Endoscopic ultrasound-guided fine-needle aspiration in the diagnosis of multiple myeloma accompanied by portal extramedullary plasmacytomas

Keiichi MORIYA, Hideto TAMURA, Masahiro OKABE, Toshio ASAYAMA, Mika SUNAKAWA, Yasuko KURIBAYASHI and Koiti INOKUCHI

A 67-year-old man presented with plasmacytomas in the hepatic portal region, as diagnosed with endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). Laboratory blood tests showed no myeloma-related symptoms such as hypercalcemia, renal failure, and anemia, and normal levels of serum immunoglobulins. However, bone marrow examination demonstrated approximately 15% of atypical plasma cells in bone marrow mononuclear cells, and serum tests showed an abnormal serum free light-chain ratio and monoclonal protein of Bence Jones lambda upon immunoelectrophoresis. Positron emission tomography/computed tomography demonstrated high 18F-fluorodeoxyglucose uptake in the portal hepatic tumors and several bone lesions accompanied by osteolysis. The patient was treated with bortezomib plus dexamethasone followed by high-dose melphalan with autologous stem cell transplantation, resulting in a complete response.

Lymph nodes are common sites of extramedullary myeloma disease associated with poor prognosis. EUS-FNA is less invasive than open surgical biopsies and thus it is recommended in the differential diagnosis of plasmacytoma in cases such as ours. EUS-FNA may enable early treatment, resulting in a good response even in myeloma patients with unfavorable prognoses.

Key words: multiple myeloma, extramedullary disease, endoscopic ultrasound-guided fine-needle aspiration

Introduction

Multiple myeloma (MM) is a mature B-cell malignancy characterized by bone marrow infiltration of clonal plasma cells with clinical features such as hypercalcemia, renal insufficiency, anemia, and bone lesions. Extramedullary plasmacytomas (EMPs) are seen in 7–15% of MM patients at the time of diagnosis, and the presence of EMPs is associated with poor prognosis in both newly diagnosed and relapsed MM patients [1]. Common sites of EMPs are the gastrointestinal tract, pleura, testis, skin, peritoneum, liver, endocrine glands, and lymph nodes [1, 2]. It was reported that fewer than 1% of patients with newly diagnosed symptomatic MM have lymphadenopathy [3]. We report a case of MM diagnosed by endoscopic ultrasound (EUS)-guided fine-needle aspiration (FNA) of the swollen lymph nodes in the hepatic portal region.

Case Report

A 67-year-old man visited our hospital with suspected malignant lymphoma. He had a history of hypertension and insomnia and had undergone abdominal computed tomography (CT) due to occult blood in the urine detected in a mass screening. The CT images demonstrated swelling of multiple lymph nodes in the hepatic portal region (Fig. 1). The physical examination was normal, and no surface lymph node was palpable. The laboratory data showed slight elevation of serum uric acid, but no myeloma-related events such as hypercalcemia, renal failure, and anemia, and levels of serum lactate dehydrogenase (LDH) and soluble interleukin (IL)-2 receptor were normal (Table 1). Total-body CT, esophagogastroduodenoscopy, and colonoscopy were performed, although they showed no tumor or abnormal mass lesion except for the previously detected lymph nodes. Biopsy of the lymph nodes by laparotomy was deemed too invasive, and thus diagnostic EUS-FNA was performed. EUS at the duo-

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denum revealed marked swelling of lymph nodes in the hepatic portal region, and FNA yielded an adequate sample. The biopsy specimen showed small-sized lymphocytes and plasma cells (Fig. 2A), which were positive for CD38 (Fig. 2B), CD56, and CD138, and lambda light-chain restriction. Flow cytometric and chromosomal analyses were not performed because the amount of aspirated sample obtained by EUS-FNA was insufficient. These findings indicated that the lymph nodes contained plasmacytomas, and thus we performed bone marrow examination and positron emission tomography (PET)-CT to detect myeloma cells and bone lesions, respectively. The bone marrow contained 15% clonal plasma cells (Fig. 2C), which were CD19−CD56+CD45+MPC-1+CD20+/− cytoplasmic lambda-positive cells in CD38 high-positive fractions.

**Table 1.** Patient’s laboratory data at diagnosis

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<tbody>
<tr>
<td>WBC</td>
<td>6000/μL</td>
<td>AST</td>
<td>24 IU/L</td>
<td>Ca</td>
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<tr>
<td>Stab</td>
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<td>ALT</td>
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<td>Seg</td>
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<td>LDH</td>
<td>146 IU/L</td>
<td>Alb</td>
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<tr>
<td>Eo</td>
<td>0.5%</td>
<td>ALP</td>
<td>261 IU/L</td>
<td>CRP</td>
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<td>Ba</td>
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<td>gGTP</td>
<td>19 IU/L</td>
<td>Glu</td>
</tr>
<tr>
<td>Mo</td>
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<td>T-Bil</td>
<td>0.5 mg/dL</td>
<td>sIL-2R</td>
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<td>Lym</td>
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<td>UA</td>
<td>7.6 mg/dL</td>
<td>IgG</td>
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<tr>
<td>RBC</td>
<td>409 × 10⁴/μL</td>
<td>BUN</td>
<td>13.3 mg/dL</td>
<td>IgA</td>
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<tr>
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<td>13.8 g/dL</td>
<td>Cre</td>
<td>0.73 mg/dL</td>
<td>IgM</td>
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<tr>
<td>Ht</td>
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<td>Na</td>
<td>144 mEq/L</td>
<td>β2MG</td>
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<tr>
<td>Plt</td>
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<td>K</td>
<td>4.0 mEq/L</td>
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<tr>
<td>Ret</td>
<td>8‰</td>
<td>Cl</td>
<td>106 mEq/L</td>
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**Figure 1.** CT image at diagnosis. Coronal slice of the portal area shows swelling of two lymph nodes (yellow arrow).

