Necrotising Sarcoid Granulomatosis of the Spinal Cord: Case Report

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A B S T R A C T

We report a patient who presented with leg weakness and cervical lymphadenopathy. Thoracical magnetic resonance imaging showed an inhomogenously increased signal in the thickened portion of the cord. Multilevel laminectomy and spinal cord biopsy revealed granulomatous infiltrations with necrosis. Review of the histopathological finding established the diagnosis of necrotising sarcoid granulomatosis (NSG) of the spinal medulla, cytological FNA diagnosis of the neck lymph node was granulomatous inflammation with necrosis, but histopathological analysis of the same neck lymph node disclosed granulomatous inflammation without necrosis. On further radiographic chest evaluation mediastinal lymphadenopathy was found. Immunophenotyping of lymphocytes in bronchoalveolar lavage fluid (BALF) was indicative of sarcoidosis. After the administration of corticosteroid therapy the patient’s clinical condition improved, and laryngeal and mediastinal lymph nodes subsided with minor changes remaining in the spinal medulla, which, based upon MR assessment, were considered to be irreversible. To our knowledge, this is the first described case with finding of granulomatous inflammation with and without vasculitis in various organs, consistent with the Churg’s study who believes NSG to be a histological variant of sarcoidosis.

Key words: sarcoidosis, spinal cord diseases, central nervous system diseases, neurosarcoidosis

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown aetiology which has a propensity for the lungs, and relatively rarely, nervous sistem1. Involvement of the central nervous sistem (CNS) is clinically apparent in 2 to 7% of patients with sarcoidosis (with or without pulmonary involvement), but asymptomatic disease has been identified in autopsy cases in as many as 14% of patients2. Neurosarcoïdosis has a predilection for the base of the brain, but any part of the CNS or peripheral nervous system may be affected3. Involvement of the spinal cord by sarcoidosis is very rare4.

Necrotising sarcoid granulomatosis (NSG) was first described by Liebow in 19735. This is a disease entity that represented either necrotising angiitis with sarcoid-like reaction or sarcoidosis with necrosis of granulomas and adjacent blood vessels. Necrotising sarcoidosis has been reported most commonly in the lungs and rarely in other organ systems6. Some cases of neurosarcoïdosis (NS) with NSG with or without concomitant systemic disease have been described previously7. We report a histologically proven case with NSG which affected the thoracic spinal cord, and granulomatous inflammation of the lymph nodes and their response to corticosteroid therapy.

Case Report

A 40-year old male, mechanic by profession, presented initially in 1993 with flue-like symptoms and en-
larged lymph nodes. Considered to have respiratory infection, the patient was treated with a penicillinc antibiotic, which resulted in partial subjective improvement. Since then, the patient had been experiencing continuous fatigue and general weakness accompanied by occasional headaches, instability during walking, and dizziness, which he had been ascribing to his psychological condition (war circumstances in the Republic of Croatia). Since 1996, in addition to the previous discomforts, persistent weakness, tingling and numb sensation in the legs had been present and the patient was diagnosed as suffering from lumbosacral syndrome. Physical therapy failed to achieve any improvement. The symptoms became increasingly marked, and in 2000 the patient underwent magnetic resonance imaging (MRI) of the spine. T2-weighted image in the sagittal plane showed an inhomogenously increased signal in the thickened portion of the thoracic spinal cord, along with cord edema extending proximally (Figure 1). Tumour of the spinal medulla was suspected and surgery indicated. Basic biochemical tests and a chest radiograph gave normal results. Laminectomy at T8 to T12 along with reduction of the intramedullar process were performed, and the histopathological examination showed granulomatous inflammation. Postoperatively, the patient continued to experience the disturbance of deep sensation and weakness of the right leg, and received physical therapy with no significant clinical improvement whatsoever. Two months following surgery, temperature of up to 37.5 °C and fatigue recurred. Erythrocyte sedimentation rate was 34 mm/h. Complete blood cell count, biochemical findings, serum angiotensin converting enzyme (ACE) levels, anti-streptolysin O titers, antinuclear antibodies, and antineutrophilic cytoplasmic antibodies were within the reference ranges. A chest radiograph and ECG were normal. Microbiologic investigation of blood, bone marrow, sputum, urine and nasopharyngeal swab were negative to bacteria, fungi and Mycobacterium tuberculosis. The tuberculin skin test with 2 tuberculin units was negative. Serologic studies for toxoplasma, Leishmania, adenoviruses, Epstein-Barr virus, cytomegalovirus, virus Parvo B 19, Coxiella burnetii and Mycoplasma pneumoniae were negative, as were the antibodies to human immunodeficiency virus-type 1 and 2. Gallium scintigraphy showed pathological accumulation in the laryngeal and mediastinal lymph nodes. Antituberculous therapy was initiated (2 months of isoniazid, rifampicin and pyrazinamide, followed by another 2 months of isoniazid and rifampicin) to which the patient responded by reversal to the afebrile state.

