Intravascular large B-cell lymphoma diagnosed on a nasal mucosal biopsy with the guide of FDG-PET/CT imaging study

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Received 2016/5/19; accepted 2016/5/26; released online 2016/7/15

Keywords: intravascular large B-cell lymphoma, nasal mucosal biopsy, FDG-PET/CT

Figure 1. FDG-PET/CT. The anterior view of the maximum intensity projection images (A) and representative axial images of the head and chest (B to E) are shown. The maximum standardized uptake value (SUVmax) of the nasal cavity was 8.92 (arrows in B and C), and that of the right maxillary bone lesion and sub-aortic arch lymphoma node (arrows in D and E) was 3.73, and 6.91, respectively. In A, increased FDG uptake in the vertebrae and nodular accumulation in the body of the right humerus (arrowheads) suggest involvement of the bone marrow. The FDG uptake in the bilateral shoulder, elbow, and wrist joints may reflect metabolic activity of underlying polyarthritis.
Intravascular large B-cell lymphoma (IVLBCL) is an extranodal subtype of diffuse large B-cell lymphoma, characterized by exclusive or predominant proliferation of lymphoma cells within the lumen of small blood vessels, and currently represents a separate entity in the WHO classification. However, in spite of increased knowledge of the features of this rare condition, IVLBCL remains a diagnostic challenge in the clinical scene.
because biopsies of expected tissue and/or organs may not necessarily provide evidence of the disease.

A 58-year-old man was referred to our department for suspected hematologic malignancy. He exhibited a stuffy nose 3 months prior, and then developed a fever of >39.0°C associated with night sweats, exertional dyspnea, and anorexia. He had also lost 10 kilograms of body weight. Blood tests at a primary care hospital showed anemia, thrombocytopenia, and an elevated level of lactate dehydrogenase (LDH). He had received treatment for hypertension, hyperuricemia, gastric ulcer, and chlamydia urethritis. On examination, his body temperature was 36.5°C after taking acetaminophen, blood pressure was 127/75 mmHg, pulse rate was 98 beats per minute, and oxygen saturation was 100% while breathing ambient air. There was no surface lymphadenopathy. The liver and spleen were not palpable. His performance status was ECOG 1. His hemoglobin level was 8.0 g/dL, white cell count was \(3.52 \times 10^3/\mu L\), and platelet count was \(92 \times 10^3/\mu L\). The white cell differential was 24.0% lymphocytes, 9.0% monocytes, 6.5% eosinophils, 1.0% basophils, 51.5% segmented neutrophils, and 8.0% banded neutrophils. The level of LDH was 499 IU/L, aspartate aminotransferase was 26 IU/L, alanine aminotransferase was 57 IU/L, uric acid was 7.8 mg/dL, C-reactive protein was 4.7 mg/dL, soluble interleukin-2 receptor was 892 U/mL, and ferritin was 638 ng/mL. The bone marrow showed infiltration of macrophages but lacked hemophagocytosis.

Equivocal lymphadenopathy in the mediastinum and splenomegaly were observed in a computed tomography (CT) of the body with contrast media, although no abnormalities were found in the head and neck regions. \(^{18}\)F-fluorodeoxyglucose-positron emission tomography combined with CT (FDG-PET/CT), however, showed significant tracer uptake within the nasal cavity, extending to the ethmoid bone and sinus of both sides (Figure 1). There was an FDG-accumulated nodule in the right maxillary bone. A sub-aortic arch lymph node was FDG-avid and the level of splenic uptake was higher than that of the liver.

Although the nasal mucosa appeared normal on endoscopic examination, biopsies of the mucosa obtained from the inferior concha and nasal septum revealed multiple clusters of lymphoma cells that filled up the intravascular space, which was delineated by anti-CD31 immunostaining (Figure 2). The cells were large in size and showed high nucleus/cytoplasm ratio with conspicuous nucleoli. The cells were CD5\(^-\), CD10\(^-\), CD20\(^+\), CD30\(^-\), CD56\(^-\), BCL2\(^+\), BCL6\(^+\) (partial), and MUM1\(^+\) on immunohistochemistry.

A diagnosis of IVLBCL was made, and the patient was treated with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy. After receiving 1 cycle of R-CHOP, his constitutional symptoms resolved. He underwent a total of 6 cycles of R-CHOP followed by high-dose methotrexate for prophylaxis of the central nervous system lymphoma in-filtration. The patient has been free from disease for 18 months.

In a Japanese series, pathological specimens for the diagnosis of IVLBCL were most frequently obtained from the bone marrow.\(^2\) From the initial report by Asada et al.,\(^3\) random biopsies of “normal” skin without any abnormalities have been proven diagnostic of the disease. On the other hand, FDG-PET/CT has been useful to not only detect unexpected disease involvement but also guide the appropriate sites of biopsy, including brain, lung, kidney, adrenal gland, vagina, and uterus.\(^4\) To our best knowledge, this is the first report demonstrating the microscopic evidence of IVLBCL in nasal mucosal biopsy with the guide of FDG-PET/CT imaging study. Although IVLBCL can involve virtually any tissue/organ containing small vessel structures,\(^1\) there may be predominant sites of involvement in each case. Thus, when IVLBCL is considered, biopsies of appropriate tissues/ organs suggested by FDG-PET/CT may contribute to early diagnosis of the disease and initiation of effective therapy.
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