Characteristic Imaging Patterns of Muscle Involvement in Polyarteritis Nodosa: Case Report and Review of the Literature

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Abstract

Objective: Polyarteritis nodosa (PAN) is a rare disease with complex clinical manifestations that are difficult to diagnose. Imaging diagnoses of previously reported patients have focused on vascular manifestations. Magnetic resonance imaging (MRI) has been used to detect muscle involvement in PAN. Here, we reviewed imaging findings pertaining to muscle involvement in patients with PAN. Methods: Twelve articles concerning muscle involvement in PAN were published during the period 1980–2020; 21 patients, including our patient, were examined in this study. Results: Across the published articles, the male to female ratio was 1:1, the mean patient age was 40.76 ± 18.28 years, and there were 17 patients with calf involvement and 3 with thigh involvement. The T1WI and T2WI findings were both isointense in one patient, and the T1WI findings alone were isointense in seven patients. The T1WI findings were slightly hyperintense in five patients, and no T1WI images were available for the remaining seven patients. The T2WI signal was diffusely hyperintense in 10 patients, and “patchy villous hyperintense” in 9 patients. Among the 12 patients with enhanced images, most exhibited diffuse or cotton-like enhancement, while some showed involvement of the fascia and periosteum. The comprehensive imaging analysis of our patient included muscle and blood vessel MRI and computed tomography (CT) examinations. Our patient’s disease involved the calves and thighs, with T1WI isointensity and T2WI patch-like hyperintensity, as well as cotton-like enhancement centered on blood vessels. Computed tomography angiography (CTA) and magnetic resonance angiography (MRA) examinations of the lower limbs showed beadlike changes in the arterial branches, and the lower leg arterial branches were obvious. Head MRA revealed stenosis and occlusion of the right middle cerebral artery. Additionally, the superior mesenteric artery was locally dilated around a tumor, with the greatest width being approximately 9 mm. Cerebral perfusion analysis indicated cerebral blood flow (CBF) was lower in the right cerebellar hemisphere. Conclusions: PAN should be considered in the presence of patchiness or diffuse muscle signal changes on MRI of the lower leg (or thigh), followed by vessel-centered cotton-like enhancement accompanied by fascial or periosteal enhancement. Our findings suggest that systemic examination of small and medium arteries in patients with PAN can aid early prevention and treatment.

Keywords: MRI-CT- Polyarteritis nodosa- Muscle
PAN is a segmentalized, necrotizing vasculitis that primarily involves small and medium arteries, as well as arterioles. It was defined at the Chapel Hill Conference in 2012. This rare disease may present with multiple organ involvement and complicated clinical manifestations, and is difficult to diagnose early [3]. The present report summarizes the typical magnetic resonance imaging (MRI) manifestations of patients with PAN, as described in the English-language medical literature. The shrin exhibits patchy-like T1WI isointensity and T2WI hyperintensity, with diffuse or vascular foci. After enhancement, the shrin exhibits cotton-like enhancement with vascular foci and focal accumulation in the periosteum and fascia. In our patient, plain and contrast-enhanced muscle MRI showed typical imaging manifestations, but plain and contrast-enhanced computed tomography (CT) revealed no abnormalities. The clinical manifestations of other extramural organs were normal, but computed tomography angiography (CTA) and magnetic resonance angiography (MRA) findings suggested stenosis of cranial vessels or aneurysmal dilation of the mesentery, and vascular lesions precluded clinical manifestations.

Case Report

Clinical manifestations and treatment process
The patient was a 55-year-old man who had a 1-year history of bilateral nodal erythema with swelling, but no itching desquamation, fever, or discomfort. He presented to the First Affiliated Hospital of Guangzhou University of TCM and the Fifth Affiliated Hospital of Sun Yat-sen University. He was first diagnosed with nodular erythema, and treated with hydroxychloroquine, prednisone, and Chinese medicine. These treatments did obviously relieve his symptoms, and he gradually developed nodal erythema on the wrist, left elbow, and thighs. Approximately 4 months later, he developed pain in both knee joints, accompanied by pain during exertion of the bilateral thigh muscles. He also experienced muscle fatigue, swelling and pain in the left ring finger, and limited fist clenching ability in both hands. However, there was no morning stiffness or skin tightness. Three months later, he developed nonspecific fever, primarily at night, with a maximum temperature of 39.0°C. This temperature returned to normal in the mornings. Based on the absence of other symptoms (e.g., oral and genital ulcers, sore throat, cough and expectoration, and abdominal pain), the patient was diagnosed with PAN. He was treated with prednisone acetate (30 mg/day) and methotrexate (12.5 mg/week). These treatments reduced the intermittent fever.

