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CASE REPORT

# A case of multiple myeloma with pancreatic involvement diagnosed via endoscopic ultrasound-guided fine needle aspiration

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**Abstract**

This report highlights the importance of considering multiple myeloma in the differential diagnosis of a pancreatic tumor with bone lesions. sampling not only from the pancreatic lesion but also from bone lesions may reach an accurate diagnosis.

**KEYWORDS**

endoscopic ultrasound-fine needle aspiration, multiple myeloma, pancreatic tumor

## 1 | INTRODUCTION

Pancreatic nonepithelial neoplasms, which comprise only 1%–2% of all pancreatic neoplasms, are difficult to differentially diagnose due to their rarity, and their clinical imaging features are similar to those of pancreatic ductal adenocarcinoma.[1] Among pancreatic nonepithelial neoplasms, pancreatic myeloma is rare, accounting for only less than 0.1% of pancreatic tumors.[1] The accurate diagnosis of pancreatic masses is important for selecting appropriate treatment and predicting prognosis. Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) and fine needle aspiration biopsy (FNB) have been recommended for histological diagnosis of pancreatic solid masses.[2] However, the diagnostic accuracies of EUS-FNA and EUS-FNB in pancreatic tumors have been reported to be 88% and 90%, respectively.[3] Adequate sampling with EUS-FNA remains challenging in some cases. Some tips are required to achieve an accurate diagnosis in such cases. Here, we present a rare case of multiple

myeloma with pancreatic involvement that was diagnosed through a combination of EUS-FNA of a pancreatic lesion and computed tomography (CT)-guided fine needle biopsy of a bone lesion.

## 2 | CASE PRESENTATION

A male patient in his 50s presented with a main complaint of left hip pain for two months. A hip magnetic resonance imaging (MRI) scan, performed by his primary physician, revealed a bone tumor and, coincidentally, a pancreatic tumor. He was diagnosed with pancreatic cancer with bone metastasis, and he came to our hospital for further examinations. He had a history of hyperlipidemia but no history of cancer, smoking, or alcohol consumption.

Contrast-enhanced computed tomography (CT) revealed a slightly enhanced pancreatic mass and soft tissue behind the left iliac bone (Figure 1A–C). 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) was also performed. FDG uptake was seen in the pancreatic body and left iliac bone (maximum standardized uptake value, SUVmax = 5.4) (Figure 2A,B). In order to obtain pathological diagnosis, we first performed EUS-FNA of the pancreatic lesion. We used a 22G FNA needle (EZ Shot 3 Plus; Olympus, Tokyo, Japan) and a 25G FNA needle (SonoTip Pro Control; Medi-globe) with the wet suction method, connected to a 10- or 20-mL suction syringe. Initially, a 22G FNA needle was used, but it was difficult to puncture the tumor repeatedly with this needle. Hence, we also used a 25G FNA needle; however, no adequate specimens were obtained due to a large amount of blood contamination. Based on the EUS-FNA results, we decided to perform CT-guided fine needle bone biopsy. On CT, the target lesion of the left pelvis was detected as an internally heterogeneous and hypodense mass (Figure 3A). The tumor cells were primarily composed of atypical cells with a high proportion of eccentrically placed nucleus with pale perinuclear area, while adenocarcinoma cells were not obtained (Figure 3B–D). CD138 and CD79a immunoreactivity was diffusely observed in the tumor cells (Figure 3E,F). Furthermore, there was a clear difference

