Case Report

A rare case of isolated cervical intramedullary neurosarcoidosis, successfully treated using a combination of prednisolone and mycophenolate mofetil

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ABSTRACT

Isolated spinal cord intramedullary neurosarcoidosis (NS) in the absence of systemic involvement is exceptionally rare, and the diagnosis can be challenging. A 41-year-old female presenting with bilateral limb weakness was referred to us with a clinical and radiological diagnosis of an intramedullary spinal cord tumor. A biopsy done from the mass was suggestive of an inflammatory lesion with no evidence of neoplasia. Following the report, she was treated with steroids that resulted in an initial symptomatic relief followed by worsening without regression of the mass. Hence, a laminotomy and decompression of the mass were done. The intraoperative smear examination showed a granulomatous lesion that was characterized on histopathology as a non-necrotizing chronic granulomatous meningomyelitis. A final diagnosis of isolated intramedullary NS was considered based on clinical features of waxing and waning response to steroids, intramedullary and leptomeningeal enhancement on radio imaging, histopathological findings of non-necrotizing granulomatous lesion, and exclusion of systemic disease. She was treated with steroids along with mycophenolate mofetil. On follow-up, there was a significant improvement in clinical symptoms.

Key words: Intramedullary Neurosarcoidosis, Mycophenolate Mofetil, Isolated Neurosarcoidosis

Sarcoidosis is a systemic, granulomatous disease most commonly involving the lymph nodes, skin, lungs, and eyes. Central nervous system involvement (neurosarcoidosis) occurs in 5–15% of cases, and the spinal cord involvement in 6–8% of patients; however, the incidence of sarcoidosis involving the spinal cord alone is only 0.43% [1-4]. Although radiographic findings and laboratory values may lead to the diagnosis, a biopsy of the involved organ systems is the gold standard [5]. Spinal neurosarcoidosis (NS) can mimic an inflammatory demyelinating process or a neoplasm both clinically and on imaging studies, particularly on magnetic resonance imaging (MRI) [1,5,6]. We present a case of isolated cervical intramedullary NS which was diagnosed as a spinal cord neoplasm on clinical and radiological examination and which required repeated surgical intervention for definitive diagnosis.

CASE REPORT

A 41-year-old female was referred to our hospital with a history of progressive bilateral upper and lower limbs weakness for the last month with a working clinical diagnosis of spinal intramedullary neoplasm, based on the imaging done.

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Clinical examination showed grade 3 power of the upper and lower limbs and stable vitals. The initial full segment spinal MRI showed a heterogeneously contrast-enhancing intramedullary lesion with dural enhancement extending from C3 to D2 involving predominantly the posterior part of the spinal cord (Fig. 1a). The laboratory investigations showed elevated acute phase reactants and normal angiotensin-converting enzyme (ACE) levels.

She underwent a limited C5 laminectomy and biopsy of the tumor that showed a chronic inflammatory lesion involving the spinal cord, dura with no evidence of neoplastic changes (Fig. 2a and b). Unfortunately, the biopsy was inconclusive for any other definitive pathological lesions. The patient was treated with steroids for a period of 1 week with symptomatic improvement.

A follow-up MRI imaging showed reduced cord widening, contrast enhancement, and extent of the lesion as compared to the previous scan (Fig. 1b). In view of the initial response, steroids were continued. Two weeks later, the patient, however, started developing progressively worsening symptoms and quadriparesis. A repeat MRI scan showed an increase in the transverse dimension of the intrinsic lesion involving the cervicodorsal cord. There was also an increase in the degree and extent of enhancement along the dorsal aspect of the cord with contiguous enhancement and abnormal T2/STIR signal in the adjacent paraspinal muscles (Fig. 1c).

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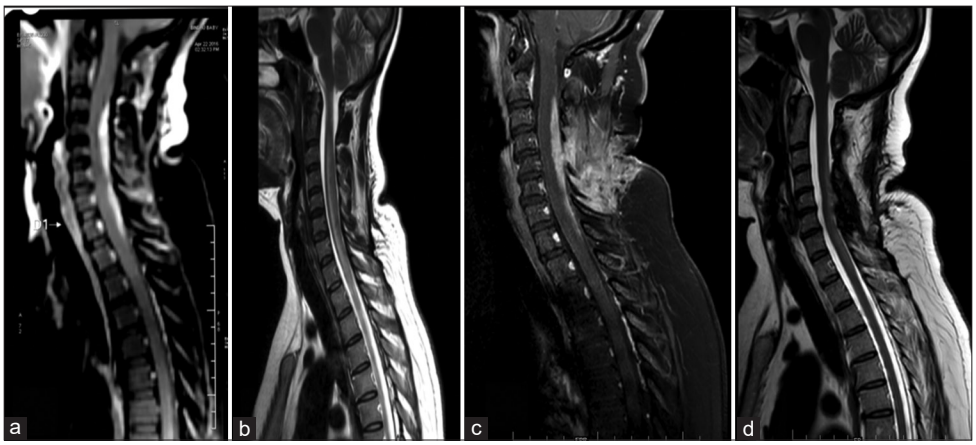

