

# Sciatic nerve sarcoidosis: utility of magnetic resonance peripheral nerve imaging and treatment with radiation therapy

## Case report

ANDREW T. DAILEY, M.D., MATTHEW T. RONDINA, M.D., JEANNETTE J. TOWNSEND, M.D., DENNIS C. SHRIEVE, M.D., PH.D., J. RICHARD BARINGER, M.D., AND KEVIN R. MOORE, M.D.

*Department of Neurosurgery, University of Washington, Seattle, Washington; Departments of Internal Medicine, and Pathology, University of Utah School of Medicine; and Departments of Radiation-Oncology, Neurology, and Radiology, University of Utah Health Sciences Center, Salt Lake City, Utah*

✓ Sarcoidosis may involve both the central and peripheral nervous system, although peripheral nerve manifestations are usually seen late in the disease. In this report, the authors describe a case of sarcoidosis in a 22-year-old woman who presented with a foot drop. Although results of conventional lumbar magnetic resonance (MR) imaging were normal, MR peripheral nerve imaging of the thigh showed a mass in the sciatic nerve indicating tumor. An intraoperative biopsy sample revealed noncaseating granulomas consistent with sarcoid. The patient was treated with steroid drugs to control the manifestations of her disease but exhibited early signs of femoral bone necrosis, which required discontinuation of the steroids. She was then treated with local radiation therapy. At her 2-year follow-up visit the patient demonstrated relief of her symptoms and improvement on MR peripheral nerve imaging. This case demonstrates that sarcoidosis may present with peripheral nerve manifestations. The appearance of a diffusely swollen nerve on MR imaging should prompt clinicians to include sarcoidosis in the differential diagnosis and plan surgery accordingly. Patients who are not responsive to or who are unable to tolerate medical therapy may be treated with radiation therapy.

**KEY WORDS** • sarcoidosis • peripheral nerve • radiation therapy • magnetic resonance peripheral nerve imaging

**S**ARCOIDOSIS is a systemic, idiopathic granulomatous disease that involves the CNS in approximately 5% of patients.<sup>16,22,24,26</sup> Of the patients with neurological involvement, most present with CNS or cranial nerve manifestations. Peripheral nervous system manifestations are seen only rarely in patients with sarcoidosis and are usually encountered later in the course of the disease. In one clinical series of patients with neurosarcoidosis, only 10% of patients had primarily peripheral nerve or muscle lesions, whereas the majority (90%) had primarily CNS or cranial nerve involvement.<sup>19</sup> Most patients who have peripheral nerve or muscle lesions only display the peripheral signs or symptoms after first exhibiting CNS involvement.

Confirming the diagnosis of sarcoidosis is often difficult. Although CNS sarcoidosis can be diagnosed using contrast-enhanced MR imaging,<sup>25</sup> the diagnosis of PNS sarcoidosis is more difficult. With conventional imaging modalities such as MR imaging and computerized tomography scanning providing a limited spatial and contrast resolution of the PNS, suspected peripheral nerve disease may require surgical exploration without the aid of imaging. Recently, the development of high-resolution MR peripheral nerve imaging sequences has provided clinicians with improved resolution of peripheral nerve structures.<sup>3,8,17</sup>

The treatment of sarcoidosis is also subject to some con-

trovery. The rarity of this disease makes randomized trials difficult. Most patients are treated with a combination of steroid and immunosuppressant medications. Although many patients respond to these modalities, often they are unable to tolerate the side effects associated with these drugs or do not respond to them. To date there have been several case reports of patients with CNS sarcoidosis that is refractory to steroid therapy who have received local radiation therapy, with varying degrees of success.<sup>1,5,6,12,18,20,21,27,29</sup>

We report on the case of a young woman whose initial presentation was a foot drop. A diagnosis of sciatic nerve sarcoidosis was made after using MR peripheral nerve imaging to guide an intraoperative biopsy procedure. Although the patient was maintained on high-dose steroid drugs for 2 years, she exhibited early signs of bone necrosis. Local radiation therapy was performed, resulting in improvement in her symptoms.