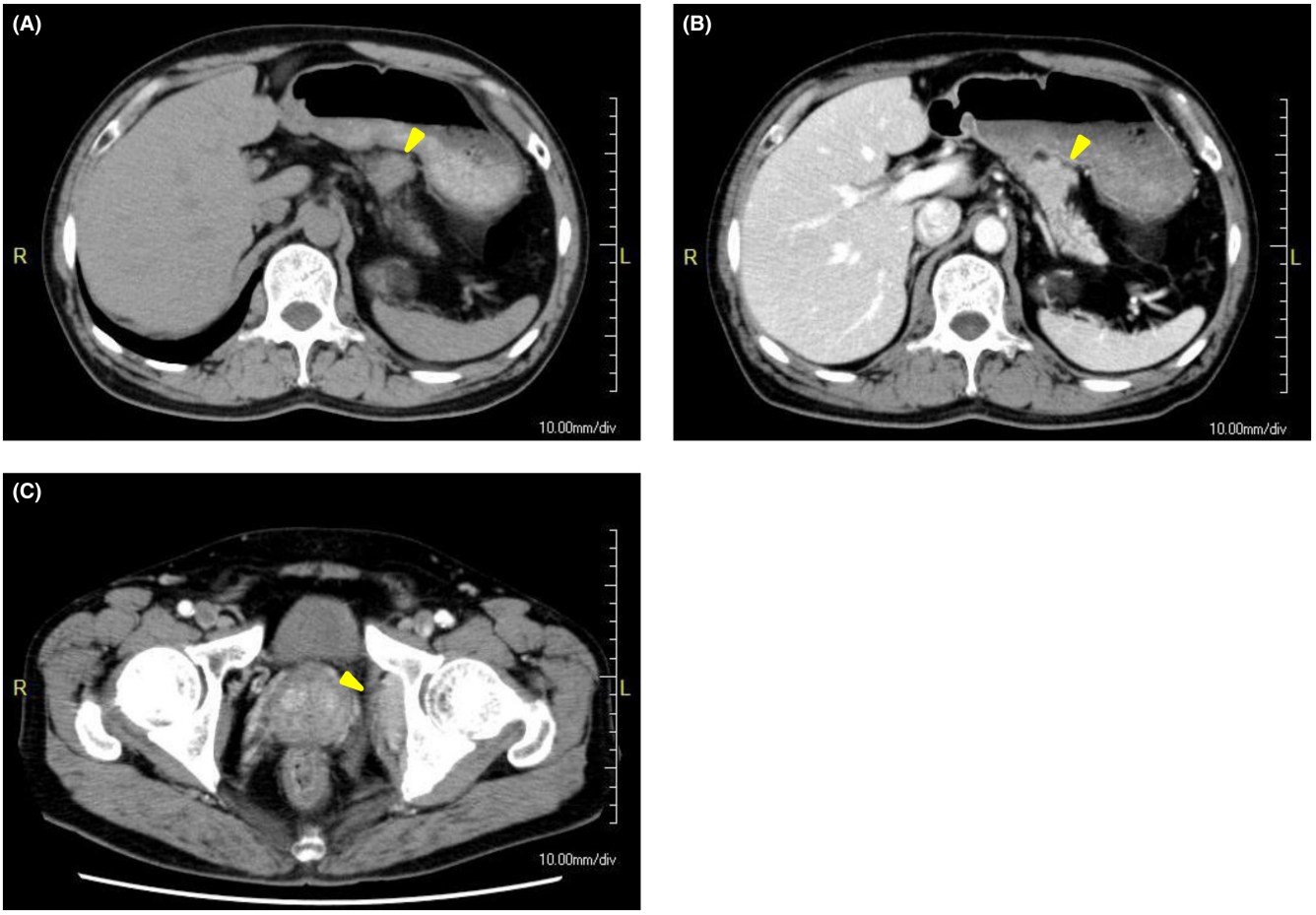


**FIGURE 1** Abdominal computed tomography (CT) images. (A,B) The pancreatic tumor was observed (arrowhead) on plain CT (A) and contrast-enhanced CT (B). The tumor was demonstrated as a slightly contrast-enhanced lesion in pancreatic body. (C) The bone lesion was revealed as soft tissue behind the left iliac bone on contrast-enhanced CT.

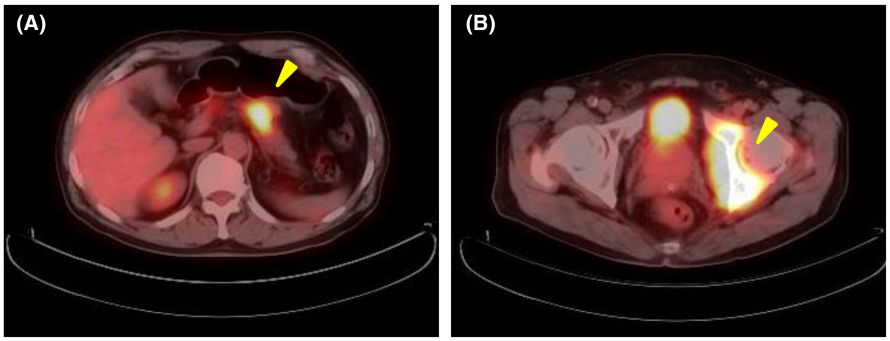


**FIGURE 2** Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET-CT) images. (A,B) FDG PET-CT showed FDG uptake in the whole pancreas (maximum standardized uptake value (SUVmax) of 5.4, arrowhead) (A) and left iliac bone (SUVmax of 5.4, arrowhead) (B).

