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CASE REPORT

Potential Role of Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography in Immunoglobulin G4-related Systemic Disease

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ABSTRACT

We report on a 60-year-old man who presented with painless obstructive jaundice, suspicious of hilar cholangiocarcinoma. Positron emission tomography–computed tomography (PET-CT) demonstrated markedly fluorodeoxyglucose-avid bilateral enlarged submandibular masses and extensive hypermetabolic supra- and infra-diaphragmatic lymphadenopathy. Left submandibular excisional biopsy revealed immunoglobulin G4-related systemic disease. Compared with CT or magnetic resonance imaging, fluorine-18 fluorodeoxyglucose PET-CT not only allows whole-body imaging, but also offers metabolic information that helps to reflect disease activity. Fluorine-18 fluorodeoxyglucose PET-CT is a potential useful tool for diagnosis, treatment response assessment, and relapse detection of this systemic disease that is worth further exploration.

Key Words: *Fluorodeoxyglucose F18; Immunoblastic lymphadenopathy; Immunoglobulin G; Lymphoma; Positron-emission tomography and computed tomography*

中文摘要

氟脱氧葡萄糖PET—CT在免疫球蛋白G4相關性系統性疾病中的潛在作用

龔本霆、黃治平、歐陽定勤、唐卓敏

本文報告一名60歲男子，病發時出現無痛性梗阻性黃疸，懷疑是肝門部膽管癌。正電子發射斷層掃描—電腦斷層掃描（PET—CT）顯示氟脱氧葡萄糖明顯濃聚的雙側下頜下腺增大的腫塊和橫膈上下方廣泛代謝增高的腫大淋巴結。左側下頜下腺切除活檢顯示免疫球蛋白G4相關性系統性疾病。與CT或磁共振相比，18氟脱氧葡萄糖PET—CT不僅可作全身顯像，而且還提供了代謝信息，有助反映病情活動。氟18氟脱氧葡萄糖PET—CT是一種潛在的有用工具，可用作該系統性疾病的診斷、治療反應評估和復發檢測，值得進一步探討。

INTRODUCTION

This report is of a middle-aged man with immunoglobulin G4–related systemic disease (IgG4-RSD), a new disease entity characterised by numerous IgG4-positive plasma cells and lymphoplasmacytic infiltrates.[1,2] Fluorodeoxyglucose positron emission

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tomography–computed tomography (FDG PET-CT) may play a complementary role in the diagnosis, treatment response assessment, and relapse detection of this systemic disease.

CASE REPORT

A 60-year-old man presented with painless bilateral submandibular masses in October 2010. He found the masses progressively enlarging for the past 3 weeks. He had no previous history of malignancy. Ultrasonography of the neck showed enlarged bilateral submandibular glands with rounded and mildly lobulated contours associated with heterogeneous hypoechoic echo pattern. Mildly increased vascularity was shown on Doppler imaging. The features were suggestive of Küttner's tumour. Fine-needle aspiration of the right submandibular gland revealed no malignant cells. The patient presented again in March 2011 with painless obstructive jaundice. A biliary stent was inserted. CT and endoscopic retrograde cholangiopancreatography findings were suspicious of cholangiocarcinoma. FDG PET-CT was performed in June 2011 for staging.

For the PET-CT, the patient was fasted for 6 hours before intravenous injection of FDG 370 MBq. Scanning was initiated 60 minutes after administration of FDG. PET-CT images were taken from the head to the proximal thigh with the Discovery LS scanner (GE Healthcare, Amersham, UK) with a spatial resolution of 6.6 mm in the centre of the field of view. Seven bed positions were performed with 3 minutes per bed position. CT was performed for attenuation correction, lesion localisation, and characterisation. The obtained images were reconstructed using the ordered subsets expectation maximisation iterative reconstruction algorithm. The regions of interests were drawn for FDG uptake quantification on visible lesions with increased uptake, and the maximum standardised uptake value (SUV_{max}) was semiquantitatively analysed with the following equation:

$$SUV=A/(ID/BW)$$

where A represents the decay- and attenuation-corrected activity in tissue (in MBq/ml), ID the injected dose of FDG (in MBq), and BW the patient's body weight (in g).