## Case Report

*History and Examination.* This 22-year-old woman presented to her primary care physician with numbness and burning in the sole of her right foot. The sensory changes progressed over 8 months to include the dorsum of her right foot and her right anterior calf. She subsequently experienced an unsteady gait and was referred for neurological consultation. On physical examination, sensation below the

*Abbreviations used in this paper:* CNS = central nervous system; MR = magnetic resonance; PNS = peripheral nervous system.

## Sarcoidosis of the sciatic nerve

right knee was found to be impaired in both the tibial and peroneal nerve distributions, with preservation of sensation within the saphenous nerve distribution along the medial aspect of the calf. There were no palpable leg masses. Motor strength was 5/5 (Medical Research Council<sup>23</sup> grading) throughout the left lower extremity. In the right lower extremity, hamstring strength was 4/5 and quadriceps strength was 5/5. The patient had 0/5 strength in dorsiflexion, plantar flexion, extension of the hallucis longus, foot eversion, and foot inversion; she had an absent right ankle jerk. The rest of her reflexes were 2+ and symmetrical. She had a circumducting gait with a right foot drop. Her station was normal. Results in the remainder of the neurological examination were normal.

**Neuroimaging Procedures.** Magnetic resonance imaging of the brain and spinal axis revealed no abnormalities. Subsequent examinations concentrating on the right pelvis and thigh revealed some tenderness to deep palpation of the midportion of the posterior thigh. High-resolution MR peripheral nerve imaging and standard MR imaging of this area were performed using a 1.5-tesla MR unit (Signa; General Electric Medical Systems, Waukesha, WI) equipped with a torso phased-array surface coil. After a coronal localizer sequence was acquired, axial T<sub>1</sub>-weighted, fast-spin echo inversion-recovery, and T<sub>1</sub>-weighted contrast-enhanced MR images were obtained throughout the thigh. The MR peripheral nerve imaging revealed an extensive enhancing mass within the right sciatic nerve (Fig. 1) that extended from the ischial tuberosity to 6 cm proximal to the tibioperoneal bifurcation. The mass was hypointense on T<sub>1</sub>-weighted MR images and enhanced after intravenous contrast administration. A T<sub>2</sub>-weighted image revealed low signal intensity within the mass, and hyperintense fascicular enlargement proximal and distal to it. The MR peripheral nerve images also revealed denervation changes within the biceps femoris and semimembranosus muscles.

**Operation.** With the aid of the MR peripheral nerve imaging findings, intraoperative sciatic nerve exploration was performed. A 13-cm incision was made from 3 cm below the right posterior superior iliac spine to just inferior to the right buttock crease. The incision was infiltrated and the fascia overlying the long head of the biceps femoris and semitendinosus muscles was opened. The muscles were spread to expose the right sciatic nerve. The fascia was opened and both palpation and visualization revealed diffusely thickened and swollen sciatic nerve fascicles with no discrete lesion. There appeared to be a diffusely infiltrating process extending the entire length of the exposed sciatic nerve. The nerve was isolated from adjacent soft tissues and separated into its lateral peroneal and medial tibial component; both the peroneal and tibial components of the sciatic nerve were firm and woody. Internal neurolysis was performed and there were no electromyographic responses in the gastrocnemius or the tibialis anterior muscles or nerve action potentials recorded across the thickened fascicles on nerve stimulation. Biopsy samples of visually abnormal nerve fascicle were sent for frozen and permanent section analysis. The frozen sections were consistent with a diffuse, infiltrating, chronic inflammatory process with noncaseating granulomas, characteristic of sarcoidosis (Fig. 2).