Laboratory examination
The initial laboratory findings were as follows: monocytes, 14.34%; absolute monocyte count, 1.19 × 10^9/L; PLT, 391.00 × 10^9/L; PT, 13.7 s; INR, 1.22 †; fibrinogen, 6.78 g/L; activated partial thromboplastin time, 33.8 †s; ESR, 44 mm/h; complement C3, 1.72 g/L; and high-sensitivity C-reactive protein, 107.73 mg/L. The patient had negative findings for cytoplasmic ANCA, formaldehyde-sensitive pANCA, glomerular basement membrane antibody, proteinase 3 target antigen, myeloperoxidase-resistant Sm antibodies, anti-SSB antibody, anti-SSA antibody, Ro-52 antibody, Scl-70 antibody, Jo-1 antibody, centromere-resistant double-stranded DNA antibody, and nucleosome-resistant antibody. The extremity electromyography (EMG) findings were as follows: abnormal bilateral median nerve F wave, bilateral ulnar nerve F wave, and bilateral tibial nerve H reflex; these findings suggested proximal nerve root involvement.

Follow-up laboratory findings were as follows: lymphocytes, 68.5%; monocytes, 10.8%; absolute monocyte count, 0.87 × 10^9/L; Hb, 128.00 g/L; HCT, 39.7%; MCH, 26.7 pg; RDW, 15.5%; MPV, 8.90 fl; PDW, 9.50 fl; ratio of large platelets, 16.3%; aspartate aminotransferase, 13.2 U/L; and 2019-nCoV nucleic acid, negative. The patient again had negative findings for cytoplasmic ANCA, formaldehyde-resistant pANCA, formaldehyde-sensitive pANCA, glomerular basement membrane antibody, proteinase 3 target antigen, myeloperoxidase-resistant Sm antibodies, anti-SSB antibody, anti-SSA antibody, Ro-52 antibody, Scl-70 antibody, Jo-1 antibody, centromere-resistant double-stranded DNA antibody, and nucleosome-resistant antibody.

Imaging findings
MRI of both lower limbs revealed swelling of both lower legs, as well as large abnormal shadows scattered in the calf muscle groups on both sides. T1WI showed mainly uneven hypointensity, and a few slightly hyperintense “internal shadows”. Fat-saturated T2WI and T2WI showed large shadows with blurred edges. Occasional hypointense signals on T1WI and hyperintense signals on T2WI were...
evident in the middle tibiofibular region on both sides, along with cotton-like enhancement centered on blood vessels (Figure 1A–D). CT of both lower extremities revealed no abnormalities (Figure 1E, F).

Bilateral lower limb MRA revealed normal findings in the abdominal aorta, bilateral common iliac arteries, bilateral external iliac arteries, bilateral internal iliac arteries, bilateral femoral arteries, bilateral popliteal arteries, bilateral anterior tibial, and posterior tibial arteries and their branches, although they had slightly rough walls. The vessels of the lower limb arteries showed beadlike changes, and the branches of the bilateral calf artery were obvious (Figure 2A).

CTA of the bilateral lower limbs revealed normal findings in the abdominal aorta, renal artery, celiac axis and its branches, superior mesenteric artery, bilateral common iliac arteries, bilateral external iliac arteries, shallow bilateral femoral artery, deep artery, popliteal artery, peripheral artery, and posterior tibial artery and its branches. The vessels exhibited rough walls, with a double leg artery and its branches, the local change a beaded samples, superior mesenteric artery local expansion in tumor samples, at its widest point is about 9 mm, bilateral popliteal artery, double pretibial, posterior tibial artery and its branches development shallow light, double leg visible early show great saphenous vein, small saphenous vein, abnormal muscle did not see reinforcement (Figure 2B).

Figure 2. 2-A, MRA of Lower Extremity Vessels; 2-B, CTA of Lower Extremity Vessels. MRA and CTA showed beadlike changes in the branches of lower extremity arteries, as well as obvious branches of lower leg arteries.

Table 1. Diagnosis and Treatment Process

| Month | Diagnosis and Treatment |
|-------|-------------------------|
| May 2018 | Erythema nodosum on both legs was suspected by the First Affiliated Hospital of Guangzhou University of TCM and the Fifth Affiliated Hospital of Sun Yat-sen University. Epitrochlear lymph nodes were also noted. |
| March 2019 | No venous abnormalities were observed in either lower limb. The diagnosis of erythema nodosum was confirmed by biopsy of subcutaneous nodules. Erythema nodosum is a clinical syndrome characterized by red, tender nodules on the lower legs, typically associated with arthritis, vasculitis, or infections. |
| March 2020 | Mesenteric arteriovenous CTA showed a slightly wider localized superior mesenteric artery. Ultrasound showed no abnormalities in the bilateral renal arteries, carotid arteries, or vertebral arteries. |
| March 2020 (follow-up) | Prednisone acetate and methotrexate treatments yielded joint pain relief and normal temperature. Injection of recombinant human tumor necrosis factor receptor II antibody led to substantial lower limb pain and fatigue reduction, but no fever. |
| July 2020 | Arthritis pain was relieved by prednisone acetate and methotrexate treatment, and his body temperature returned to normal. |
lower in the right cerebellar hemisphere than in the left cerebellar hemisphere at DLP1.5, although both sides were equivalent at DLP2.5. These findings were indicative of ischemic changes in the right cerebellar hemisphere (Figure 4).

EMG of both lower extremities revealed an abnormal tibial nerve H reflex on both sides, which implied proximal nerve root involvement.

**Diagnosis and treatment process**

See Table 1.