**Figure 2.** Microscopic images. The EUS-FNA sample smear shows proliferation of plasma cells with HE staining (A) and these were CD38+ in immunohistochemistry (B). A bone marrow aspiration sample smear shows proliferation of plasma cells with Wright-Giemsa staining (C).
EUS-FNA in the diagnosis of myeloma as shown by flow cytometric analysis. Adverse chromosomal abnormalities such as t(4;14), t(14;16), and 17p- were not detected by fluorescence in situ hybridization. PET-CT demonstrated high 18F-fluorodeoxyglucose (FDG) uptake by lymph nodes of the hepatic portal region and several bone lesions of the right scapula and thoracic vertebrae accompanied by some osteolysis (Fig. 3). Serum and urinary electrophoresis showed monoclonal lambda light-chain protein with serum free light-chain kappa/lambda 141/1730 mg/L, and serum β2MG was 4.7 mg/dL. We therefore diagnosed Bence Jones lambda type MM in Durie & Salmon stage IIIA and International Scoring System stage II.

The patient was treated with bortezomib plus dexamethasone (BD) with concurrent radiotherapy of the vertebrae because of lumbar with high FDG uptake. After 1 course of BD therapy, the serum free light-chain kappa/lambda ratio normalized (Fig. 4). After four courses of BD were administered, abdominal CT demonstrated no swelling of lymph nodes in the hepatic portal region. High-dose melphalan treatment with autologous peripheral blood stem cell transplantation (APBSCT) was performed, and the patient continued to show a complete response for 4.3 years after transplantation with no maintenance therapy.

Discussion

In our patient, histological diagnosis of swollen lymph nodes in the portal region was needed because no myeloma-defining signs were evident in the laboratory blood test results. EUS-FNA revealed MM accompanied by portal EMPs, which contributed to the early start of treatment and resulted in a good response in this case of myeloma with an unfavorable prognosis.

The diagnosis of EMPs requires the demonstration of monoclonal plasma cell proliferation in the tumor site. Minimally invasive surgical procedures are preferred, especially for elderly patients, and CT-guided core needle biopsy (CTNB) is a common procedure to obtain tumor samples. However, it is sometimes difficult to perform CTNB because of the high risk of pneumothorax, hemorrhage, and air embolism in some patients. In some cases, plasmacytoma biopsy is performed in invasive procedures such as open surgical biopsy, although EUS-FNA is a less invasive, well-established technique. There have been several reports of EMPs in the pancreas, omentum, liver, and gallbladder, as well as of mediastinal and mass lesions near the aortoiliac bifurcation diagnosed by EUS-FNA [4–11]. Furthermore, the incidence of complications with
EUS-FNA is lower than with CTNB because of the fine needle used in FNA. However, the small amount of sample obtained is a disadvantage of EUS-FNA, which may result in difficulty in pathophysiologic diagnosis and biological/genetic analyses in hematologic area. On the other hand, the diagnostic accuracy of lymph nodes for metastatic pancreatic cancer is very high when combined with radiologic evaluation, and some studies showed that EUS-FNA has a sensitivity of 79–98% and a specificity of 98–100% in diagnosing mediastinal and intra-abdominal lymphadenopathies [12]. It is difficult to diagnose some lymphomas in detail, but it was reported that the accuracy of EUS-FNA in combination with flow cytometry in diagnosing lymphoma was 94.2% [13], and therefore EUS-FNA is a useful tool in the diagnosis of lymphadenopathy.

The incidence of extramedullary lesions in MM is 7–15% at initial diagnosis, and the majority of those cases have a single plasmacytoma [1, 3]. Patients with EMPs at diagnosis have shorter progression-free survival compared with others. Solitary plasmacytomas are usually treated with radiation [14], but there is no standard therapy for patients with multiple EMPs. Because there were several reports on the efficacy of bortezomib-based combination therapy in extramedullary MM, our patient was administered BD as induction therapy, achieving a significant therapeutic effect [15, 16]. Several reports mentioned that high-dose chemotherapy followed by APBSCT can overcome the negative impact of EMPs on prognosis [1, 3]. Previous studies found that the prevalence of EMPs was significantly higher in younger than in elderly patients [17, 18]. Transplant-eligible patients with EMPs should be treated with triplet induction therapy followed by high-dose melphalan with APBSCT and triplet consolidation therapy [19]. However, our patient did not receive triplet induction/consolidation therapy because the triplet regimen was not standard at the time of treatment.

In summary, EUS-FNA has some disadvantages such as the small amount of specimen yielded, but it is very useful for the diagnosis of early-stage high-risk MM accompanied by EMPs. In our patient, EUS-FNA led to the diagnosis of MM and made urgent treatment possible.

**Authorship**

K.M. and H.T. analyzed the clinical status of the patient, analyzed the data, and prepared the manuscript; M.O., T.A., M.S., Y.K., and K.I. analyzed the data and the clinical status of the patient.

**Conflicts of Interest**

The authors declare no competing financial interests.