INTERNAL MEDICINE

□ CASE REPORT □

Intriguing Findings of the Muscle on Magnetic Resonance Imaging in Polyarteritis Nodosa

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Abstract

Polyarteritis nodosa (PAN) confined to the muscle is rare and hard to diagnose. Recently, the utility of magnetic resonance imaging (MRI) for detecting muscle involvement of PAN has been introduced. We herein report the case of biopsy-proven, refractory PAN confined to the lower limb muscles with enhanced MRI demonstrating discretely granular hyperintensities, which was contrary to previous reports. Our results, with those of previous reports, suggest that the MRI findings of muscles in PAN reflect the vessel size involved and disease severity.

Key words: polyarteritis nodosa, magnetic resonance imaging, muscle

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Introduction

Polyarteritis nodosa (PAN) is a medium vessel vasculitis affecting systemic organs. PAN involves multiple organs, therefore, single organ involvement except for the skin is rare. In particular, little is known about PAN limited to the muscles. Most cases only present symptoms of myalgia and a fever without the elevation of creatine kinase, leading to a difficulty in the diagnosis (1, 2). Recently, some groups have reported the utility of magnetic resonance imaging (MRI), which demonstrates diffuse high intensity signals in affected muscles (3, 4). We herein report the case of biopsy-proven PAN confined to the lower limb muscles with unusual MRI findings, which were discordant from previous reports.

Case Report

A 69-year-old man was hospitalized because of a spiking fever and lower limb weakness and pain that persisted for a month. On physical examinations, there was no eruption, ocular abnormal finding, oral ulcer, respiratory manifestation, arthritis, or any abnormal neurological signs except for rapidly progressive lower proximal muscle weakness. Manual muscle testing revealed the following (right/left): deltoid 5/5, biceps 5/5, triceps 5/5, iliopsoas 3/4, quadriceps 3/3, biceps femoris 5/5, gastrocnemius 5/5, and tibialis anterior 5/5. Blood testing showed an elevated C-reactive protein (CRP) level of 20 mg/dL, low levels of creatine kinase (CK) of less than 20 U/L and normal levels of aldolase of 4.9 IU/L (2.7-5.9 IU/L). Antinuclear antibody was negative, and both anti-proteinase 3 antineutrophil cytoplasmic antibodies and myeloperoxidase antineutrophil cytoplasmic antibodies were negative. Furthermore, cytoplasmic staining using indirect immunofluorescence of human epithelial cells was negative. Other laboratory testing showed alanine aminotransferase levels of 11 U/L (5-40 U/L), aspartate aminotransferase levels of 14 U/L (10-35 U/L), serum creatinine levels of 0.63 mg/dL (0.7-1.1 mg/dL), KL-6 levels of 125 U/mL (0-500 U/mL), and SP-D levels less than 17 ng/mL (0-109 ng/mL). Hepatitis B antigen, hepatitis B antibody, and hepatitis C antibody were all negative. A urinalysis showed a red blood cell count of 3-5/HPF, a white blood cell count of 3-5/HPF, trace protein and no red blood cell casts. A chest X-ray showed no significant findings. Although an electromyogram showed a mild positive sharp wave in the gluteus maximus, enhanced MRI demonstrated

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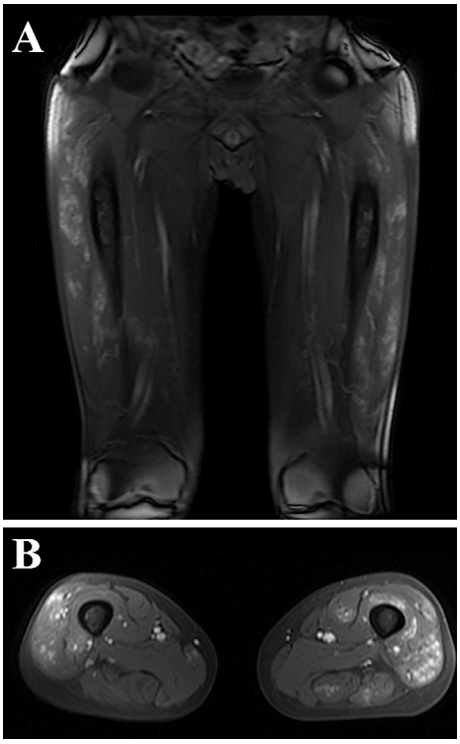

