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A rare presentation of POEMS syndrome on magnetic resonance neurography: a case series

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***Abstract*:** Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes (POEMS) syndrome is a multisystem disease associated with underlying plasma cell neoplasm. Here, we present two cases of POEMS syndrome that manifested on magnetic resonance neurography as an increasing bone mass with cortical disruption, direct invading nerve roots and lumbar gluteal muscles. These features have not been previously reported. We also report a case with diffuse hypertrophy and enhancement of the brachial and lumbosacral plexus, which mimics the most common chronic inflammatory demyelinating polyradiculoneuropathy. Moreover, we detected perineurium effusions in the plexus, coupled with a variety of myofascitis and atrophy in denervated muscle. The case series is of concern to atypical magnetic resonance imaging findings of POEMS syndrome in the bone and peripheral nerve system as critical attacked target organs, which would be facilitating diagnosis.

Keywords: bone mass, endocrinopathy, magnetic resonance neurography, monoclonal plasma cell disorder, organomegaly, plexus, polyneuropathy, skin changes

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Introduction

Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes (POEMS) syndrome is a rare and diagnostically elusive condition.[1–3] Polyneuropathy is not only an essential feature of POEMS syndrome but has also been associated with underlying plasma cell neoplasm.[1,4] Increased permeability of the blood–nerve barrier (BNB) is a key factor in development of pathological changes in immunoreaction, which have been attributed to M-protein-mediated activation and tight junction microvasculature opening induced by elevated vascular endothelial growth factor (VEGF).[4,5] The disease is often missed or misdiagnosed, owing to a lack of typical characteristics and its rarity. All three patients reported in the present study were initially misdiagnosed as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). However, magnetic resonance imaging (MRI) revealed abnormal findings that were hard to explain by CIDP.

In this report, we describe rare radiological manifestations, which on MRI appeared to be enhanced bone mass with cortical disruption, direct invading nerve roots, lumbar–gluteal muscles in patients with POEMS syndrome. Furthermore, we detected abnormalities in directly invaded nerve roots, as well as throughout the lumbosacral (LS), brachial plexus, cauda equina, and adjacent muscles and musculararfascia. The case series is of concern to atypical imaging findings of the POEMS syndrome in the bone and peripheral nerve system as critical attacked target organs, which might be emphasized to aid in diagnosis.

Materials and methods

POEMS syndrome was diagnosed using previously published criteria.[1] Next, we obtained each patient's data from electronic medical records, including their demographics (namely gender and age at onset), symptoms and signs, laboratory,

electrophysiological and radiological findings, as well as clinical outcomes. Magnetic resonance neuropathy (MRN) examination was performed on a 3.0 T MRI scanner (MAGNETOM Trio, Siemens Healthcare, Germany). The MRN protocol, for the brachial, LS plexus and cauda equina, was as previously reported.[6] Routine lumbar spine imaging was acquired through the T1- and T2-weighted turbo spin-echo (TSE) sequences on the sagittal plane. The volumetric interpolated breath-hold examination (VIBE), turbo inversion recovery magnitude (TIRM) and sampling perfection with application-optimized contrasts using different flip angle evolution (SPACE) sequences were performed on coronal plane for the plexus. Moreover, contrast-enhanced T1-weighted TSE and VIBE sequences were performed again after gadolinium administration (Gadovist, Bayer Healthcare). Specific sequence parameters are outlined in supplementary Table 1. No statistical analysis was performed.

Results

A summary of demographic and clinical characteristics, including each patient's neuropathy symptoms, and time of POEMS syndrome onset, is outlined in Table 1.

Case studies

Case 1

A 68-year-old woman initially presented with numbness of both the calf, that progressed down below the level of the knee joint, coupled with weakness and instability with repeated falls. The tendinous reflex was absent or disappeared, with no evidence of pathological and kerning signs. The muscle strength, in her lower extremities, was 5-grade and accompanied by hyperalgesia, pitting edema, and generalized hyperpigmentation. Laboratory results revealed renal dysfunction, hypercalcemia, hypophosphatemia, elevated thyroid-stimulating hormone, thyroid peroxidase antibodies and anti-TG and VEGF. Immunofixation electrophoresis revealed presence of M-protein IgG/λin serum. Electromyography (EMG) demonstrated severe sensorimotor polyradiculoneuropathy with coexisting acute and chronic impairment. Bone marrow aspiration revealed active bone marrow hyperplasia.

