Usefulness of L-[Methyl-11C]Methionine Positron Emission Tomography in the Treatment of Idiopathic Hypertrophic Cranial Pachymeningitis
—Case Report—

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Abstract

A 53-year-old man suffered from pulsating headache for 2 months. Magnetic resonance imaging with gadolinium revealed a linear or nodular mass along the left fronto-parietal convexity. Positron emission tomography (PET) with L-[methyl-11C]methionine (11C-MET) demonstrated increased uptake in the enhanced lesion. Biopsy, obtained by craniotomy, demonstrated granulation with lymphocyte and plasma cell infiltration, suggesting inflammatory changes, and a diagnosis of idiopathic hypertrophic cranial pachymeningitis (IHCP) was made. Steroid therapy resulted in improvement of the clinical symptoms and shrinkage of the enhanced lesion in a week. Follow-up 11C-MET PET study, after 18 months of steroid therapy, demonstrated significantly decreased uptake in the lesion, so the steroid therapy was discontinued. Neither clinical nor radiological recurrence was observed one year after discontinuation of the steroid therapy. This case of IHCP with increased 11C-MET uptake, which then decreased after steroid therapy suggests that 11C-MET PET is a useful monitoring modality for therapeutic efficacy against IHCP, and can indicate the appropriate timing of therapy discontinuation.

Key words: idiopathic hypertrophic cranial pachymeningitis, L-[methyl-11C]methionine positron emission tomography, high-dose corticosteroid therapy, headache, immunoglobulin G4-related disease

Introduction

Hypertrophic cranial pachymeningitis is a rare inflammatory disease which causes diffuse thickening of the dura mater.10,12,13,19) If the investigations fail to reveal the etiology, idiopathic hypertrophic cranial pachymeningitis (IHCP) is considered. At the onset, IHCP patients present with chronic headache, with or without neurologic manifestations.5,20,21,24) Usually, IHCP patients are treated with corticosteroids. However, corticosteroid therapy does not always arrest the clinical progression of IHCP. Positron emission tomography (PET) with L-[methyl-11C]methionine (11C-MET) provides information about not only the metabolism of brain tumor but also the uptake of inflammatory cells in non-neoplastic brain lesions.8) Serial evaluations using 11C-MET PET also provide useful information to monitor the therapeutic efficacy in non-neoplastic brain lesions.14)

We present a case of IHCP using 11C-MET PET as a useful monitoring modality to evaluate the therapeutic efficacy in a patient who responded well to low-dose oral corticosteroid therapy after high-dose corticosteroid therapy.

Case Report

A 53-year-old man initially complained of frontal headache. After 2 months, his headache exacerbated, and subsequently, he was admitted to our hospital. Neither motor weakness nor sensory disturbances were noted. The clinical history revealed gastric cancer in the lamina propria, but no recurrence after partial removal 6 years previously. Laboratory examinations revealed no abnormalities in the serum and urine. The serum immunoglobulin G (IgG) concentration and IgG isozyme level were normal. Chemical screening tests of the cerebrospinal fluid were negative except for slightly elevated cell count (7/mm³, monocyte/polycyte 6/1).

Cranial computed tomography revealed a slightly high density area in the left fronto-parietal lobe, but no bony thickening or thinning was detected (Fig. 1A). T1-weighted magnetic resonance (MR) imaging revealed an isointense area (Fig. 1B), and T2-weighted MR imaging showed a mass of thickened dura mater in the isointense area with surrounding hypointense area (Fig. 1C). T1-weighted MR
imaging with gadolinium showed homogeneous enhancement of the meninges (Fig. 1D–F). Left internal carotid angiography revealed no vascular abnormality (Fig. 1G), whereas left external carotid angiography showed faint tumor staining supplied by the middle meningeal artery (Fig. 1H, I). PET with 2-deoxy-2-[18F]fluoro-D-glucose ([18F]FDG) demonstrated slightly increased uptake compared to the normal brain (lesion/normal [L/N] ratio 1.55, maximum standardized uptake value [SUVmax] 8.53) (Fig. 1J). However, high [11C]-MET uptake (L/N ratio 4.47, SUVmax 4.59) was observed in an area corresponding to the enhanced lesion on MR imaging (Fig. 1K). Although we can discriminate IHCP from malignant lymphoma and metastatic brain tumor by observing increased accumulation of [18F]FDG and [11C]-MET, meningioma and IHCP cannot be differentiated even with both PET studies. Therefore, to distinguish IHCP from meningioma, left parietal craniotomy was performed and the dura-based mass was partially resected with a multimodal navigation system including [11C]-MET PET and MR imaging.

The dura was remarkably thick, and the mass extended into the brain and adhered strongly to the adjacent brain parenchyma (Fig. 2A). Histological examination of the dural biopsy revealed thickened fibrous tissue with marked lymphocyte infiltration without granuloma or necrosis. Immunohistochemical studies for CD20, CD3, κ, λ, CD68, and IgG4 showed that the infiltrating lymphocytes, plasma cells, and histiocytic cells were polyclonal (Fig. 2B–H). By exclusion, we diagnosed this lesion as IHCP. Since it was not an infection, we did not perform microbiological culture of the tissue sample.

The patient was treated with high-dose pulse therapy using intravenous methylprednisolone (1000 mg/day, for 3 days) (Fig. 3). One week after the first steroid pulse therapy, MR imaging revealed that the mass had spontaneously regressed (Fig. 3A). He received the high-dose steroid pulse therapy two more times. Subsequently, he was treated with prednisolone at 20 mg/day orally for one month, followed by 15 mg/day for another month, and we tapered prednisolone off at 1 mg in one month for 10 months. He was continually treated with prednisolone at 5 mg/day for 6 months. Follow-up PET studies demonstrated significantly decreased [11C]-MET uptake (L/N ratio 0.94) and decreased [18F]FDG uptake (L/N ratio 0.88) in the left parietal lobe (Fig. 3C). After these PET studies, the steroid therapy was discontinued. Neither clinical nor imaging (MR imaging and PET) manifestations of recurrence were observed one year after discontinuation of the steroid therapy (Fig. 3D).