Figure 1. MRI findings of the lower limb muscles. (A) Coronal section. (B) Horizontal section.

discretely granular hyperintensities on T1 in the gluteus maximus and femoral muscles (Fig. 1), which were not consistent with inflammatory myositis. A biopsied specimen of the femoral muscle revealed fibrinoid necrosis of small-sized arteries (100 μm) with inflammatory cell infiltrate and disruption of the elastic lamina of the vessel wall without findings of myonecrosis (Fig. 2). A computed tomography angiogram did not show any other lesions related to PAN, including aneurysms. According to these findings, the patient was diagnosed with PAN with limited involvement in the muscle and treated with methylprednisolone pulse therapy (1,000 mg/day ×3 days) followed by prednisolone of 60 mg/day. His fever subsided and the CRP level temporarily decreased, but re-increased within 5 days. We added monthly intravenous cyclophosphamide (IVCY) of 1,000 mg, which resulted in normalization of the CRP level (Fig. 3). Sulfamethoxazole/trimethoprim was switched to pentamidine inhalation for prophylaxis against pneumocystis pneumonia due to drug-induced leukocytopenia. However, after two episodes of bacterial pneumonia requiring intravenous antibiotics, a sustained elevation of the CRP level was observed with a decrease in the PSL dose and intermission of IVCY. We regarded the CRP elevation to be related to PAN activity, and switched PSL to betamethasone (BMZ) and reinitiated IVCY to control PAN inflammation. The MRI findings of the limb muscles improved after the second course of IVCY. However, 27 days after the third course of IVCY, he developed *Pneumocystis jiroveci* pneumonia that was diagnosed with elevated (1→3)-β-D-glucan (31.9 pg/mL) and the presence of *Pneumocystis jiroveci* DNA from his sputum, although pentamidine inhalation was periodically performed. Despite methylprednisolone pulse therapy (1,000 mg/day×3 days) and sulfamethoxazole/trimethoprim, his respiratory condition deteriorated, and he died 14 days after the diagnosis of pneumocystis pneumonia.

Discussion

We present a case of refractory, biopsy-proven PAN with only muscle involvement that showed unusual findings of discretely granular hyperintensities on T1-weighted MRI with contrast enhancement in the femoral muscles.

Ten cases of PAN confined to the lower limb muscles with MRI finding were previously reported with MRI images (Table). MRI in those cases (2-10) showed homogenous hyperintensities within the muscles resembling inflammatory myositis without CK elevation (one case showed an elevated CK level). The possibility that these findings reflect functional ischemia inside the muscles is of great interest in considering the pathological differences between PAN and inflammatory myositis.

We then classified the MRI findings of the ten previous reports and our case as diffuse, patchy and granular hyperintensities. We classified the MRI findings into patchy and diffuse according to either the description or the area and homogeneity of T2 high intensity lesions in muscle MRI images in the previous reports. Although the difference in MRI resolution might affect the findings between patchy and speckled hyperintensities, no previous reports described the resolution of MRI used.

Furthermore, we divided the diameters of the affected vessels into small, small to medium or medium-sized according to the descriptions in the articles. We classified the affected vessel diameter of our case as small according to the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (11). There was a trend that cases with affected small-sized vessels showed patchy or granular high intensity lesions on MRI, while those with medium-sized vessels showed diffuse lesions. As medium-sized vessels are mainly localized in the epimysium and perfuse large areas of muscle fibers, medium-sized vessels can cause broad ischemia leading to vasogenic edema, which shows diffuse hyperintensities on MRI. On the other hand, small-sized vessels are distributed around the perimysium closer to the muscle fibers. Localized ischemia and inflammatory cell infiltration spreading from the affected small vessels to muscles can project patchy hyperintensities on MRI. The discrete and granular hyperintensities on MRI in our case with small-sized vasculitis suggested that MRI could confirm the vessel size involved in PAN. Alternatively, those findings can be associated with the severity of vascular inflammation, for our case was refractory whereas other cases responded well to glucocorticoids.

Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) affects mainly small-sized vessels. Although AAV commonly involves the lungs and kidneys, a few cases with

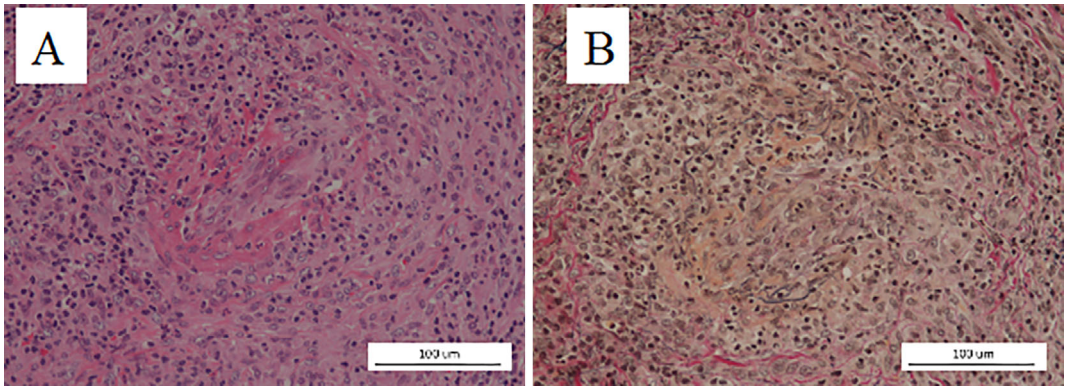

Figure 2. **A muscle biopsy of the femoral muscle. (A) Fibrinoid necrosis of a medium-sized vessel (Hematoxylin and Eosin staining, 400×). (B) Disruption of the elastic lamina of the vessel wall (Elastica van Gieson stain, 400×).**