MRN results revealed an enhanced irregular regiment at the right wing of the iliac, which was further attached to the adjacent muscles, stretching from the erector spinae, iliopsoas to the gluteus, and appeared as widespread myofascitis with hyperintensity on T2-weighted images (T2WI). The bone regiment manifested uniformity isointense on T1-weighted images (T1WI) but appeared hyperintense on T2WI, suggesting a high-water content. In addition, inhomogeneous and focal hyperintense was observed in the LS plexus, while the right L5 nerve root appeared as mild fusiform hypertrophy. Mild enhancements were observed in the cauda equina and LS plexus nerve roots, and this was accompanied by the effusion and swelling perineurium (Figure 1).

Case 2

A 45-year-old female patient presented at our neurology outpatients department with numbness and weakness in arms and legs. She was diagnosed with probable CIDP and had poorly responded to steroid treatment at a local community hospital. Results from blood routine analysis, biochemical indices, tumor markers, rheumatoid factors, coagulation, thyroid, and renal function were all within normal ranges. The cerebrospinal fluid (CSF) was clear, with a total protein concentration of 1.34 g/L. Nerve conduction velocity was markedly reduced across all extremities, especially the right lower extremity. The EMG revealed a denervated pattern with no evidence of F-wave generation. Abdominal ultrasound revealed a hepatomegaly and splenomegaly.

MRN showed an irregularly shaped bone mass at the right sacroiliac joint, which was isointense and hyperintense based on T1WI and T2WI, respectively. Notably, the mass invaded the LS nerve roots, adjacent muscles, and fascia flaps directly. Affected right L5–S1 nerve roots and branches were detected as swelling and focal hypertrophy, with effusion perineurium, accompanied by extensive lumbar gluteal myofascitis and atrophy in denervated muscle. Furthermore, we detected heterogeneous enhancements were detected in the bone mass, as well as the nerve roots and cauda equina after gadolinium administration (Figure 2).

Case 3

A 50-year-old man, with a 4-year history of continuity numbness in his feet, presented with weakness, imbalance and asynergy, and rapid

Table 1. Clinical features of POEMS patients.

No.	Age sex	Time of onset	Neuropathy symptoms	Endocrine alteration	Organomegaly	Skin changes	CSF protein*
1	68y F	67 years old	Weakness, numbness LE > UE	Hypothyroidism Hypercalcemia Hypophosphatemia	Hepatomegaly Splenomegaly	Generalized hyperpigmentation Leg edema	0.91 (g/L) YES
2	45y F	44 years old	Weakness, numbness, LE = UE	None	Hepatomegaly	Leg edema	1.34 (g/L) YES
2	50y M	53 years old	Weakness, numbness LE > UE	Diabetes erectile dysfunction	Hepatomegaly Splenomegaly	Hyperpigmentation in both feet leg edema	0.48 (g/L) YES

CSF, cerebrospinal fluid; F, female; LE, lower extremity; M, man; UE, upper extremity; y, years.
*Whether or not an albuminocytological dissociation was detected in the CSF fluid. (YES/ No).