**Discussion**

Hypertrophic pachymeningitis is characterized by dense fibrosis with scattered inflammatory cells, and the peripheral margin of the lesion contains highly vascularized arachnoid membrane. These features probably cause the enhancement of the dura mater observed on MR imaging with gadolinium.4) In the present patient, MR imaging with gadolinium showed an enhanced area of the left fronto-parietal lesion, similar to that seen in patients with malignant lymphoma, meningioma, and metastatic tumors. We were unable to exclude the possibility of neoplastic disease until the histological examination. IHCP has been described with unusual and misleading manifestations mimicking other diseases on morphologic neuroimaging diagnostic modalities such as MR imaging.16) In this study, we used [18F]FDG PET and [11C]-MET PET to distinguish these diseases by functional and metabolic imaging methods. Accumulation of [18F]FDG and [11C]-MET is much increased in malignant lymphoma and metastatic brain tumor, so these lesions can be distinguished from IHCP.8,14) However, meningioma and IHCP cannot be discriminated even if [18F]FDG PET and [11C]-MET PET are
Fig. 2  A: Intraoperative photograph showing the dura mater in the fronto-parietal lesion was thickened.  B–H: Photomicrographs of the resected mass lesion showing collagen fibers containing lymphocytes, plasma cells, and histiocytic cells.  Hematoxylin and eosin (B), CD20 (C), CD3 (D), γ (E), l (F), CD68 (G), and immunoglobulin G4 stain (H), original magnification × 200.

Fig. 3  Illustration showing the profile of steroid therapy and the changes in the lesion/normal (L/N) ratio in the lesion as evaluated by 2-deoxy-2-[18F]fluoro-D-glucose ([18F]FDG) (blue line) and L-[methyl-11C]methionine ([11C-MET]) (red line) positron emission tomography (PET) during the treatment.  A: Follow-up T1-weighted magnetic resonance (MR) images with gadolinium after the first steroid pulse therapy revealing that the enhanced mass had decreased.  B: Follow-up T1-weighted MR images with gadolinium (upper row), [18F]FDG PET scan (left lower, L/N ratio 1.02), and [11C-MET] PET scan (right lower, L/N ratio 1.78) after 12-month steroid therapy following biopsy showing decreased uptake.  C: [18F]FDG PET scan (left lower, L/N ratio 0.88) and [11C-MET] PET scan (right lower, L/N ratio 0.94) showing no uptake in the lesion after continuation of prednisolone (5 mg/day) for 6 months.  D: At one year after discontinuation of the oral steroid therapy, T1-weighted MR images with gadolinium (upper row) showing no enhanced mass and [18F]FDG PET (left lower) and [11C-MET] PET scans (right lower) showing no uptake.
used. $^{11}$C-MET uptake shows variable increase in meningiomas that are hypo- or isometabolic on $^{18}$F-FDG PET.1,2) Similarly, the uptake of $^{11}$C-MET is increased in granulomatous lesions and pachymeningitis that are hyper- or isometabolic on $^{18}$F-FDG PET.3,11) We emphasize the necessity for considering IHCP in the differential diagnosis of meningiomas.

Recently, IgG4-related disease has received significant attention in patients with pachymeningitis.5,15,23) This disease is characterized by elevated serum IgG4 levels, abundant infiltration of IgG4-positive plasma cells, and high-grade sclerosis including autoimmune pancreatitis.31) Although infiltration of IgG4-positive plasma cells was detected in this patient, we suggest that the pachymeningitis was not related to IgG4 because we could not find high serum IgG4 levels.

The treatment for IHCP is steroid therapy with or without a short course of high-dose pulse therapy. Some patients experience frequent relapses with corticosteroid therapy tapering, and such cases are considered to represent corticosteroid dependence.18) To avoid corticosteroid dependence, high-dose pulse therapy using intravenous methylprednisolone has been recommended.25) If those therapies are ineffective, the patients are treated with immunomodulators, such as azathioprine and cyclophosphamide,4) although their efficacy has not been proven yet. The response to corticosteroid therapy is assessed based on any changes in the clinical manifestations and MR imaging findings. However, the timing of tapering and discontinuation of steroid therapy is difficult to judge only by neurological examination and MR imaging. $^{11}$C-MET PET clearly demonstrates viable and infiltrative zones of inflammatory cells and is accurate for the diagnosis of the exact border of the disease.23) Furthermore, $^{11}$C-MET PET distinguishes between active lesions and inactive portions. In the treatment of gliomas and germinoma, $^{11}$C-MET PET is a useful biological monitoring modality to find active tumor tissues, because it reflects the biological nature of the tumors.6,7,17) The present case illustrates the usefulness of $^{11}$C-MET PET in monitoring the therapeutic efficacy in IHCP. In this patient, the lesion became inactive because the $^{11}$C-MET uptake significantly decreased, and then the steroid therapy was discontinued. Neither clinical nor radiological manifestations of recurrence were observed one year after discontinuation of the steroid therapy. Further experience of cases is obviously needed to confirm whether the lesions with decreased $^{11}$C-MET uptake never relapse after steroid discontinuation.

In conclusion, PET in a 53-year-old man with IHCP revealed marked accumulation of $^{11}$C-MET. $^{11}$C-MET PET was very useful for accurately locating the biopsy target and helpful to decide on continuation of the steroid therapy by providing useful information in monitoring the therapeutic efficacy against IHCP.

References


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