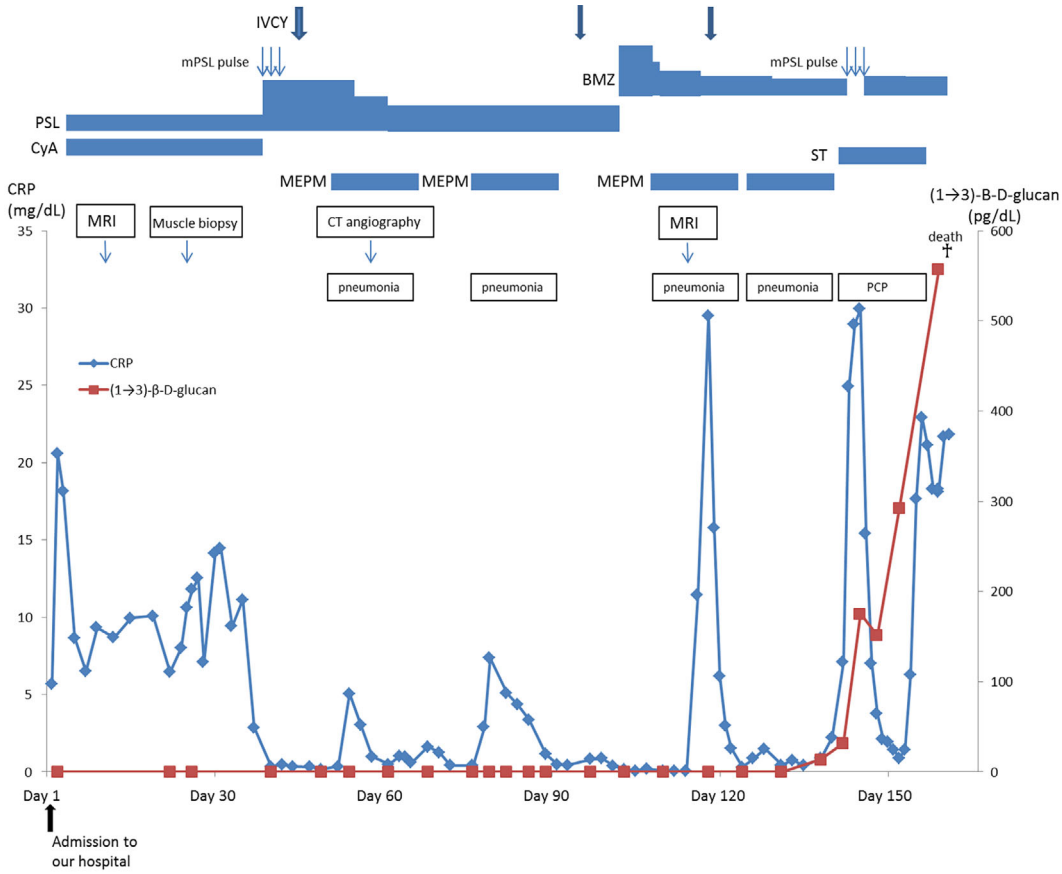

Figure 3. **The clinical course of the patient. The x-axis indicates the date and the y-axis indicates the CRP levels (mg/dL) and (1→3) -β-D-glucan levels (pg/dL). PSL: prednisolone, mPSL: methylprednisolone, BMZ: betamethasone, IVCY: intravenous cyclophosphamide, MEPM: meropenem, ST: sulfamethoxazole/trimethoprim, MRI: magnetic resonance imaging**

muscle involvement have been reported (12, 13), among which only one case presented with a muscle MRI image showing a diffuse pattern (12). Since AAV affects smaller vessels than PAN, vasculitis might cause diffuse edema in the muscles resulting in diffuse hyperintensities on MRI.

Unfortunately, our case died of *Pneumocystis jiroveci* pneumonia. Although this case was refractory to glucocorticoid requiring intensive immunosuppressive therapy, we should have titrated the initial IVCY dose and continued sulfamethoxazole/trimethoprim in such an immunocompromised case. Other treatment choices such as intravenous immunoglobulin can be considered in order to avoid susceptibility to infection such as in our case (14).

In summary, we experienced a rare form of PAN with a unique MRI finding. A greater accumulation of cases is necessary to clarify whether this MRI finding accurately reflects

Table. Clinical Features of Patients with Polyarteritis Nodosa Confined to Lower Limbs.

Reference No.	Age	Gender	CK elevation	High intensities on MRI	Contrast enhancement	Affected vessel size	Glucocrticoid	Immunosuppressants
Present case	69	M	-	discretely granular	+	small (100μm)	mPSL pulse +PSL 60mg, BMZ	IVCY 1000mg
2	38	F	-	patchy	not enhanced	small	PSL 15mg	-
5	57	F	-	patchy	not enhanced	small	PSL 30mg	-
3	38	M	-	patchy	not enhanced	small and medium	PSL 20mg	-
6	56	M	-	diffuse	not enhanced	small and medium	PSL 30mg	-
4	40	M	-	patchy*	+	medium (250μm)	PSL 40mg	-
4	45	F	-	diffuse*	not enhanced	medium	PSL 40mg	IVCY
7	36	F	-	diffuse	not enhanced	medium	TRI 16mg	-
8	65	F	+	diffuse*	not enhanced	medium	PSL 1.0mg/kg	-
9	NA	NA	-	patchy	+	NA	PSL 0.5-1.0mg/kg	-
10	26	M	-	diffuse*	+	NA	PSL 60mg	-

CK: creatine kinase, mPSL: methylprednisolone, BMZ: betamethasone, IVCY: intravenous cyclophosphamide, TRI: triamcinolone, PSL: prednisolone, NA: not available
* According to the description in the manuscript.

the course of PAN.

The authors state that they have no Conflict of Interest (COI).

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