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Expect the Unexpected: Unusual Neurological Presentation of Bone Marrow Sarcoidosis

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Abstract. Bone marrow granulomas are rare and, when they occur, sarcoidosis is an uncommon etiology. This report describes a case of a 58-year-old man who presented with a five-month history of bilateral lower limb paresis. His paresis was associated with urinary and fecal incontinence and impotence, but without any loss of sensations. Head, chest, abdominal, and pelvic CT scans and MRI images, and a full-body Gallium 67 scan were all within normal limits. A CT-guided biopsy of the L1-L2 vertebral bodies showed non-caseating granulomatous inflammation. Serum angiotensin-converting enzyme (ACE) level was elevated. A diagnosis of bone marrow sarcoidosis was made after other differential diagnoses were excluded. *(Sarcoidosis Vasc Diffuse Lung Dis 2014; 31: 67-70)*

Key words: Sarcoidosis, Paresis, Incontinence, Impotence, Angiotensin-Converting Enzyme.

Case report

Our patient is a 58 year-old male with a past medical history of coronary artery disease, hypertension, and hyperlipidemia, who presented with lower extremity weakness which started five months ago. The weakness started in the right lower limb, but later became bilateral and more severe on the right side. At the time of his presentation, the patient described bilateral paraparesis more severe on the left. He also described tingling and numbness sensations bilaterally on the lateral side of the thighs radiating toward the anterior aspect of the knees. He described two episodes of uncontrolled urination in public settings without having felt an urge to urinate. He also complained of gradual onset of urinary incontinence, fecal incontinence, and impotence. Due to his inability to stand or ambulate, he had been lying in bed for approximately five months prior to admission. He denied any cough, fever, chills, chest pain, shortness of breath, and weight loss. He had been taking captopril, atenolol, hydrochlorothiazide, aspirin, isosorbide mononitrates, and biogabalin.

Physical exam revealed normal cranial nerve functions. Muscle strength in the lower limbs was 2/5 (R) and 0/5 (L). There was no deficit of pain or touch sensations in any aspect of his body. Tendon reflexes were normal in both upper extremities. However, he had hyperreflexia bilaterally in his lower extremities, in addition to bilateral positive Babinski sign. His exam also showed clonus bilaterally up-

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on passive dorsiflexion of his feet. There was normal muscle tone in the lower limbs. Passive flexion of his left leg was painful. He was unable to stand or ambulate. Neurological examination of his upper limbs was insignificant. Rectal tone was loose. Upon admission, he had an external urinary catheter in place, and he had been using these catheters since he started having urinary incontinence. There was grade II pitting edema in his ankles bilaterally. The pulse on the dorsum of the right foot was not palpable, other peripheral pulses were normal. His right calf was mildly tender and distinctly warmer than his left calf. The patient was aware and well oriented to time, place, and people. His cardiac and chest exams were within normal limits, and his abdominal exam was insignificant.

Complete blood count with differential, electrolytes, ESR, renal and liver function tests, vitamin B12 serum levels, serum CA-19.9 and CEA were all within normal limits. His blood hemoglobin was 17 mg/dL, and blood RBC was 7.6 million/mL. ParaTyphi (AO), Typhi (O), ParaTyphi (BO), Typhi (H) serology, as well as Brucella Abortus and Brucella Meliteasis serology were all negative. Treponema pallidum recombinant screening test was nonreactive.

CSF was clear, colorless; white blood cells (WBC) were rare; red blood cells (RBC) were rare; CSF glucose, 110 mg/dL (normal 40-80 mg/dL); and CSF protein, 55 mg/dL (normal 15-58 mg/dL). No malignant cells or oligoclonal bands were detected. CSF viral, bacterial, and fungal cultures and cytology were negative. The patient had normal serum free PSA and total PSA levels and normal blood protein electrophoresis. The skin tuberculin test and the serum tuberculosis serology (IgG and IgM) were negative. Urinalysis and urine culture showed severe lower urinary tract infection (UTI) with Klebsiella with over 100,000 colonies. Co-amoxiclav was added to the patient's regimen.

An electrocardiogram showed normal sinus rhythm with signs of left ventricular hypertrophy. A chest x-ray revealed mediastinal dilatation, diffuse reticulonodular infiltrations, and suspicion of a mass above the left hilum. This was followed by a chest, abdomen, and pelvis computed tomography (CT) scans with contrast which indicated fibrous reticulonodular infiltrations diffusely across both lungs, minor basal collapsing lamellae with minor bilateral pleural effusions. Multiple pulmonary emboli in the segmental and subsegmental arteries bilaterally (most distinct in the lower lung lobes) were also seen. There were no abdominal masses, abdominal lymphadenopathy, or free fluids in the peritoneum. Osteoarthritic changes were seen in the spine with osteoporotic signs. Lack of homogeneity in the density of the vertebral bodies was noted.