FDG PET-CT showed diffuse supra- and infra-diaphragmatic lymphadenopathy, including enlarged porta-hepatis lymph nodes, with an SUV_{max} of 6.1 (Figure 1). Homogenous mildly increased splenic FDG

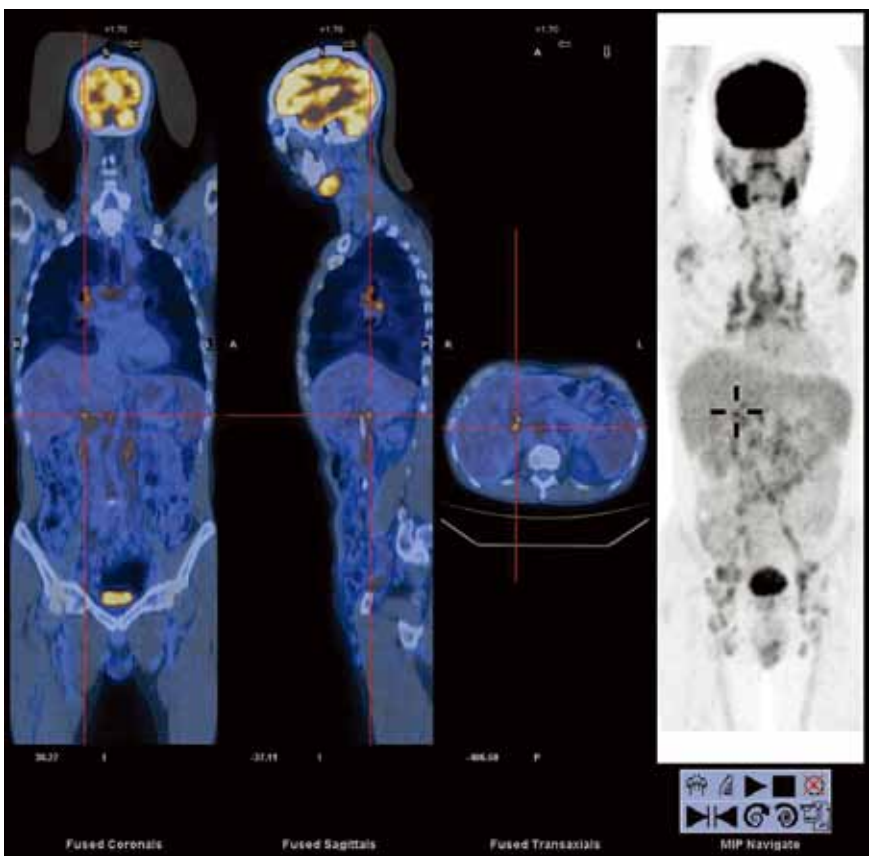

Figure 1. Positron emission tomography–computed tomography shows diffuse supra- and infra-diaphragmatic lymphadenopathy, including an enlarged porta-hepatis lymph node with a maximum standardised uptake value of 6.1.

metabolism was detected, with an SUV_{max} up to 3.1. No hypermetabolic liver lesion was identified. In view of the extensive hypermetabolic lymphadenopathy, the attending nuclear medicine physician provided differential diagnoses, including lymphoproliferative disease. Markedly hypermetabolic bilateral submandibular masses with an SUV_{max} up to 7.5 were thought to be related to either tumour infiltration or inflammation (Figure 2). Excisional left submandibular, right groin, and ampulla biopsies revealed abundant plasma cells, mostly IgG- and IgG4-positive plasma cells. The ratio of IgG4- to IgG-positive plasma cells was more than 40%. The features were consistent with IgG4-RSD. Serum IgG4 and IgE levels were markedly raised. The patient was treated with oral prednisolone (from 30 mg daily in August 2011 to 7.5 mg daily in January 2012) and oral azathioprine (50 mg daily from October 2011 to February 2012). Liver function and amylase level subsequently normalised with treatment. Follow-up PET-CT in November 2011 showed considerable metabolic improvement of the lymphadenopathy and bilateral submandibular masses (Figure 3). To date, the patient continues to receive oral azathioprine (50 mg daily) treatment.