between kappa and lamda chains in the ISH (in situ hybridization) images of immunoglobulin light chains, which we judged to be a neoplastic change caused by B cells or plasma cells (Figure 3G,H). Based on these findings, we diagnosed the bone lesions as plasma cell neoplasm; however, we needed to differentiate whether the pancreatic tumor was invasion from myeloma or another primary pancreatic tumor. As a result, we performed EUS-FNA once again for the pancreatic target. On EUS imaging, the pancreatic mass exhibited a 2–3 cm heterogeneous diffusely hypoechoic mass in the pancreatic body with partially unclear demarcations between the mass and the pancreatic parenchyma (Figure 4A). We reduced the aspiration pressure to 5 or 10 mL to avoid blood contamination, used a 22G FNA needle (EZ Shot 3 Plus; Olympus, Tokyo, Japan) and elongated the stroke length of the needle to ensure a sufficient sample volume. The obtained pancreatic tumor cells were similar to those from the bone tumors, with a high proportion of eccentrically placed nucleus with pale perinuclear area (Figure 4B). Most of the tumor cells were positive for CD138 and CD79a (Figure 4C,D). No adenocarcinoma cells were found in the pancreatic lesions. Based on the results of CT-guided bone biopsy and EUS-FNA, the histologically diagnosis was multiple myeloma with pancreatic invasion. To determine the stage and type of myeloma, we measured serum immunoglobulin (Ig) levels, serum M protein, and urine M protein. The following tests were performed to determine the stage and the type of myeloma: immunoglobulin (Ig) G level of 2664 mg/dL, IgA level of 324 mg/dL, IgM level of 51 mg/dL, kappa lambda ratio of 2.28, and β2-microglobulin of 2.2 mg. L and an M protein level of 2.39 g/L (accounting for 29.5%). The urine test showed no M protein. Although bone marrow and chromosome examinations were performed, the bone marrow indicated no monoclonal plasma cells, and the chromosome examinations showed no pathological findings. Based on these results, the patient was diagnosed with stage I symptomatic multiple myeloma, IgG kappa type, classified according to the International Staging System (ISS). According to this accurate diagnosis, he received high-dose melphalan followed by autologous stem cell transplantation after four cycles of induction therapy with bortezomib, lenalidomide, and dexamethasone. Two years after the initiation of induction therapy, the patient was under lenalidomide maintenance and doing well with stringent complete response.

## 3 | DISCUSSION

We present a case of extramedullary multiple myeloma, pathologically diagnosed via EUS-FNA of the pancreas and CT-guided needle biopsy of the left pelvis. It is important to include multiple myeloma in the differential diagnosis of pancreatic tumors with bone lesions. Extramedullary disease in myeloma is not frequent but can arise anywhere in the body, although the majority of cases occur in tissues rich in reticuloendothelial tissues, including the spleen, liver, kidney, and lymph nodes.[4] Clinically, extramedullary lesions in multiple myeloma are present in only 7%–8% of cases at diagnosis,[4] and pancreatic invasion is rare in extramedullary lesions.[5] However, the rate of bone metastasis from pancreatic cancer has been reported to be 6.7%, which is higher than the rate of pancreatic invasion in myeloma.[6] Pancreatic involvement in myeloma is rare but is an important factor in differential diagnosis because of the differences in treatment regimens and overall survival. Previously, patients with multiple myeloma have demonstrated a favorable prognosis, with a five-year survival rate of approximately 70%.[7] Recent advancements in medicine have further improved this survival rate. With the current generation of drugs, some targeted drugs have recently been used to treat multiple myeloma in the clinic, including proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), immunomodulatory drugs