An intraoperative spinal tap was performed and the cerebrospinal fluid angiotensin-converting enzyme level was

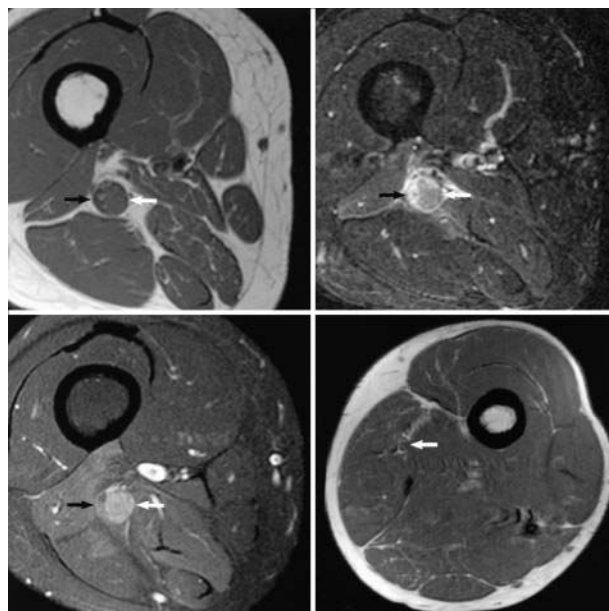


FIG. 1. *Upper Left:* Magnetic resonance peripheral nerve image of the sciatic nerve sarcoidosis mass. Axial T<sub>1</sub>-weighted image through the midthigh demonstrating marked enlargement of the sciatic nerve, in particular the tibial division (*white arrow*). The peroneal division is minimally enlarged and shows mild hypointensity of compressive edema (*black arrow*). *Upper Right:* Magnetic resonance peripheral nerve image of the sciatic nerve sarcoidosis mass. Axial fast-spin echo inversion-recovery image acquired at the same level as in *upper left* panel, demonstrating hypointensity and enlargement of the tibial division (*white arrow*) with loss of normal internal architecture. The peroneal division (*black arrow*) reveals abnormal hyperintensity with relative preservation of internal architecture, implying compressive edema with no mass infiltration. *Lower Left:* Magnetic resonance peripheral nerve image of the sciatic nerve sarcoidosis mass. Axial T<sub>1</sub>-weighted contrast-enhanced image through the midthigh confirms mild homogeneous enhancement of the mass within the tibial division (*white arrow*), but no abnormal enhancement of the peroneal division (*black arrow*). *Lower Right:* Magnetic resonance peripheral nerve image of a healthy sciatic nerve (*white arrow*).

measured along with the serum angiotensin-converting enzyme level; these were both within normal limits. Fungal cultures, yeast preparations, an acid-fast bacillus stain, and tuberculosis cultures of the nerve were all negative. Postoperatively, a tuberculin test and chest x-ray were performed to exclude other granulomatous diseases such as tuberculosis or other evidence of sarcoid lesions; results of both tests were negative.

**Steroid Treatment.** The patient was placed on a regimen of steroid drugs in consultation with the neurology service and continued to receive these drugs for approximately 2 years. She experienced a gradual but significant resolution of her weakness while receiving high-dose steroid agents, which were tapered slowly over several months. Nevertheless, while she was being maintained on a minimal alternate-day dose, her weakness recurred. Resumption of a higher dose produced cushingoid side effects with early signs of femoral bone necrosis that were evident only on MR images. She was referred for radiation therapy of the thigh.

