

Histological findings in the spleen affected by adult-onset Still's disease: a report of three cases

Sirs,

Diagnosis of adult-onset Still's disease (AOSD) is based on sets of several clinical and laboratory criteria because no specific test is available. The differential diagnosis includes malignant lymphoma and infectious diseases. A recent case series using positron emission tomography/computed tomography (PET/CT) showed high frequency accumulation of injected ^{18}F -fluorodeoxyglucose (FDG) in the spleen and bone marrow of AOSD patients (1). Cell types contributing to the splenic ^{18}F -FDG accumulation in AOSD have not been identified, while granulocytic hyperplasia in bone marrow reported as a common feature of AOSD may be responsible for the FDG uptake by bone marrow (2). Here we describe three female cases presenting fever of unknown origin, in which accumulation of ^{18}F -FDG was found in both the spleen and bone marrow on PET/CT, and on whom spleen and bone marrow biopsies were performed to distinguish AOSD and malignant lymphoma. The histological analysis ruled out the possibility of malignant lymphoma, and the diagnosis of AOSD was made according to the Yamaguchi criteria in each case.

Case 1

A 48-year-old Japanese woman was admitted to our hospital with a high spiking fever and polyarthralgia. Laboratory examination revealed neutrophilia and elevated lactate dehydrogenase (LDH), C-reactive protein (CRP), and ferritin levels. PET/CT demonstrated a profound ^{18}F -FDG accumulation in the spleen, bone marrow, and cervical, axillary, mediastinum and para-aortic lymph nodes (Fig. 1a). Biopsy specimen from left inguinal lump did not include lymph node tissue, and the every superficial lymph node in other areas seemed inadequate for biopsy because of their small size. Thus the percutaneous CT-guided spleen biopsy and bone marrow biopsy were conducted to distinguish between AOSD and malignant lymphoma. The spleen biopsy showed extensive infiltration of neutrophils and mild infiltration of plasma cells, lymphocytes, and eosinophils in the red pulp (Fig. 1d). In the bone marrow, neutrophil hyperplasia and histiocytic hemophagocytosis were observed.

Case 2

A 37-year-old Japanese woman was admitted to our hospital with a high spiking fever, rash on her hands and left arm, and swollen lymph nodes in the bilateral submandibular areas. Laboratory tests showed mild elevation of LDH and CRP levels. PET/CT revealed mild hepatomegaly, mild

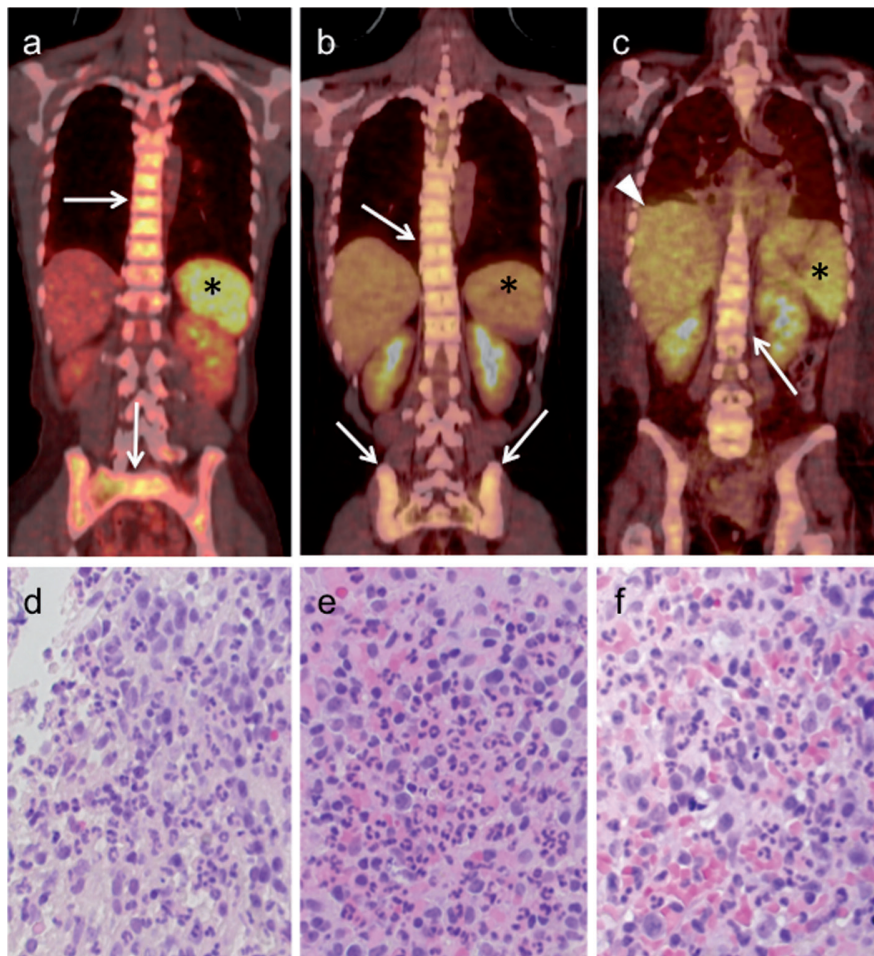


Fig. 1. ^{18}F -FDG PET/CT images and histological findings of the spleen in AOSD.