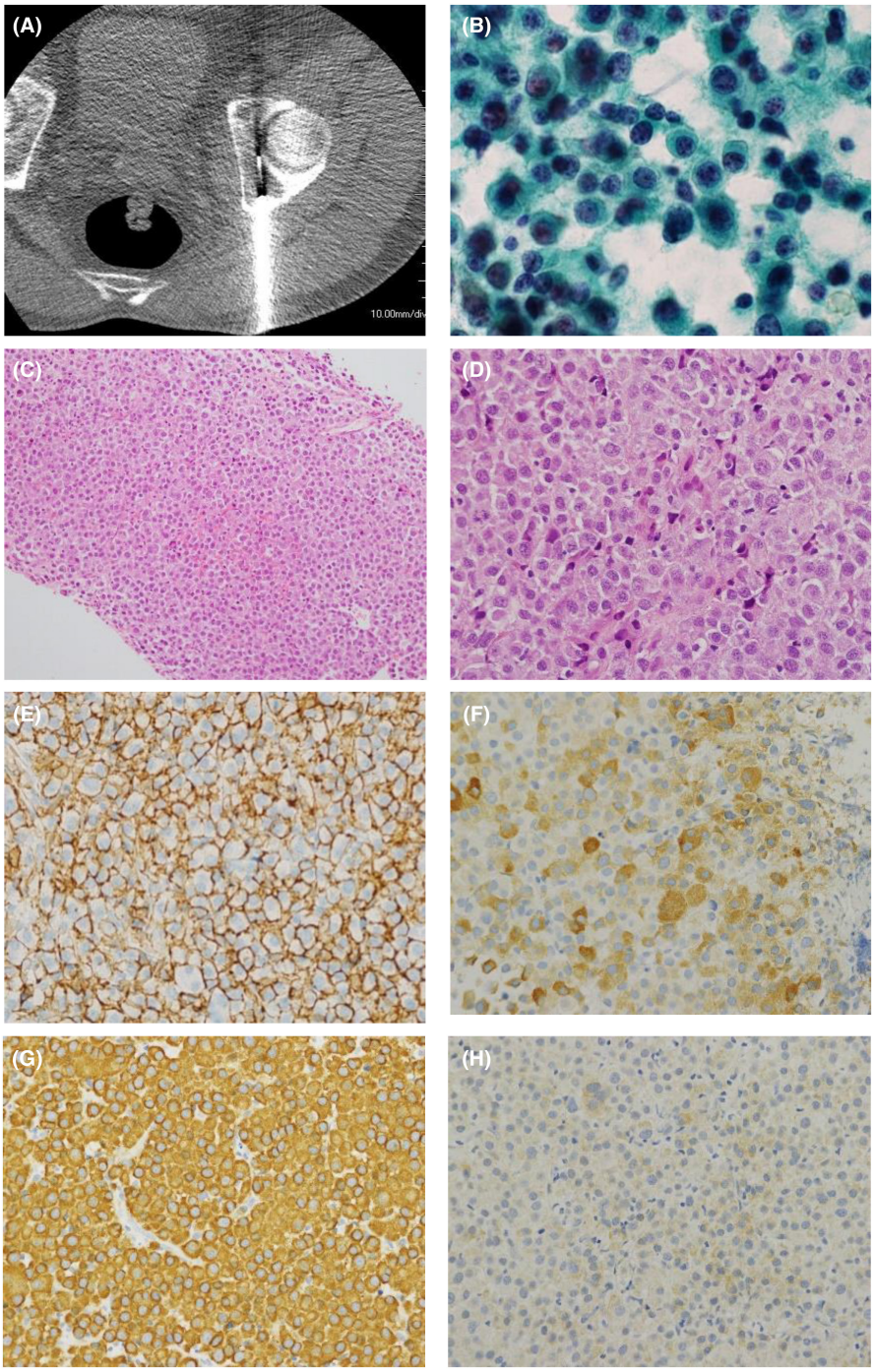


**FIGURE 3** Pathological examination with CT-guided fine needle biopsy for left iliac bone. (A) CT image showing the bone lesion as the target, which appears as an internally heterogeneous and hypodense mass. (B) Cytological staining with the Papanicolaou stain (×400). (C,D) Immunohistochemical staining with hematoxylin–eosin. (×200, ×400). (E,F) Immunohistochemical staining with CD138 (E) and CD79a (F) (×400). (G,H) In situ hybridization for kappa (G) and lambda (H) light chains (×400). Only kappa light chains were found.