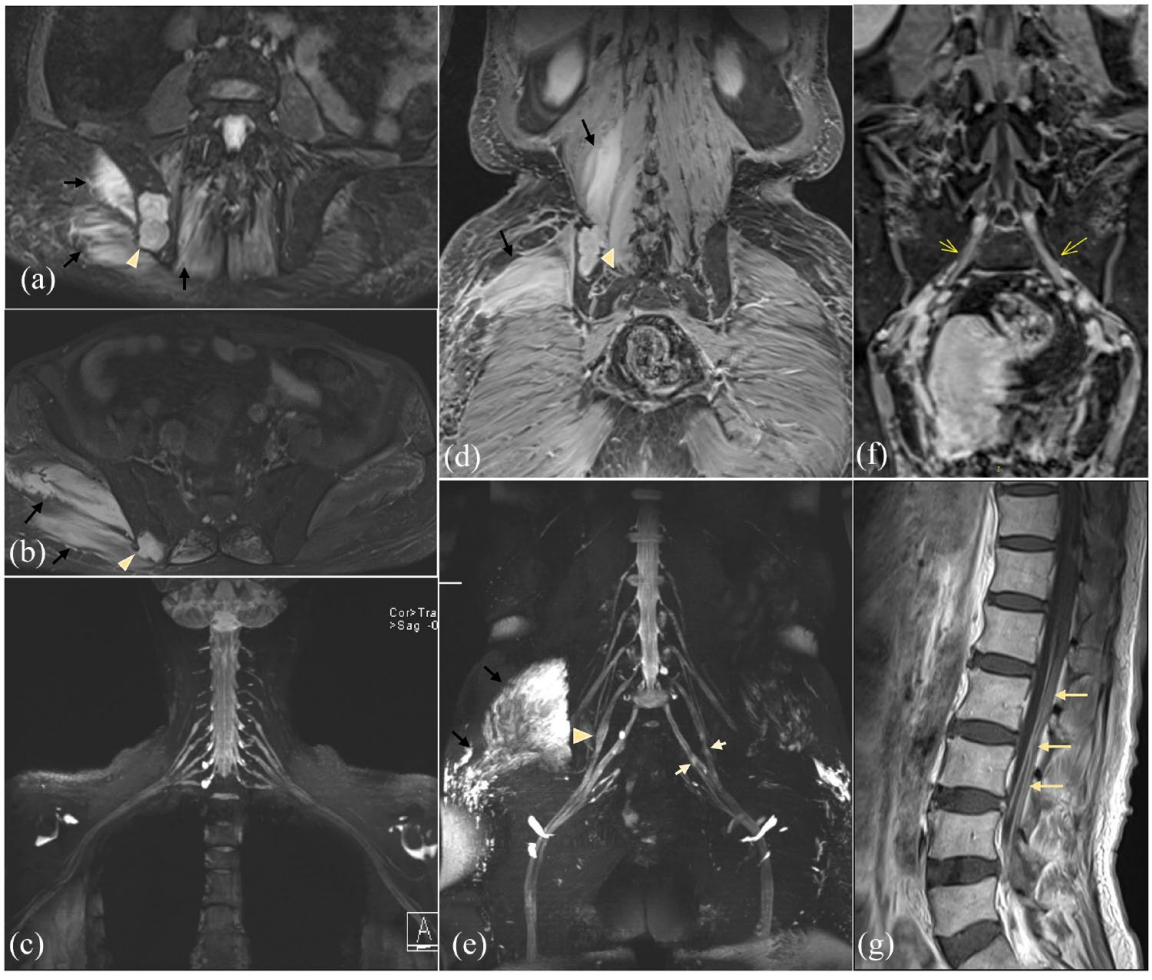

Figure 1. Images (a), (b) and (d) demonstrated an irregular regiment at the right wing of iliac (triangles) with hyperintense on PDWI [(a) and (b)] and obvious enhancement (d), further attached to the erector spinae, iliopsoas and gluteus, appeared as widespread myofascitis [black arrows in (a), (b), (d) and (e)]. MRN showed inhomogeneous and focal hyperintense in LS plexus [yellow arrows in (e)] and mild fusiform hypertrophy in the right L5 nerve root (triangles). Enhancements were observed in bilateral nerve roots [arrows in (f)] and cauda equina [arrows in (g)]. Normal performance in the brachial plexus (c)

