CASE REPORT

Positron emission tomography findings in a patient with multiple myeloma of polymyalgia rheumatica-like symptoms caused by paraneoplastic syndrome

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SUMMARY

A 50-year-old Japanese man was referred to our department with pain in his limb joints persisting for 3 months. Although his joints showed no redness, swelling or tenderness, he had a limited range of motion of his hip and shoulder joints, suggesting a diagnosis of polymyalgia rheumatica (PMR). However, his relatively young age and subacute course along with the absence of morning stiffness made the diagnosis uncertain. We performed positron emission tomography/CT, which revealed 18F-fluorodeoxyglucose uptake in bilateral upper and lower joints, consistent with PMR. There was also uptake by a sacral tumour, suggesting a diagnosis of paraneoplastic syndrome. Immunoglobulin A- κ type M protein was detected in serum and bone marrow aspiration/biopsy identified diffuse proliferation of atypical plasma cells, confirming a diagnosis of multiple myeloma. The patient received chemotherapy, which alleviated his limb pain, and achieved stringent complete remission after autologous peripheral blood stem cell transplantation.

BACKGROUND

Polymyalgia rheumatica (PMR) is an inflammatory disease that generally causes pain and stiffness in the shoulders and/or pelvic region of patients over 50 years of age.¹ Although PMR is relatively common, there is no specific test for its detection, and the differential diagnosis includes a wide variety of diseases such as malignancies, seronegative polyarthritis, systemic lupus erythematosus, polymyositis and ankylosing spondylitis.² Positron emission tomography/CT (PET/CT) is reported to be useful for diagnosing PMR and excluding other possibilities,³ but the PET/CT findings in patients with PMR-like symptoms secondary to paraneoplastic syndrome (PNS) have been unclear. Here we report a patient in whom we confirmed a diagnosis of multiple myeloma as the underlying cause of PMR-like symptoms. In this patient, PET/CT showed 18F-fluorodeoxyglucose (FDG) uptake in bilateral upper and lower joints that was consistent with PMR. PET/CT was also most helpful in providing information that led to an early correct diagnosis, although his symptoms, physical findings and laboratory data at presentation did not suggest a diagnosis of multiple myeloma.

CASE PRESENTATION

A 50-year-old Japanese man was referred to our hospital with bilateral knee pain persisting for

3 months. The onset of his knee pain had been gradual and it had reached a plateau after approximately 2 months. There was slight rest pain in the knees, which was worsened by ambulation. However, he had no morning stiffness and no systemic symptoms such as fever or weight loss. Also, there was no significant history or family history and he was not on any medications. The physical findings, including vital signs, were unremarkable. His upper and lower limb joints showed no redness, swelling or tenderness, but Patrick's test was positive with pain radiating to the knees. The range of motion of both shoulder joints was limited due to pain. There was no muscle pain or pain in other joints or the spine, and he had neither muscle weakness nor lymphadenopathy.

INVESTIGATIONS

Laboratory tests showed a haemoglobin of 12.4 g/dL with a mean corpuscular volume of 87.1 fL, total protein of 7.6 g/dL, serum albumin of 3.8 g/dL, C reactive protein of 5.0 mg/dL and erythrocyte sedimentation rate of 45 mm/h, indicating that he had mild normocytic anaemia, hypoalbuminaemia and inflammation. Renal function tests, electrolytes such as serum calcium and inorganic phosphate were all normal and urinalysis showed no proteinuria. There were no significant findings on X-ray films of the shoulders, knees and hips. Gastrointestinal endoscopy and colonoscopy were unremarkable. PET/CT revealed FDG uptake by a tumour in the sacrum (figure 1), as well as uptake by the limb joints (figure 2). Examination of globulin fractions demonstrated marked elevation of IgA to 1408 mg/dL (IgM was 91 mg/dL and IgG was 1653 mg/dL). Immunofixation electrophoresis of his urine was negative for Bence-Jones protein,

Figure 1 Positron emission tomography/CT. Sacral tumour showing 18F-fluorodeoxyglucose uptake.

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Figure 2 Positron emission tomography/CT. 18F-fluorodeoxyglucose uptake is seen in the bilateral shoulder, elbow and hip joints (arrows).

but IgA- κ type M protein was detected in the serum. Bone marrow aspiration/biopsy demonstrated diffuse proliferation of atypical plasma cells, indicating a diagnosis of multiple myeloma.

TREATMENT

Treatment with bortezomib and dexamethasone alleviated his limb pain within a few days. He received a total of six courses of treatment with these drugs and had no recurrence of pain even during intermittent periods. After the fifth course, peripheral stem cells were harvested and autologous peripheral blood stem cell transplantation was performed.