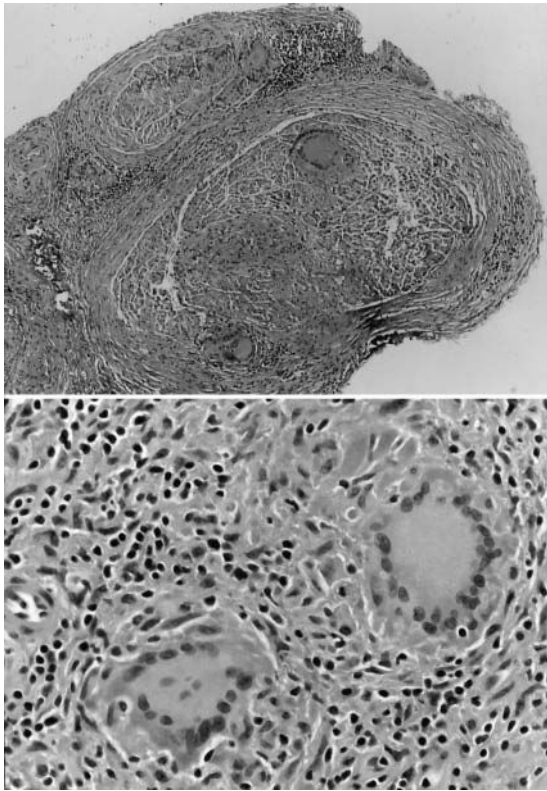


FIG. 2. *Upper:* Low-power photomicrograph of a fascicular biopsy specimen obtained in the tibial component of the sciatic nerve, showing thickened epineurium with marked lymphocytic infiltration as well as multinucleated giant cells and noncaseating granuloma formation. In addition, there is also evidence of endoneurial granuloma formation and lymphocytic infiltration. H & E, original magnification  $\times 10$ . *Lower:* High-power photomicrograph of an endoneurial section showing granuloma formation and multinucleated giant cells. H & E, original magnification  $\times 40$ .

**Radiation Treatment.** Radiation treatment was delivered with a 10-MVp photon beam produced by a linear accelerator. The treatment volume was based on MR images of the right thigh, computerized tomography-based simulation, and three-dimensional treatment planning. The swollen sciatic nerve was contoured as the gross target volume. The length of nerve targeted extended from the level of the lesser trochanter to just superior to the level of the femoral condyles. A total dose of 20 Gy was delivered in 10 fractions over a period of 12 days. The prescription dose was specified at the 97% isodose line. The patient reported prompt improvement in muscle tone and decreased pain at the end of radiation treatment. No adverse reactions were encountered.

**Posttreatment Course.** Since she completed her radiation therapy the patient has been clinically stable and has attained considerable resolution of her symptoms. She has experienced a modest but significant improvement in strength following radiation treatment: she has 4/5 dorsiflexion strength and 5/5 plantar flexion, hallucis longus extension, foot eversion, and foot inversion strength. She has not had substantial changes in sensory abnormalities. She no longer needs to wear a brace, although she continues to walk with a slight right steppage gait. An MR peripheral nerve image

obtained 24 months after radiation treatment demonstrated diminished sciatic nerve enhancement compared with MR peripheral nerve images acquired before treatment.

## Discussion

The frequency of neurological involvement in sarcoidosis ranges from 1 to 27% (mean 5%).<sup>4,19</sup> In patients with neurosarcoidosis, peripheral nerve symptoms are very rarely the presenting complaint and only 5 to 10% of patients with neurosarcoidosis ever experience PNS involvement. In a series of 50 patients, only four experienced solely PNS symptoms and only one of these accompanied acute sarcoidosis.<sup>1,8</sup> The patient described in our report demonstrated no evidence of extrasciatic nerve involvement on physical examination or on neuroimaging. This unusual presentation of sarcoidosis should be kept in mind during the differential evaluation of peripheral nerve disease.

As far as we know, this case is the first one in which sarcoidosis has been diagnosed with the help of MR peripheral nerve imaging. Although the MR modality traditionally has been used in the imaging of soft tissues, conventional MR imaging has limited spatial and contrast resolution and often suffers from motion artifacts resulting from long imaging times. Furthermore, routine MR imaging protocols do not clearly demonstrate the individual components of the lumbosacral plexus or sciatic nerve. Recent technological advances have led to the development of MR peripheral nerve imaging, which provides significantly better depiction of peripheral nerve structures.<sup>3,7</sup> With this modality, peripheral nerves have a characteristic fascicular architecture that distinguishes them from adjacent blood vessels, muscle, and adipose tissue. Clinically, MR peripheral nerve imaging may provide important information regarding peripheral nerve anatomy, internal nerve signal changes, and the presence of intraneural pathological lesions.<sup>13</sup> Recent investigations have found that MR peripheral nerve imaging also may aid in the diagnosis of nerve entrapment,<sup>15</sup> cervical radiculopathy,<sup>3</sup> and peripheral nerve entrapment.<sup>11</sup>