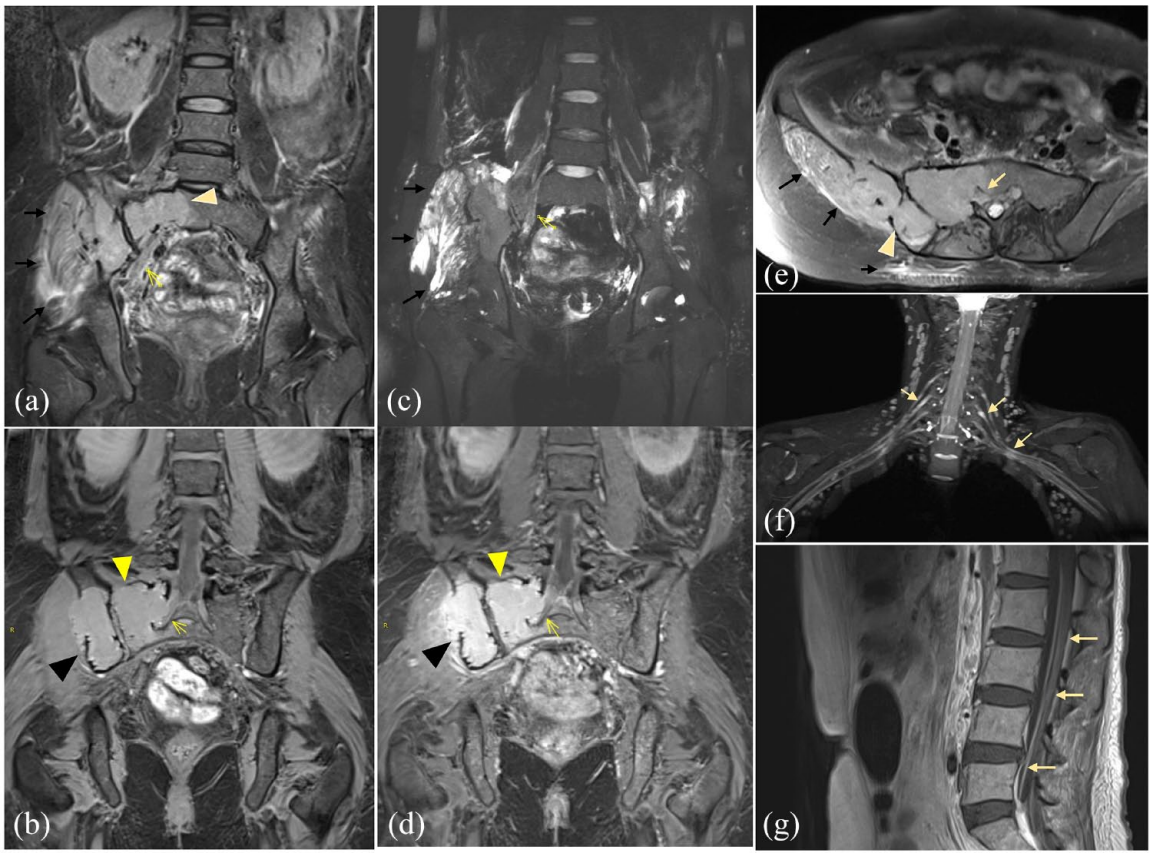

Figure 2. MRN showed an irregular greatly mass at right sacroiliac joint, with hyperintense on T2WI [triangles in (a) and (e)], isointense on unenhanced T1WI [triangles in (b)], and uniform enhancement after gadolinium administration [triangles in (d)]. Cortical disruptions were detected with involvement of sacroiliac joint [triangles in (b), (d) and (e)]. Affected right L5–S1 nerve roots [yellow arrows in (a)–(e)] were detected as swelling and mild hypertrophy with effusion perineurium (a), accompanied by extensive lumbar gluteal myofascitis [black arrows in (a), (c), and (e)]. MRN showed heterogenous signal intensity in the brachial plexus (f) with focal hyperintense in nerve roots and branches (arrows). Image G showed mild enhancement in the cauda equina [arrows in (g)].

weight loss of about 10 kg in the last 3 months. The muscle strengths were 3-grade and 4-grade in the lower and upper extremities, respectively, with hyperpigmentation in the feet. Neurological examination revealed characteristic clinical findings, such as the Kerning's, Babinski's, and Lasesue's signs among positive, and deep tendinous reflect disappeared in the extremities.

IgM kappa monoclonal gammopathy was detected in both the serum and *via* urine immunofixation electrophoresis. The total protein markedly rose to 2.89 g/L in the CSF, with increased protein from IgG, IgM, and IgA, while no CSF-oligoclonal bands (CSF-OCB) were observed. Similarly, no abnormalities were observed in the thyroid, biochemical indices and tumor markers. EMG revealed severe diffuse sensorimotor polyneuropathy with both demyelination and axonal loss.

Moreover, MRN revealed symmetrical hypertrophies with heterogenous signal intensity of the brachial and LS plexus nerve roots and its branches, as well as sciatic and femoral nerves, which were accompanied by slight to moderate enhancements. Notably, the neural stems exhibited a *worm-like* signal reduction, suggesting increased permeability in the BNB that consistent with enhancement after gadolinium administration. Moreover, we detected perineurium effusions in the plexus, which were accompanied by a wide range of myofascitis and atrophy in the denervated muscles. Results from MRI skeletal survey revealed multiple subtle lesions with hyperintensity on T2WI within the sacroiliac bone (Figure 3).