DISCUSSION

IgG4-RSD is characterised by extensive IgG4-positive plasma cells and T-lymphocyte infiltration.[1,2] IgG4-RSD usually affects elderly or middle-aged men. Patients usually have good clinical status with no constitutional symptoms or fever.[3] IgG4-RSD can involve single or multiple organs in the form of mass lesions. Typically, IgG4-RSD involves the pancreas, salivary gland, bile duct, gallbladder, retroperitoneum, kidney, lung, and prostate.[3] Biochemically, high serum IgG, IgG4, and IgE concentrations and abundant IgG4-bearing plasma cell infiltration are the hallmarks of IgG4-RSD.[3-5] Within the spectrum of IgG4-RSD, autoimmune pancreatitis and Mikulicz's disease are the two most commonly encountered conditions. Autoimmune pancreatitis is closely associated with a variety of extra-pancreatic lesions, such as sialadenitis.[6] In this patient, Küttner's tumour was initially suspected. Küttner's tumour is a fibro-inflammatory salivary gland disease involving one or both submandibular glands, which contain IgG4-positve plasmacytes.[7] Both Küttner's tumour and Mikulicz's disease appear to be within the spectrum of IgG4-RSD.[8,9] Concomitant lymphadenopathy is

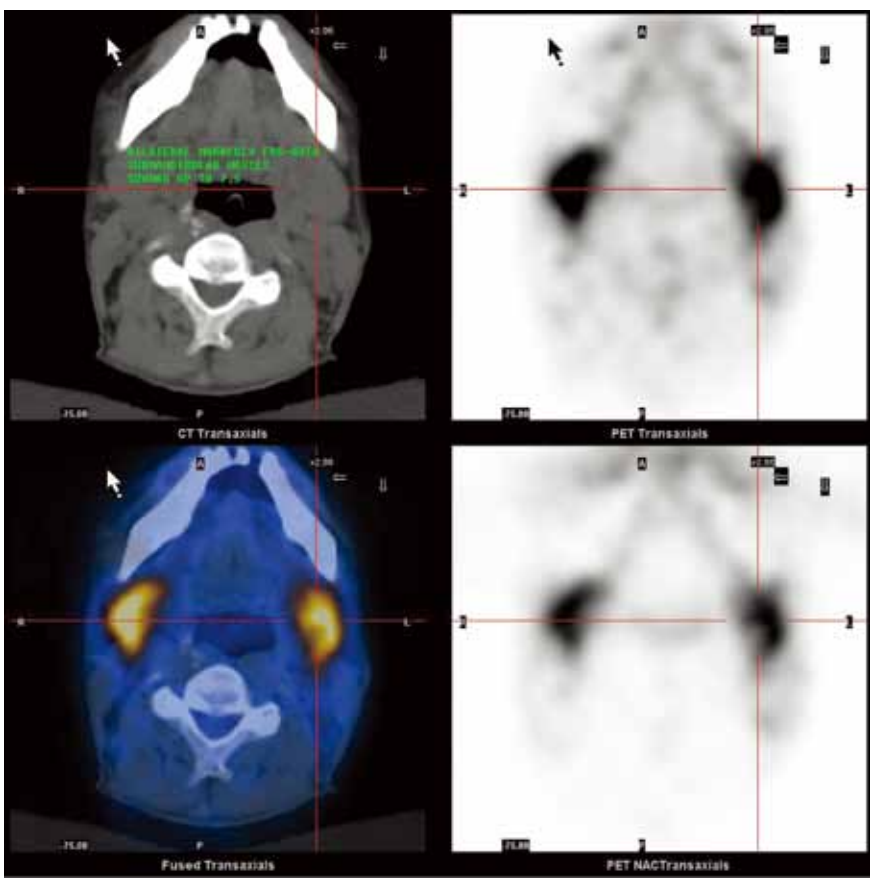

Figure 2. Positron emission tomography–computed tomography shows markedly hypermetabolic enlarged bilateral submandibular masses with a maximum standardised uptake value up to 7.5. Subsequent left submandibular biopsy revealed immunoglobulin G4-related systemic disease.