Figure 1: (a) Magnetic resonance imaging (MRI) at presentation; (b) MRI after 1 week of steroid therapy; (c) MRI post-biopsy; (d) MRI – 6-month post-treatment

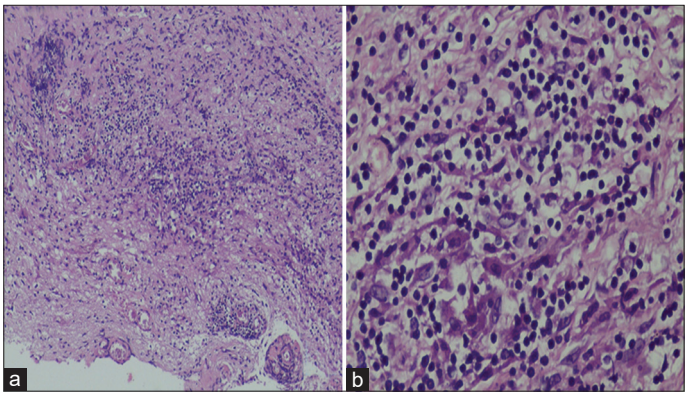

Figure 2: (a and b) Chronic inflammatory lesion involving the spinal cord, dura, and no evidence of neoplasm

She subsequently underwent C3-C6 laminotomy and decompression of the lesion with intraoperative electrophysiologic monitoring. The intraoperative squash smear showed a chronic granulomatous lesion with giant cells. The biopsy also showed perivascular dense chronic inflammation and fibrosis. The second biopsy specimen showed reactive nervous tissue with infiltration of multiple discrete small, well-defined non-necrotizing epithelioid granulomata with giant cells. Few giant cells showed Schaumann bodies in the cytoplasm (Fig. 3a-c). The dural tissue also showed granulomatous inflammation (Fig. 3d). Special stains for acid-fast bacilli and fungal elements were negative. The diagnosis of non-necrotizing chronic granulomatous meningomyelitis suggestive of NS was offered based on this.

Further, MRI scan of the brain and whole-body fluorodeoxyglucose-positron emission tomography scan did not show any other significant systemic involvement. She was treated with 1 mg/kg of prednisolone along with mycophenolate mofetil. On follow-up, she recovered from quadriparesis. MRI scan done at 6 months follow-up showed significant improvement with reduction of signal intensity, extent, and enhancement of the intramedullary and dural lesion (Fig. 1d). After 1 year, her steroid was stopped completely, and presently she is only on mycophenolate mofetil.

DISCUSSION

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology that most often affects the lungs followed by other systems such as the eyes, skin, liver, spleen, and nervous system [1,2,3,7]. NS was first reported in 1904 and is often a part of systemic sarcoidosis with superimposed neurological manifestations [1,3,4]. Isolated NS is uncommon, and the ones restricted to the spinal cord are exceptionally rare. Spinal sarcoidosis when involved shows a predilection for the cervical, thoracic, and lumbar spinal cord in their frequency of location.

The incidence of spinal sarcoidosis is estimated to be 0.43–0.8% and the disease can present as intramedullary lesions (35%), intradural-extramedullary lesions (35%), a combination of these two lesion types (23%), or extradural lesions (7%). Spinal sarcoidosis can present with varied symptoms, including weakness; paresthesia's; back pain or radicular pain, myelopathy; depending on the site of involvement, NS cannot be differentiated from other common spinal cord lesions as demyelination or neoplasms [1,3-8].

The non-specific symptoms, varied clinical presentation, rather non-specific imaging findings make the diagnosis of NS quite challenging. Tissue biopsy and histopathological examination are still the gold standard for diagnosis [1,2,3,7]. The diagnosis can be established on skin or lymph node biopsy in cases of multisystem involvement. In the absence of reliable laboratory findings, imaging features of neoplasm and clinical progression after the periodical waning of symptoms as in our case a definitive diagnosis was possible only through tissue biopsy [1,2,3]. Spinal sarcoidosis most commonly demonstrates smooth or nodular leptomeningeal enhancement with patchy peripheral cord enhancement because of infiltration of the perivascular spaces. The radio imaging spectrum of spinal sarcoidosis varies from diffuse intramedullary T2 hyperintensity to mass-like intramedullary enhancement [2,6-8].