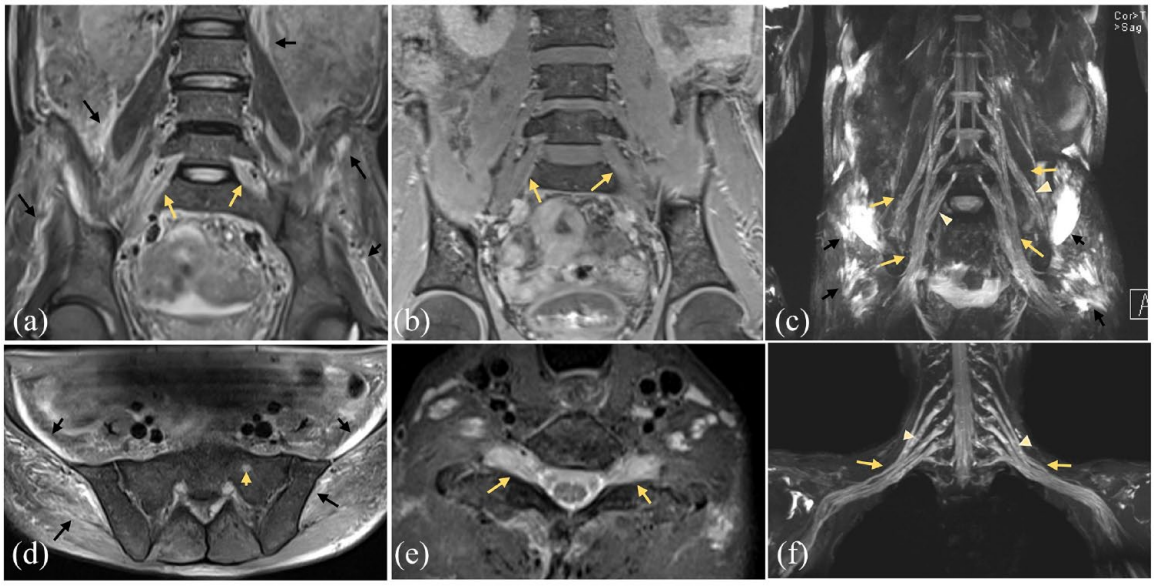

Figure 3. MRN revealed symmetrical diffuse hypertrophy with heterogenous increased signal intensity and mild enhancement, markable effusions of perineurium in the LS plexus [yellow arrows in (a)–(c)], brachial plexus [(e) and (f)] and its branches. Neural stems exhibited the worm-like signal reductions in LS [triangles in (c)] and brachial plexus [triangles in (f)]. A markable wide range of myofascitis and atrophy in denervated lumbar gluteal muscles were detected [black arrows in (a), (c) and (d)]. Image D showed a subtle bone lesion with hyperintensity on T2WI in the sacroiliac bone (yellow arrow).

Discussion

POEMS syndrome is a rare, complicated, and plasma cell proliferative disease, whose diagnosis remains a challenge for clinicians.[2,3] Polyneuropathy, clonal plasma cell disorder, sclerotic bone lesions, elevated VEGF, and the presence of Castleman disease were the main criteria for the syndrome.[1] The diagnosis is based on three of the major criteria, two of which must include polyneuropathy and monoclonal plasma cell disease, and at least one of the minor criteria.[1]

In this study, we report a rare occurrence of MR findings in POEMS syndrome patients, presenting with a bone mass coupled with cortical disruption, which further invaded adjacent nerve roots and soft tissue. These abnormal MRI findings made it difficult for us to interpret CIDP, therefore, the initial CIDP diagnosis were overturned, which may probably have had decisive significance in the final diagnosis of these cases. MRI is advantageous in that it allows detection of two important sites of involvement, the peripheral nerves and bone marrow, as well as minor criteria like organomegaly, which subsequently are vital for diagnosis of POEMS syndrome. At present, multisequence MRN not only allows imaging to clearly identify deep nerves and bone marrow conspicuously and to accurately locate lesions, but it also serves as of the sites for bone marrow biopsy to increase the diagnostic efficiency. However, CT/PET-CT is not efficacious in presenting the peripheral nerves systems. In addition, electrophysiology is affected by major limitations, such as the inability to assess nerves at all sites and morphology. This is particularly so in the proximal nerve roots of the deep plexus that are often involved. Previous reports have shown that MRI has results in higher sensitivity than skeletal CT/PET-CT in distinguishing active osteolytic lesions from osteosclerotic ones, as well as more subtle lesions than CT in POEMS syndrome.[7,8] Moreover, MRN is superior to CT/PET with regards to evaluating innervated muscles. To date, however, use of MRI to identify bone lesions or peripheral nerves in POEMS syndrome remains relatively uncommon.[7–10]