Magnetic resonance peripheral nerve imaging may be helpful in the evaluation of PNS masses or lesions. In a recent study the use of MR peripheral nerve imaging was investigated in 13 patients with neuropathic leg pain connected to the lumbosacral plexus or the sciatic nerve. All patients had undergone lumbar spine MR imaging and in all 13 cases the lumbar MR images did not reveal the cause of the symptoms. Nevertheless, MR peripheral nerve imaging demonstrated an abnormality that accounted for the patients' symptoms in all 13 cases.<sup>17</sup>

Magnetic resonance peripheral nerve imaging may be used to identify focal peripheral nerve abnormalities, which will allow for more directed surgical exposure and treatment planning. Although the most common cause of extraspinal nerve injury is focal trauma, peripheral nerve sheath tumors, focal entrapment and focal neuropathies must all be included in the differential diagnosis. Our case illustrates the wide spectrum of disease encountered in focal nerve lesions.

Treatment for neurosarcoidosis has typically involved large doses of steroid agents to suppress the symptoms, followed by tapering down to a maintenance dose.<sup>1,10,14</sup> Nevertheless, many patients are unable to tolerate prolonged oral



steroid treatment or experience adverse side effects and need other therapeutic interventions. In one large series of patients with neurological manifestations of sarcoidosis, investigators found that less than 30% of patients tolerated maintenance steroid medications.<sup>14</sup> Medications such as methotrexate and cyclophosphamide are successful 75 to 90% of the time<sup>1,28</sup> in patients who are unable to tolerate high-dose steroid drugs. Nevertheless, the addition of these medications warrants monitoring for adverse side effects.

Prior to the development of immunosuppressive therapies, pulmonary sarcoidosis was occasionally treated with radiation therapy. The initial reports described clinically and radiographically confirmed improvement for doses between 20 and 25 Gy,<sup>2,18,20</sup> although not all series demonstrated improvement at these dose levels.<sup>5</sup> Other authors have described the use of radiation therapy to treat a variety of other manifestations of sarcoid. After radiation therapy, a lower maintenance dose of steroid agents was successful in stabilizing disease.<sup>5,9,12,20,29</sup>

With regard to neurosarcoidosis, radiation therapy has been used to treat both meningitic and solitary parenchymal lesions. Doses ranging from 10 to 30 Gy have reduced the size of the lesions or allowed the patient to be maintained on a lower dose of steroid drugs. Although the exact mechanism is unclear, Stelzer, et al.,<sup>27</sup> have hypothesized that radiation therapy may interfere with lymphocytic proliferation or it may inhibit the inflammatory cascade that is the result of lymphocytic invasion.

We believe this is the first report of external-beam radiation therapy being used in a case of sarcoidosis with a discrete peripheral nerve lesion. The patient's course illustrates the wide spectrum of presentations that comprise neurosarcoidosis and demonstrates the variety of treatment options available to combat these problems.

### Conclusions

This case report illustrates that, although it is considered primarily a disease of the CNS, sarcoidosis can present with peripheral nerve disease. The diagnosis of peripheral nerve sarcoidosis may be made earlier with the use of new high-resolution MR peripheral nerve imaging protocols. Magnetic resonance peripheral nerve imaging can also aid surgical planning for exploration and treatment. Once the diagnosis is confirmed a wide variety of treatment modalities, including steroid medications and radiation therapy, may be used to stabilize the patient's clinical course.

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Address reprint requests to: Matthew T. Rondina, M.D., Department of Internal Medicine, University of Utah School of Medicine, 30 North 1900 East, Room 4C106, Salt Lake City, Utah 84132. email: matthew.rondina@hsc.utah.edu.