The laboratory investigations such as elevated cerebrospinal fluid (CSF) oligoclonal bands, serum, and CSF ACE levels can be supportive of the diagnosis of NS; however, due to lack of sensitivity and specificity, the absence of these does not rule out the diagnosis as was in our case. The imaging findings of

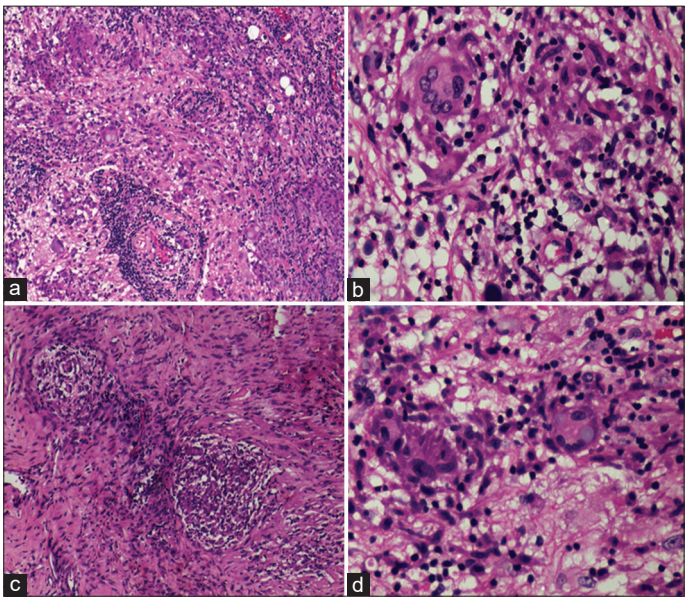

Figure 3: (a-c) Reactive nervous tissue with infiltration of multiple discrete small well-defined non-necrotizing epithelioid granulomata with giant cells. Few giant cells showed Schaumann bodies in the cytoplasm; (d) dural tissue showing granulomatous inflammation

spinal sarcoidosis can mimic other disease processes such as neoplasm, demyelinating processes, post-infectious myelitis, spondylotic compressive myelopathy, lymphoma, cord ischemia, and paraneoplastic processes [6-9].

The review of reported cases in the literature demonstrates that suspicion of sarcoidosis should be high in patients with contiguous multi-segmental intramedullary T2 signal hyperintensity with a combination of leptomeningeal and/or focal patchy intramedullary enhancement without significant cord expansion in patients in the absence of significant stenosis [7-10]. The retrospective review of radio imaging in our case supports this observation.

Treatment with steroids may result in decreased enhancement. Although many sarcoid-related MRI abnormalities are not associated with correlating symptoms, there is a high degree of concordance between changes in clinical symptoms and MRI abnormalities, particularly in the cranial vault and spinal cord [1,9].

Although the initial treatment of sarcoidosis is with steroid, which can be administered on a presumptive diagnosis based on certain imaging and biopsy features as described above, in the appropriate clinical context, the response to steroids can be variable as was in our case and in other cases described in the literature [2,5]. This makes surgical intervention and tissue diagnosis mandatory, although invasive. Studies have reported that spinal cord sarcoidosis is one of the steroid-refractory lesions among NS and often requires additional immunosuppressant therapy which suggests that the absence of response to steroid does not rule out NS once again, highlighting the importance of biopsy [2,11].

The intraoperative pathological examination can be useful to assess the nature of the lesion to decide on the extent of resection required. In our case, proving that it was a granulomatous lesion helped to avoid aggressive resection and subsequent operative morbidity. A leptomeningeal and dural biopsy may also be useful for the confirmation of the diagnosis of NS as intramedullary involvement by perivascular spread is also a well-known proposed mechanism. The histopathological hallmark of sarcoidosis is non-necrotizing granulomatous lesions which can sometimes show asteroid bodies or calcified Schaumann bodies as in our case (Fig. 3c). The histopathological workup should include special stains to rule out differential diagnoses of tuberculosis and fungal infections.

According to Zagilek's criteria, NS can be diagnosed as definite, probable, and possible based on clinical symptomatology, MRI features, laboratory findings, presence or absence of systemic sarcoidosis, exclusion of alternative diagnosis, and positive nervous system histology. There have been no randomized, double-blind, and placebo-controlled treatment trials for NS, but there is a consensus that these patients should be treated with corticosteroids [12]. Patients who deteriorate despite aggressive corticosteroid treatment, who cannot tolerate corticosteroids, or who have a primary contraindication to corticosteroid treatment may benefit from alternative therapies [2-4]. In our case, the patient responded well to mycophenolate mofetil that was added to the steroid therapy.

CONCLUSION

Isolated spinal intramedullary NS is extremely rare in the absence of other systemic involvement. The clinical and radiological features of intramedullary NS can be variable and non-specific. Manifestations mimicking an intramedullary neoplasm are common and a relapsing-remitting neurological course is known. The intramedullary infiltrating lesion with leptomeningeal enhancement on MRI should raise the possibility of NS. A complete systemic workup for evaluation of systemic involvement needs to be done. Biopsy of the spinal lesion can be used for definitive diagnosis in cases of isolated spinal NS. A high index of suspicion and a multidisciplinary approach is essential for accurate diagnosis and management of isolated involvement of NS.

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