a-c: ^{18}F -FDG PET/CT images of cases 1 (a), 2 (b), and 3 (c). Uptake of ^{18}F -FDG was observed in the bone marrow (arrows) and enlarged spleen (asterisks) in all three cases. ^{18}F -FDG also accumulated in the lymph nodes in case 1 (not shown) and liver in case 3 (an arrowhead). **d-f:** Histological findings of the spleen in cases 1 (c), 2 (d), and 3 (e). Severe infiltration of neutrophils was identified in the red pulp in each case. Haematoxylin-eosin staining; $\times 400$.

splenomegaly and swollen lymph nodes in the bilateral submandibular space. ^{18}F -FDG uptake was observed in the spleen and bone marrow (Fig. 1b). Spleen biopsy showed micro-abscesses characterised by focal dense infiltration of neutrophils and sparse infiltration of eosinophils, lymphocytes and plasma cells in the red pulp (Fig. 1e). Bone marrow biopsy revealed normocellular bone marrow with normal myeloid/erythroid ratio.

Case 3

A 31-year-old Brazilian woman was admitted to our hospital due to a high spiking fever. Laboratory tests detected neutrophilia, and severe elevation of liver transaminases, LDH, CRP and ferritin levels. PET/CT identified mild splenomegaly and moderate uptake of ^{18}F -FDG in the bone marrow, liver, and spleen (Fig. 1c). The spleen biopsy revealed severe infiltration of neutrophils, and moderate infiltration of plasma cells and lymphocytes in the red pulp (Fig. 1f). Normocellular bone marrow with histiocytic haemophagocytosis was identified by bone marrow biopsy.

^{18}F -FDG PET/CT is considered to be useful for monitoring disease activity in AOSD, but unable to exclude malignant lymphoma (1, 3). Exclusion of malignant lymphoma in spleen is required in some cases suspicious of AOSD presenting splenomegaly. Further, percutaneous spleen biopsy is recently considered to be a safe and effective procedure for the evaluation of neoplasm in the spleen (4). However, limited data are available regarding the histopathology of spleen biopsy specimens in AOSD. Denzur *et al.* performed minilaparoscopy-guided spleen biopsy in four patients with splenomegaly of unknown origin (5). Notably, one of these patients had a history of AOSD and the spleen biopsy showed granulocytic infiltration. Another case of AOSD with peritonitis and granulocytic infiltration in the spleen has also been reported (6). These two reports are consistent with the observations in our cases.

In summary, our cases suggest that infiltration of neutrophils into the red pulp may contribute to ^{18}F -FDG uptake by the spleen in AOSD patients.

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References

1. YAMASHITA H, KUBOTA K, TAKAHASHI Y *et al.*: Clinical value of 18F-fluoro-dexoxyglucose positron emission tomography/computed tomography in patients with adult-onset Still's disease: a seven-case series and review of the literature. *Mod Rheumatol* 2014; 24: 645-50.
2. MIN JK, CHO CS, KIM HY, OH EJ: Bone marrow findings in patients with adult Still's disease. *Scand J Rheumatol* 2003; 32: 119-21.
3. FUNAUCHI M, IKOMA S, KISHIMOTO K *et al.*: A case of adult onset Still's disease showing marked accumulation in the liver and spleen, on positron emission tomography-CT images. *Rheumatol Int [Case Reports]* 2008; 28: 1061-4.
4. TAM A, KRISHNAMURTHY S, PILLSBURY EP *et al.*: Percutaneous image-guided splenic biopsy in the oncology patient: an audit of 156 consecutive cases. *J Vasc Interv Radiol* 2008; 19: 80-7.
5. DENZER U, HELMREICH-BECKER I, GALLE PR, LOHSE AW: Minilaparoscopy-guided spleen biopsy in systemic disease with splenomegaly of unknown origin. *Endoscopy* 2002; 34: 495-8.
6. PORALLA T, HUTTEROTH T, MAYET W *et al.*: Peritonitis and massive granulocytic infiltration of the spleen in adult Still's disease. *Z Rheumatol* 1988; 47: 364-5.