Fig. 1. MR imaging after the first onset of neurological symptoms: T2-weighted image in the sagittal plane reveals inhomogenously increased signal in the thickened portion of the cord (white arrow), along with cord edema extending proximally (white arrowhead).

Fig. 2. MR imaging nine months later, after a multilevel laminectomy and intramedullar process reduction: T2-weighted image in the sagittal plane shows slightly reduced area of abnormal signal (white arrow) with less prominent spinal cord thickening in comparison with Figure 1 spinal cord edema is no longer present (white arrowhead).

Four months after the initiation of antituberculous treatment, the patient developed oliguric acute renal failure. Clinical and laboratory parameters indicated tubulointerstitial nephritis most probably caused by a hypersensitive reaction to rifampicin. Following the discontinuation of antituberculous therapy and a single haemodialysis session the kidney function was normalised. Repeated infectologic and immunologic tests showed no dynamics, except that the ACE value was at that time found to be borderline, 51.3 (the reference range 8–52). A postoperative MRI of the spine disclosed a slightly reduced area of abnormal signal with a less prominent spinal cord thickening (Figure 2), and an x-ray of the thorax.
demonstrated bilateral lymphadenopathy (Figure 3a and b). Further pulmonary investigation of bilateral lymphadenopathy was indicated.

The histopathological analysis of the lung tissue (transbronchial-lung biopsy) showed adequately thick septa containing mononuclear infiltrates (lymphocytes). Immunophenotyping of lymphocytes in bronchoalveolar lavage fluid revealed the predominance of CD3+CD4+ lymphocytes with the CD4/CD8 ratio of 3.8. Fine needle aspiration (FNA) cytology of the cervical lymph nodes showed granulomatous inflammation with necrosis (Figure 4 and 5). The histopathological finding of the extirpated neck lymph node showed the presence of well-circumscribed granulomas without central necrosis (Figure 6). Granulomatous inflammation with vasculitis was then established by the review of the previous histopathological analysis of the spinal medullar tissue (Figure 7a and b). From such histopathological finding, clinical course of the disease and the findings excluding other diseases, the diagnosis of necrotising sarcoid granulomatosis was inferred and corticosteroid therapy was instituted (metylprednisolone in a dose of 1 mg/kg of body weight).

After the 10 months administration of corticosteroid therapy the clinical picture has improved, and changes previously detected on MRI regressed. T2-weighted im-

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Fig. 3. An x-ray of the thorax demonstrated bilateral lymphadenopathy. a) AP, b) lateral.

Fig. 4. Cervical lymph node FNA smear: Small lymphocytes, cluster of epithelioid cells and multinuclear giant cell (Langhans type). MGG staining, original magnification 100x.

Fig. 5. Cervical lymph node FNA smear: Scattered small lymphocytes, few epithelioid cells and necrosis elements. MGG staining, original magnification 100x.

Fig. 6. The histopathological finding of the extirpated neck lymph node: the presence of well circumscribed granulomas without central necrosis.
age in the sagittal plane revealed a decreased size and number of abnormalities, which were now better delineated and of a higher signal intensity (Figure 8). There have remained visible changes of the spinal medulla, which according to the MRI evaluation are considered definitive and doubtful as to whether they are consequent to posttherapeutic vascularisation, or surgery.

Discussion and Conclusion

Necrotising sarcoid granulomatosis (NSG) is a rare disease first described by Liebow in 1973. The aetiology of the disease is unknown. There has been doubt as to whether NSG is a distinct disease entity, or a histological variant of sarcoidosis. According to Churg, NSG would appear to be a form of sarcoidosis, while Saldana would not seem to consider the disease to be related to classical sarcoidosis. It most commonly occurs in middle aged individuals, particularly women. Although any organ may be affected by the disease, it has shown a strong propensity for the lungs. Its occurrence in the central nervous system has been observed only in a small number of patients. The spinal cord is rarely the predominant site of involvement by both sarcoidosis and NSG. Sarcoidosis of the spinal medulla has been described in the literature in several cases, while NSG of the spinal medulla has been reported in three cases. Majority of patients with NSG demonstrate the course of the disease similar to that in classical sarcoidosis. An average of 40% of patients is symptom free, whereas the remainder of the patients have mild, nonspecific symptoms such as cough, temperature, chest pain, weakness and fatigue. The physical examination is generally non diagnostic. The diagnosis is based on the clinical picture complemented by radiological and histopathological examination of the affected organ.