(thalidomide, lenalidomide, and pomalidomide), daratumumab (an anti-CD38 monoclonal antibody), and chimeric antigen receptor (CAR)-T cells.[8] Advances in treatment options for multiple myeloma contribute to further improvements in overall survival. Nonetheless, pancreatic cancer is characterized by its aggressive nature and rapid metastasis, with a five-year survival rate of 5%–10%. In addition, only 10%–20% of patients with pancreatic cancer are diagnosed with localized, surgically resectable disease.[9] For patients with unresectable or recurrent pancreatic cancer, the therapeutic options are mainly based on combined cytotoxic chemotherapy with limited efficacy.[10–12] The definitive pathological diagnosis is important because the two diagnoses have different treatments and prognoses.

However, differential diagnosis between the two diseases is difficult based on imaging alone, such as CT or EUS. The EUS features of pancreatic invasion of myeloma remain unclear due to the paucity of cases diagnosed via EUS.[13] A literature review suggests that pancreatic invasion of myeloma often presents as a heterogeneous and hypoechoic tumor with well-defined borders.[13,14] Clear tumor borders are important for its differentiation from pancreatic adenocarcinoma.[15,16]

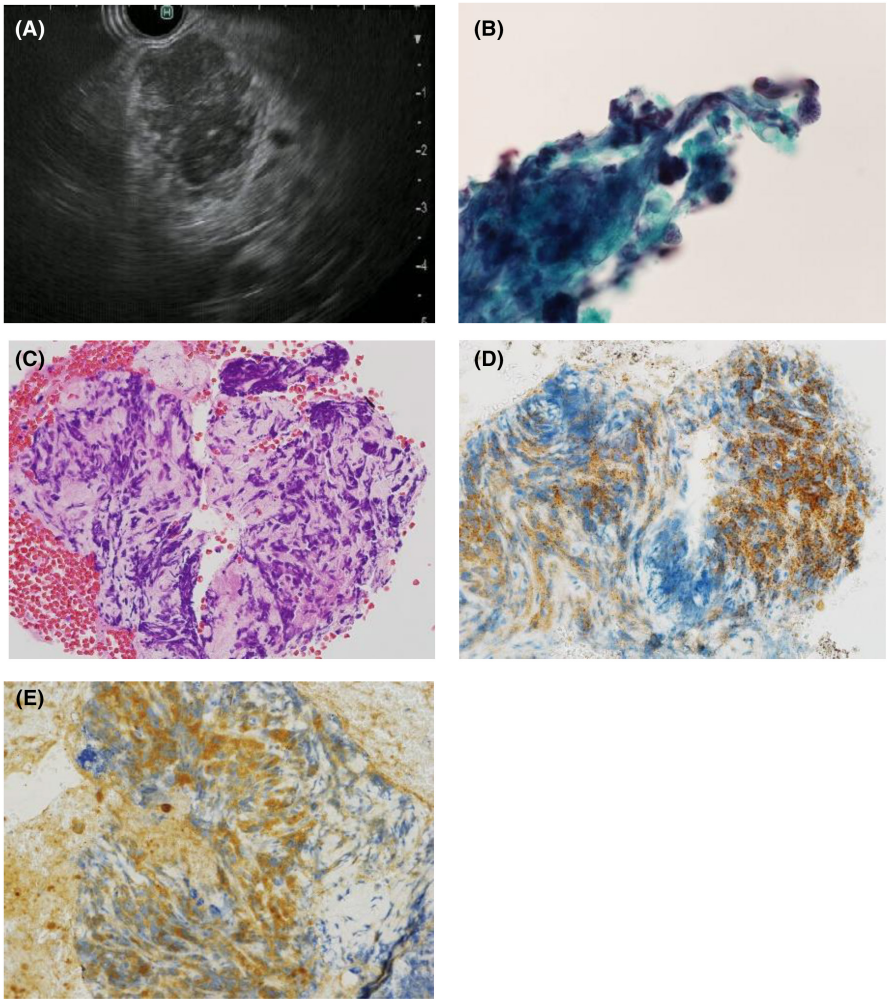


**FIGURE 4** Pathological examination with endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for the pancreatic lesion. (A) EUS image showing the pancreatic head lesion, which had an indistinct border, internal heterogeneity, and hypoechoic appearance. (B) Cytological staining with the Papanicolaou stain (×400). (C–E) Immunohistochemical staining with hematoxylin–eosin (C), CD138 (D), and CD79a (E) (×400).