**Pathological examination**

Skin biopsy of the left leg revealed findings consistent with erythema nodosum.

**Discussion**

PAN is a relatively rare rheumatic immune disease with various clinical manifestations and no specific serological markers. Therefore, it is difficult to diagnose...
and clinicians have insufficient knowledge of this disease. The pathogenesis of PAN remains unclear. Some clinicians have suggested that it is hereditary, where deletion of the autosomal recessive CecRL gene can lead to PAN [6]. Furthermore, patients with familial Mediterranean fever may present with PAN [7]. Viral infection, such as hepatitis B virus, hepatitis C virus, and human immunodeficiency virus, is an important potential etiology [8].

Patients with PAN may have nonspecific symptoms such as fever, weight loss, joint pain, and muscle pain. The corresponding organs or tissues may exhibit ischemia or bleeding due to narrowing or blockage of inflamed arteries, or microaneurysm rupture. PAN combined with cardiovascular lesions has the following imaging characteristics: extensive artery involvement, most commonly in the aorta and secondary branches; and diverse arterial lesions, primarily in the gut and lower extremities, including the renal artery and its branches. Coronary artery involvement is also common. The reported incidence of cardiac involvement of PAN ranges from 4% to 65% [9]. Vascular lesions of PAN disease show segmental changes, mainly in vascular branches, along with immune complex deposition and granuloma formation. Extensive inflammatory cell infiltration (mainly lymphocytes) is present in the lesions. Fibrosis-like necrosis is a common manifestation of active lesions, often accompanied by neutrophil infiltration [10-13].

The MRI manifestations of 21 patients (including our patient, as shown in Table 2) described in 12 English-language articles [17-28] were retrospectively analyzed: there were 17 patients (80.9%) with calf involvement, 3 (14.3%) with thigh involvement, and 1 (4.8%) with both thigh and calf involvement. The patients included 11 males and 10 females (mean age, 40.76 ± 18.28 years; range: 7–78 years). The T1WI and T2WI findings were both isointense in one patient, while the T1WI findings alone were isointense in seven patients. The T1WI findings were slightly hyperintense in five patients, and no T1WI images were available for the remaining seven patients. The T2WI signal was diffusely hyperintense in 10 patients, and “patchy villous hyperintense” in 9 patients. Among the 12 patients with enhanced images, most exhibited diffuse or cotton-like enhancement, and some patients had involvement of the fascia and periosteum. Our patient showed early disease manifestations in the calves, and late manifestations in the thighs. MRI revealed that the thigh and calf muscles were involved, with T1WI isointensity and T2WI patch-like hyperintensity, as well as cotton-like enhancement centered on blood vessels. Enhanced muscle scans did not show abnormalities (Figure 1). Focal accumulation was indicative of vascular stenosis. The bilateral leg artery and its branches showed localized headlike changes with many lesions. The wall of the profunda femoris artery was rough, with slightly localized stenosis and few lesions. It also showed aneurysmal dilation of the superior mesentry, as well as middle cerebral artery stenosis and occlusion, and ischemic compensatory changes in the right cerebellar hemisphere. However, no clinical symptoms were evident (Figures 2-4).

Currently, diagnosis of PAN is made using the American College of Rheumatology 1990 classification [14]. However, due to improvements in our understanding of vasculitis, this standard now clearly has limitations, especially because the ANCA antibody test does not reliably detect microscopic polyangiitis. PAN was defined at the Chapel Hill Conference in 2012 and determined to have no association with ANCA [3]. Some researchers have proposed combining the American College of Rheumatology, La Industrial Standard, and Chapel Hill Conference standards, such that granulomatous polyangiitis is ruled out first. If eosinophilic granulomatous polyangiitis, granulomatous polyangiitis, and microscopic polyangiitis can be excluded, then PAN may be the appropriate diagnosis [15].

Glucocorticoids are the currently preferred treatment, combined with immunosuppressants as necessary. Surgical treatment may be necessary in patients with serious complications, such as gastrointestinal perforation, visceral rupture, ischemia, or bleeding. In a retrospective database analysis conducted in 2011, the French Vasculitis Research Group found that factors associated with 5-year mortality in patients with PAN included age > 65 years, renal insufficiency (serum creatinine ≥ 150 µmol/L), symptomatic cardiac insufficiency and, especially, severe gastrointestinal involvement (e.g., perforation, hemorrhage, and/or pancreatitis) [16].

In Conclusion, in cases with patchiness or diffuse muscle signal changes in the lower leg (or thigh) on MRI, cotton-like or diffuse enhancement centered on blood vessels may be accompanied by fascial or periosteal enhancement. PAN should be considered in the differential diagnosis, and vascular CTA or MRA examinations should be added to facilitate the diagnosis. In our patient, only the skin and lower leg showed clinical symptoms, but the profunda femoris artery, celiac trunk, and cranial vessels were abnormal. Therefore, patients with PAN should undergo examinations of small and medium arteries throughout the body, to ensure early detection of diseased vessels. This may prevent or reduce damage to target organs. If focal accumulation is suspected, MRI and MRA examinations are recommended.
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