In NSG of the lungs radiologic lesions are most often demonstrated as nodular infiltrates. Bihilar lymphadenopathy is rare, with an incidence of less than 10%. NSG changes in the spinal medulla are best visualized by magnetic resonance imaging (MRI). Typical MRI findings include a thickened portion of the spinal cord and an increased signal intensity. Histologically, granulomas similar to that in sarcoidosis are found with a various degree of necrosis and vasculitis. Numerous inflammatory cells are found in the intragranulomatous space. The necrosis may affect small central areas but Churg did not require this feature for the diagnosis of NSG. Vascular involvement is prominent and affects both arteries and veins.

The differential diagnosis of sarcoid vasculitis are other primary granulomatous systemic vasculitides including Wegener’s granulomatosis, giant cell arteritis, Churg Strauss vasculitis, Takayasu’s arteritis and infection. On occasions it may be difficult to differentiate between NSG and Wegener’s granulomatosis, particularly when changes in the thoracic and renal area are found. Our patient had reversible renal damage, which was attributed to the adverse effects of rifampicin. In fact, renal functions were normalized after a single dialysis session and discontinuation of antituberculotic therapy including Rimactan. Simultaneously, ANCA (antineutrophil cytoplasmic antibody), being positive in 90% of patients with Wegener’s granulomatosis, in our patient was negative. In contrast to NSG, Wegener’s granulomatosis must have necrosis of vessel walls. Some cases of neurosarcoidosis (NS) with NSG with or without concomitant systemic disease have been described previously. We report a histologically proven case with NSG which affected the thoracic spinal cord, and granulomatous inflammation of the lymph nodes and their response to corticosteroid therapy.

In our patient paraparesis was a leading symptom of the disease. It appeared as a consequence of lesions in the spinal medullar area present at the MRI evaluation. In addition to spinal medullar lesions, enlarged lymph nodes were also found in the neck and mediastinum. Previously reported cases of NSG involving the spinal medulla...
did not show simultaneous other organ involvement. In our case granulomatous inflammation and vasculitis were found, suggesting NSG in the spinal medulla, while the neck lymph nodes were affected with granulomatous inflammation with minimal necrosis established in FNA cytology. Immunophenotyping of lymphocytes obtained by bronchoalveolar lavage fluid was supportive of granulomatous inflammation. The serum ACE level was within the normal range. Such finding of granulomatous inflammation with or without vasculitis in various organs is consistent with the Churg’s study who believes NSG to be a histological variant of sarcoidosis.

Corticosteroids are the therapy of choice. Prednisolon dosage may range from 40 to 80 mg per day, and treatment is long-term. Alternative therapy with corticosteroids include methotrexat, azathioprine, cyclophosphamide, hydrochloroquine sulfate, cyclosporine and radiation. Surgical treatment is indicated in patients who have developed complications including acute hydrocephalus and progressive neurological events where systemic therapy has proved to be ineffective. In our patient surgery was indicated because he was suspected of having an expansive process. If the previous illness was connected with the symptoms, the thorough examination could reveal the enlarged neck lymph nodes. The cytology and histopathology examination of the lymph nodes, bilateral lymphadenopaty and BAL examination would point to the right diagnosis and treatment and the surgery with all the negative consequences could be avoided.

To our knowledge, this is the first described case with finding of granulomatous inflammation with and without vasculitis in various organs, consistent with the Churg’s study who believes NSG to be a histological variant of sarcoidosis. We have found granulomatous inflammation and vasculitis, suggesting NSG in the spinal medulla, while the neck lymph nodes were affected with granulomatous inflammation with minimal necrosis. Previously reported cases of NSG involving the spinal medulla did not show simultaneous other organ involvement.

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**NEKROTIZIRAJUĆA SARKOIDNA GRANULOMATOZA KRALJEŽNIČNE MOŽDINE: PRIKAZ SLUČAJA**

**SAŽETAK**

Prikazali smo slučaj bolesnika koji se prezentirao sa slabosti u nogama i cervikalnom limfadenopatijom. Magnetna rezonanca je pokazala inhomogenog pojačani signal u zadebljanoj dijelu kralježnice, a lateralnom raščeljavanju i oksidativnom procesu, a upotreba prednog sa brzim rastom i radijacijom među limfenim maličadima je dovela do izraženog proizvoda. S obzirom na prethodne poremećaje, zapažene su znatne promene u kralježnici u skladu sa Churg-ovim priznanjem kako je NSG histološka varijanta sarkoidoze. Prema našem znanju, ovo je prvi opisani slučaj granulomatozne upale sa i bez vaskulitisa u različitim organima. Zbog toga, ovo je prvi opisani slučaj granulomatozne upale sa i bez vaskulitisa u različitim organima. Zbog toga, ovo je prvi opisani slučaj granulomatozne upale sa i bez vaskulitisa u različitim organima. Zbog toga, ovo je prvi opisani slučaj granulomatozne upale sa i bez vaskulitisa u različitim organima.