[36] Pegat B, Drapier S, Morandi X, Edan G. Spinal cord hemorrhage in a patient with neurosarcoidosis on long-term corticosteroid therapy: case report. BMC Neurol 2015;15:123.
[37] Reske-Nielsen E, Harmsen A. Periangiitis and panangiitis as a manifestation of sarcoidosis of the brain: report of a case. J Nerv Ment Dis 1962;135:399–412.
[38] Scott TF, Yandora K, Valeri A, Chieffe C, Schramke C. Aggressive therapy for neurosarcoidosis: long-term follow-up of 48 treated patients. Arch Neurol 2007;64: 691–6.
[39] Shenoy N, Tesfaye M, Brown J, Simmons N, Weiss D, Meholli M, et al. Corticosteroid-resistant bulbar neurosarcoidosis responsive to intravenous immunoglobulin. Pract Neurol 2015;15:289–92.
[40] Stern BJ, Krumholz A, Johns C, Scott P, Nissim J. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42:909–17.
[41] Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med 2010;363: 221–32.
[42] Tavee JO, Stern BJ. Neurosarcoidosis Continuum (Minneap Minn) 2014;20: 545–59.
[43] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018;169:467–73.
[44] Ungprasert P, Ryu JH, Matteson EL. Clinical manifestations, diagnosis, and treatment of sarcoidosis. Mayo Clin Proc Innov Qual Outcomes 2019;3:358–75.
[45] Vollmer TL, Guarnaccia J, Harrington W, Pacia SV, Petroff OA. Idiopathic granulomatous angiitis of the central nervous system. Diagnostic challenges. Arch Neurol 1993;50:925–30.
[46] Zajicek JP, Scolding NJ, Foster O, Rovaris M, Evanson J, Moseley IF, et al. Central nervous system sarcoidosis - diagnosis and management. Qjm 1999;92:103–17.
[47] Zella S, Kneiphof J, Haghikia A, Gold R, Woitalla D, Thöne J. Successful therapy with rituximab in three patients with probable neurosarcoidosis. Ther Adv Neurol Disord 2018;11. 1756286418805732.