OUTCOME AND FOLLOW-UP

At 1 year after the completion of treatment, serum IgG, IgA and IgM levels were normal, while both serum M protein and urine Bence-Jones protein were negative. The free light chain κ/λ ratio was within the normal range. Plasma cells accounted for 0.8% of bone marrow cells (<5%), and the marrow was negative for clonal cells by immunohistochemistry. These findings confirmed that stringent complete remission had been achieved.

DISCUSSION

PMR is an inflammatory disease that usually presents with pain and stiffness in the shoulders and/or pelvic region of patients over 50 years of age.¹ As malignant tumours occasionally cause the PMR-like symptoms, patients who display atypical manifestations should undergo detailed assessment to exclude other diagnoses including malignancy.⁴ The following atypical features are considered to be particularly important: an age younger than 50 years, involvement of only one typical site, asymmetrical involvement of typical sites, additional painful joints, an erythrocyte sedimentation rate <40 or >100 mm/h and partial

Box 1 Criteria for polymyalgia rheumatica developed by Bird *et al.* Three of the seven features are required

- ▶ Bilateral shoulder pain and/or stiffness
- ▶ Bilateral upper arm tenderness
- ▶ Onset of illness within 2 weeks
- ▶ Erythrocyte sedimentation rate >40 mm/h
- ▶ Morning stiffness >1 h
- ▶ Age >65 years
- ▶ Depression or weight loss or both

or delayed improvement (requiring longer than 48 h) after administration of 10 mg of prednisolone.⁵ Our patient was suspected to have PMR because of pain and symmetrical limitation of the range of motion affecting the bilateral shoulder and hip joints with a positive inflammatory reaction. However, he had atypical features such as a relatively young age (50 years old) and subacute course along with lack of morning stiffness,⁶ which did not meet the criteria for PMR (boxes 1 and 2).² So we performed further investigation. PET/CT may detect underlying disorders in patients with PMR-like symptoms, and FDG uptake in the shoulders or hips has a high sensitivity for PMR.⁷ PET/CT in our patient showed FDG uptake in the limb joints, which was consistent with PMR,³ but there was also uptake by a sacral tumour. Examination of immunofixation electrophoresis and bone marrow aspiration/biopsy confirmed the diagnosis of multiple myeloma.

Multiple myeloma rarely shows direct invasion into the joints and previous cases have featured asymmetrical involvement,⁸ so symmetrical pain in the proximal joints of our patient was unlikely to be caused by direct invasion. In addition, typical PET/CT findings in multiple myeloma are focal and/or diffuse uptake by the axial-peripheral skeleton, especially the spine and the pelvis,⁹ while uptake in the joints is not a feature. As chemotherapy improved our patient's pain and he did not experience recurrence while off steroids, we concluded that his PMR-like symptoms were secondary to PNS.

The most frequent cause of PNS is small-cell lung cancer, while the other malignancies that have been reported include multiple myeloma (as in our case), lymphoma, ovarian cancer, testicular cancer, bladder cancer, thymoma, rectal cancer, head and neck cancer and gastric cancer.¹⁰ To identify the malignancy underlying PNS, it is still controversial whether PET/CT is useful in patients with non-neurological symptoms.¹¹ Although it has been reported that PET/CT showed FDG uptake in the joints of a patient with polyarthritis due to PNS,¹² FDG uptake

Box 2 Criteria for polymyalgia rheumatica developed by Healey *et al.* All features are required

- ▶ Pain for at least 1 month at two or more of the following sites: shoulders, pelvic girdle and cervical spine
- ▶ Morning stiffness >1 h
- ▶ Age >50 years
- ▶ Erythrocyte sedimentation rate >40 mm/h
- ▶ Exclusion of other diagnosis
- ▶ Prompt and marked response to glucocorticoid therapy in a dosage <20 mg/day

was only seen in the affected lymph nodes and not in the joints of a steroid-treated patient who had Hodgkin disease of PMR-like symptoms induced by PNS.¹³ Therefore, this is the first report of PET/CT showing FDG uptake in the limb joints (consistent with PMR) in a patient with PMR-like symptoms due to PNS. In our case, we made a diagnosis of multiple myeloma by PET/CT before symptoms of the primary disease became apparent, suggesting that PET/CT can be useful to identify the lesion underlying PNS.

Learning points

- In patients with polymyalgia rheumatica (PMR)-like symptoms due to paraneoplastic syndrome (PNS), positron emission tomography/CT (PET/CT) shows a similar pattern of 18F-fluorodeoxyglucose uptake to that seen in PMR.
- PET/CT is useful to identify the underlying disease in patients with PMR-like symptoms caused by PNS.
- If patients with PMR-like symptoms do not meet the criteria for PMR, further investigation with PET/CT is recommended.
- When PMR is suspected in patients with atypical symptoms, the differential diagnosis includes malignant disease.

Contributors SS, MM and KS contributed to managing the patient and writing the report. MI contributed to revision of the report.

Competing interests None.

Patient consent Obtained.

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