MRN has been predominantly used to assess peripheral nerves, which could provide additional information throughout the entire nerve tracts and its branches.[6,11] To date, however, it has not been used to assess POEMS syndrome. In a previous case study, conventional MR was used to successfully detect enlargement of the proximal sciatic nerves with increased T2 signal,[4] which was consistent with our findings. In this study, MRN revealed diffuse hypertrophy with

heterogenous increased signal intensity with enhancement in the LS and/or brachial plexus nerve roots, cauda equina, and directly invading nerves. Compared with CIDP, direct primary signs of POEMS syndrome in nerves included a bone mass that invaded the adjacent nerve roots, presenting focal fusiform hypertrophy and swelling with increased signal on the basis of diffuse peripheral neuropathy. In addition, we detected edema and exudation in the fascicular membranes of the plexus nerves, indicating that the condition was more severe than CIDP. Enhancement in the nerve roots is what would be expected for the given pathophysiological events in POEMS syndrome, which might be attributed to increased permeability or even disruption of the BNB.[9] However, the presence of enhancement may not be useful in distinguishing between POEMS and CIDP, because it can also be observed in the latter group of patients.[12–14] Interestingly, it serves as a potential marker for detecting disease activity or treatment response.

So far, only one case of a mass in a single lumbar vertebra, involving paraspinal soft tissue with hypointensity on T1WI and hyperintensity on T2WI, has been reported.[15] In our cases, MRI precisely displayed the size, shape and extent of the bone mass with isointense on T1WI and slightly hyperintensity on T2WI. This was in contrast to findings from previous studies in which most bone lesions exhibited hypointensity on T1WI.[7,8] In the case 3, MRN revealed symmetrical diffuse hypertrophy and enhancement of the plexus, while EMG also showed demyelinating features, both which mimics the most common CIDP. Upon suspecting unexpectedly tiny abnormalities in the sacrum, a focal lambda-restricted plasmacytoma was confirmed by targeted marrow aspiration. This was a further reminder that clinicians need to not only pay attention to sclerotic bones lesions, but also to bone mass or subtle lesions. Moreover, we observed indirect signs of effusion and swelling of the perineurium, which were accompanied by a wide range of myofascitis and atrophy in the denervated muscles, manifested patch-shaped hyperintense on T2WI, which is even more remarkable than CIDP. The severe edema and wide range of the surrounding lesions not only just involved bone tissues and peripheral nerves but was also possibly associated with cachexia of the plasma cell tumor. This may be helpful to differentiate from the POEMS syndrome and CIDP, and it is worthy of further study.

POEMS syndrome should be considered in patients with polyradiculoneuropathy, organomegaly, characteristic skin changes and thrombocytosis. Furthermore, serum electrophoresis or bone marrow biopsy is required, although both have been associated with a certain degree of failure to detect monoclonal protein or plasmacytoma for the first test.[9,16] This is a reminder that clinicians should not solely rely on serum electrophoresis or biopsy when diagnosing POEMS syndrome.

This study had some limitation. First, we did not perform skeletal CT/PET-CT examinations, CT/PET-CT following bone lesions detected by MR findings, so as not to increase the radiation dose and economic burden of the patient. Second, none of the patients underwent X-ray, or CT examination or repeated MRI following symptomatic improvement.

In conclusion, MRN scans may not only help to identify an underlying plasmacytoma in the bone and adjacent tissues involvements, but are also significant in directly assessment of polyradiculoneuritis. Bone and peripheral nerves tissues, as critical attacked target organs, may facilitate diagnosis and could be highlighted in the POEMS syndrome patients. Furthermore, a targeted bone marrow biopsy or aspiration can be performed under MR guidance to increase the positive rate in bone lesions.

Ethics statement

The present study was approved by the ethics committee of Tongji Medical College, Huazhong University of Science and Technology (approval no. IORG0003571). All patients voluntarily signed a written informed consent prior to inclusion in the study and for publication of their medical data and images.

Consent for publication

Not applicable.

Author contributions

Xiaoyun Su: Conceptualization; Data curation; Investigation; Resources; Writing – original draft; Writing – review & editing.

Jing Wang: Data curation; Investigation; Validation.

Xiangchuang Kong: Data curation; Resources.

Zuneng Lu: Conceptualization; Project administration; Resources; Supervision.

Chuansheng Zheng: Funding acquisition; Project administration; Supervision; Writing – review & editing.

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Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials

Not applicable.

Supplemental material

Supplemental material for this article is available online.

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