In our case, the border of the tumor was partially obscured, and pancreatic cancer could not be completely ruled out. Thus, biopsy samples were also essential for obtaining an accurate diagnosis.

The pathological diagnosis of myeloma is currently based on histological and immunohistochemical confirmation of the presence of a homogenous monoclonal plasma cell. Pathologic features of the myeloma cells are characterized by heterogeneous-sized tumor cells heterogeneously sized with eccentric nuclei, enlarged nucleoli, perinuclear halo, and basophilic cytoplasm.[17] Typically, myeloma cells manifest CD138 and/or CD38.[17] CD79a, one of B cell markers, is usually positive or weakly positive in more than half of all myeloma cases.[18] In addition, the monoclonality of tumor needs to be verified via kappa/lambda light chain restriction or a PCR-based approach.[19] Occasionally, a large number of cells are necessary to confirm the degree of malignancy of the tumor, and obtaining a sufficient specimen volume is important.[20] EUS-FNA can be a useful diagnostic method for the pathological confirmation of pancreatic tumors.[13,14]

Reports of EUS-FNA for pancreatic plasmacytoma indicate that a sufficient amount of specimen was collected to achieve a diagnosis.[5,21] However, a comprehensive review of the 63 published cases of pancreatic plasmacytomas showed patients' characteristics and clinical manifestations were summarized.[21] Among 63 cases of pancreatic myeloma, only 14 (32.6%) cases were performed with EUS-FNA including some cases of recurrence. This suggests the need for a method to be devised for cases where enough samples cannot be collected by EUS-FNAs.[21] In our case, a primary CT-guided bone biopsy was beneficial for the definitive diagnosis, followed by a secondary EUS-FNA for additional diagnosis.

Furthermore, changing the EUS-FNA procedure could be important for increasing the sample volume. When we cannot obtain a sufficient amount of tumor, we need the additional devices of an FNB needle[22] or a thicker 19G needle[23] to increase the specimen volume. In the present case, based on the sufficient volume of the sample obtained via CT-guided needle biopsy of the left pelvis we first diagnosed the bone tumors as having plasmacytoid cell patterns. To obtain an accurate diagnosis for the pancreatic lesion, immunostaining against multiple antigens was needed for the pancreatic samples. Then, EUS-FNA

was performed for the pancreatic tumors, and a definite diagnosis was obtained, despite performing CD138 staining using EUS-FNA samples with a limited volume. To increase the sample volume and reduce blood contamination, the aspiration pressure was reduced, and the stroke length of the 22G biopsy needle was increased. Despite these approaches, it was difficult to sample a sufficient amount of tissue. However, we could obtain a definitive diagnosis after combining these findings with the CT-guided bone biopsy results.

In conclusion, we reported a rare case of multiple myeloma with pancreatic involvement diagnosed via EUS-FNA and CT-guided needle biopsy. Sampling from multiple sites and the ingenuity of EUS-FNA and immunostaining could be important for obtaining an accurate diagnosis.

## AUTHOR CONTRIBUTIONS

**Erika Hiraga:** Conceptualization; data curation; writing – original draft. **Takuo Yamai:** Conceptualization; data curation; writing – original draft. **Kenji Ikezawa:** Conceptualization; data curation; writing – original draft. **Yasuharu Kawamoto:** Data curation. **Takeru Hirao:** Data curation. **Sena Higashi:** Data curation. **Makiko Urabe:** Data curation. **Yugo Kai:** Data curation; writing – review and editing. **Ryoji Takada:** Writing – review and editing. **Tasuku Nakabori:** Data curation; writing – review and editing. **Hiroyuki Uehara:** Data curation. **Ayumi Ryu:** Data curation. **Sayako Yuda:** Supervision. **Keiichirou Honma:** Supervision. **Kazuyoshi Ohkawa:** Supervision.

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## CONFLICT OF INTEREST STATEMENT

The authors disclose no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data sharing are not available as no datasets were generated and analyzed in this study.

## CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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