A head, chest, abdomen, and pelvis MRI showed several foci of tissue masses (high signal in T2 and FLAIR, low signal in T1) infiltrating the bone marrow of all lumbar vertebrae and the thoracic vertebrae (T2, T3, T4, T5) with smaller other foci in the rest of the vertebrae suggesting metastases or infiltrations. Also noted were the osteoarthritic signs with cervicothoracic scoliosis. Pelvic MRI revealed abnormal signals in the bone marrow of the hip bones most evident in the iliac crests. Head MRI was unremarkable. A full-body ^{99m}techetium bone scintigraphy scan showed mild increased absorption of the radiolabelled substance in the thoracic T10-T12 vertebrae, lumbar L1-L2 vertebrae, anterior arch of the right 4th rib, and the lateral arch of the right 11th rib, suggesting secondary metastases or infiltrations.

A Doppler ultrasound of the lower limb veins showed a new-onset large deep vein thrombosis (DVT) in the right popliteal vein extending towards the beginning of the femoral vein. Intravenous low molecular weight heparin (LMWH) and subcutaneous enoxaparin were added to the patient's regimen for the DVT.

An iliac bone marrow biopsy was taken and showed mild hypercellularity (70%), myeloid and erythroid series slightly hyperplastic, and megaloblastic changes were evident. Overall, the biopsy showed focal nonspecific granulomatous inflammation with giant cells.

A full-body Gallium-67 scan came out negative. A CT-guided direct biopsy of the L1-L2 vertebral lesions revealed bone and marrow spaces showing focal fibrosis and granulomatous inflammation

with scattered multinucleated giant cells. Staining of the biopsied bone marrow sample with PAS was negative.

Vertebral biopsy re-evaluation confirmed the non-caseating granulomatous inflammation. After ruling out other causes of granulomatous inflammatory lesions, a test for serum angiotensin-converting enzyme (ACE) level was ordered and appeared 90.9 U/L (normal=8-52).

A diagnosis of bone marrow sarcoidosis was made. The patient was discharged on prednisolone 60 mg PO daily. Two months later, the patient reported mild clinical improvement. Namely, he described increased muscle strength and moderate ability to stand and ambulate with the help of a walker device alongside with improvement in fecal incontinence. No improvement in urinary incontinence or impotence was reported two months after discharge. ACE serum level decreased to 21 U/L 45 days post-treatment with prednisolone.

Discussion

Sarcoidosis is an enigmatic multisystem disease that affects people of all racial and ethnic groups and occurs at all ages (1). Given the several environmental risk factors reported to date (2), it has been hypothesized that this disease results from the cellular immune responses to various ubiquitous environmental triggers leading to the development of granulomas which are its fundamental histopathological finding (3). Sarcoidosis typically involves the lungs, eyes, and skin. However, other systems can also be involved such as the heart, gastrointestinal tract, kidneys, spleen, and central nervous system (4-6). Sarcoidosis can mimic infectious, malignant, and granulomatous conditions particularly when multiple organ systems are affected. An estimated 50% of patients are asymptomatic at the time of diagnosis, with 30-50% of the rest reporting non-specific symptoms (7). Clinical manifestations differ from one patient to another depending on the organ systems involved and the extent to which they are affected.

Bone marrow granulomas are generally rare and, when they occur, sarcoidosis is an uncommon etiology. The incidence of bone marrow granulomas is about 0.5% (8 9) and Sarcoidosis accounts for 5-9% of them. Among patients with sarcoidosis, the bone marrow is involved in 15% of cases (10). Thus, bone marrow sarcoidosis is rarely, if ever, recognized clinically (11). Neurologic manifestations of bone marrow sarcoidosis are rare, and are usually associated with spinal cord involvement (12). We hypothesize that the patient's symptoms were due to multiple spinal and spinal nerve lesions that were too small to be seen on radiological images.

The diagnosis of sarcoidosis relies on biopsy proven non-caseating granuloma and the exclusion of other differential diagnoses. Up to the date of writing this report, there is no specific diagnostic test for sarcoidosis (13) Although serum angiotensin-converting enzyme (ACE) activity can be elevated in sarcoidosis, it can also increase in other conditions such as malignancy-related hypercalcemia and primary hyperparathyroidism. Nevertheless, a decrease in serum calcium and ACE levels after the treatment with corticosteroids favors the diagnosis of sarcoidosis (14-16)

Due to the difficulty of diagnosing similar cases, treatment is often delayed. Such delays increase the risk of more serious complications of paraparesis such as pulmonary embolism, DVT, and UTI. Therefore, sarcoidosis should be considered an important differential diagnosis in cases presenting with unexplained or atypical signs of spinal nerve compression. A high suspicion of sarcoidosis must be maintained because of its ability to affect unusual tissue sites or mimic many other conditions. Tissue biopsy from affected bone marrow and other sites should be obtained to confirm the diagnosis.

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