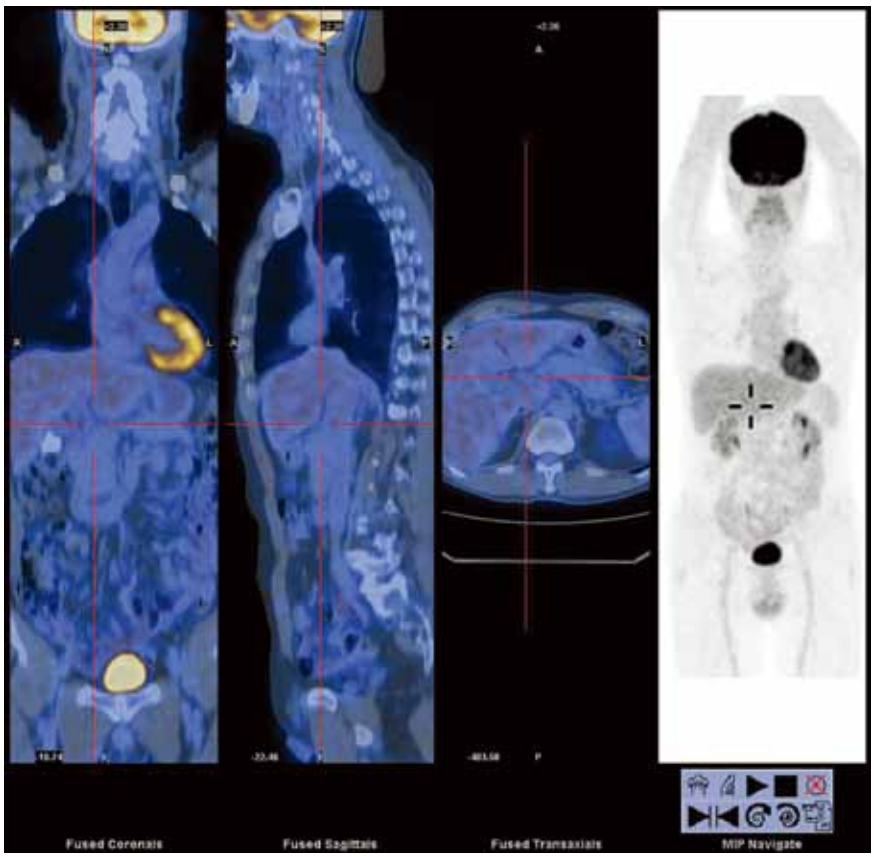

Figure 3. Follow-up positron emission tomography–computed tomography shows hypermetabolic lymphadenopathy and bilateral submandibular masses demonstrating considerable metabolic improvement. The previously noted hypermetabolic enlarged porta-hepatis lymph node demonstrates complete metabolic remission.

commonly encountered in IgG4-RSD, especially in the presence of elevation of serum IgG4 and IgE.

This patient shows that FDG PET-CT offers important information about the disease distribution in benign systemic disease. In this patient, PET-CT not only assessed the extent of involvement of this benign systemic disease, but also identified lesions with the highest FDG metabolism so as to guide the site for further biopsy. This patient was initially suspected of having lymphoma based on the PET-CT findings. Unfortunately, it is not always easy to differentiate lymphoma from IgG4-RSD, either radiologically or histologically. Also, lymphoma development during follow-up of IgG4-RSD has been reported.[10] More studies are needed to validate whether IgG4-RSD patients have increased risk of developing lymphoma.

Potentially, FDG PET-CT may play a useful role in treatment monitoring. IgG4-RSD typically shows significant response to steroid therapy. In IgG4-RSD patients, maintenance steroid therapy should be given for at least 3 years to patients with radiological and serological improvement, even if a patient is no longer symptomatic.[11] However, the long-term outcome for IgG4-RSD patients is yet to be determined. For this patient, follow-up PET-CT was done for treatment response assessment and considerable metabolic improvement was noted. By offering a semi-quantitative score (SUV_{max}), PET-CT can be used to determine the inflammatory disease activity. However, this patient was receiving steroid treatment when he underwent follow-up PET-CT, which could overestimate the treatment response. To date, there is still no consensus regarding the optimal timing of PET-CT after steroid therapy. The relatively high radiation dose also counteracts liberal use of FDG PET-CT for repeated assessments of non-malignant disease such as IgG4-RSD.

Elevated serum IgG4 or IgE are often detected in disease relapse. At present, CT, magnetic resonance imaging, and ultrasonography are used to examine patients with suspected relapse by detecting interval lesion enlargement. Nevertheless, relapse can occur in other organs that are not the primary lesion site,[11] which makes the diagnosis of relapse difficult. Since PET-CT enables whole-body imaging, its potential role for detecting disease relapse is worth further exploration.

FDG PET-CT may play a complementary role in IgG4-RSD in terms of diagnosis, biopsy site guidance, treatment response assessment, and relapse detection, although its ultimate role in this systemic disease needs to be further validated. Clinicians should be aware of this new disease entity during PET-CT reporting, particularly if the typical scintigraphic pattern is encountered in a suspicious clinical setting.

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