Kikuchi–Fujimoto disease presenting as post-traumatic pyrexia of unknown origin

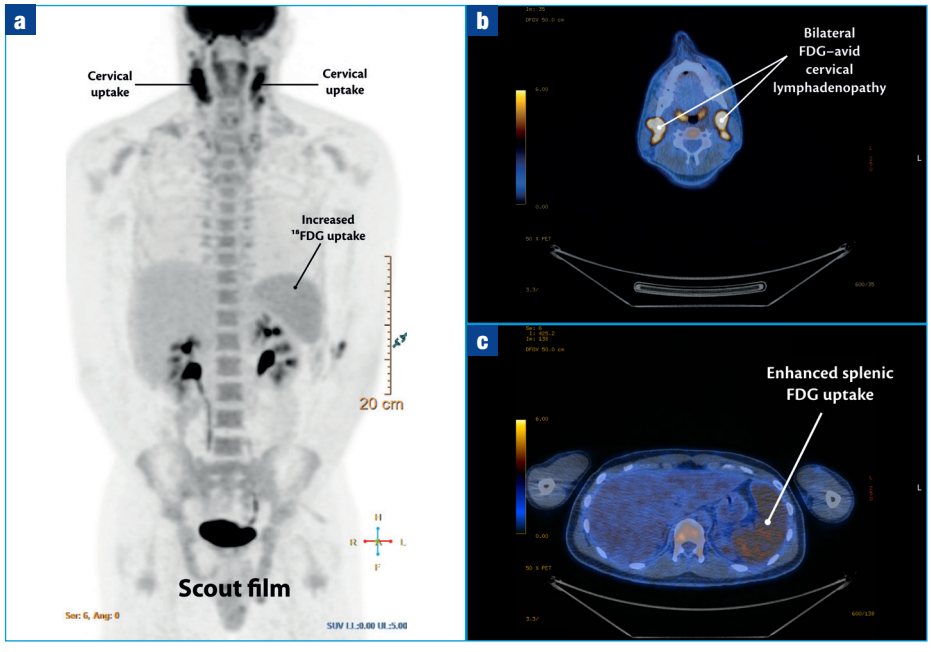
Introduction

Pyrexia of unknown origin is sustained pyrexia in patients despite comprehensive inpatient work-up. It has a varied aetiology and remains a significant diagnostic challenge for physicians. Histiocytic necrotizing lymphadenitis, or Kikuchi–Fujimoto disease, is a rare and benign disorder, which usually presents with fever and cervical lymphadenopathy in young women. This article describes an unusual case of Kikuchi–Fujimoto disease with extra-nodal splenic involvement diagnosed by combined ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography with computed tomography and subsequent lymph node biopsy in a young man with pyrexia of unknown origin following a road traffic accident. The patient was treated conservatively and had a good outcome with no recurrence at 12-month follow up.

Discussion

Petersdorf and Beeson (1961) defined pyrexia of unknown origin as patients with a temperature greater than 38.3°C on more than three occasions within a 3-week period and a failure to reach a diagnosis after 1 week of inpatient investigation. This has been updated to include patients who are diagnosed after two outpatient visits or 3 days in hospital. Pyrexia of unknown origin has a varied aetiology and relies on meticulous diagnostic work up in reaching

Figure 1. **a.** Combined ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography scan scout image showing bilateral increased uptake in the cervical lymph nodes and spleen. **b.** Axial image of the neck showing bilateral ^{18}F-FDG avid cervical lymphadenopathy (standardized uptake value (SUVmax) 12.6). **c.** Axial image of the upper abdomen, showing enhanced splenic ^{18}F-FDG uptake.



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CASE REPORT

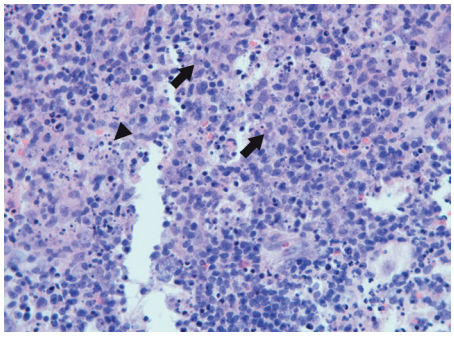
A 22-year-old Caucasian man was admitted to hospital with minor injuries following a road traffic accident. He had no other significant past medical history, or previous significant illnesses or hospital admissions. During admission, he was noted to have ongoing pyrexia (>38.3°C) and underwent extensive inpatient investigation over the course of 3 weeks.

Blood investigations revealed an elevated C-reactive protein concentration at 104 mg/litre with a leucocytosis (white cell count 12×10^9/litre), for which he was initially given broad-spectrum intravenous antimicrobial therapy. Subsequent investigations including numerous blood cultures, anti-nuclear antibodies, HIV serology, lumbar puncture and transthoracic echocardiography were all negative. A serum lactate dehydrogenase concentration was elevated at 1788 U/litre.

Two weeks into the admission, he developed a normocytic anaemia (haemoglobin 75 g/litre), with neutropenia (white cell count 1.9×10^9/litre) and thrombocytosis (platelet count 676×10^9/litre). ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography scan showed ^{18}F-FDG avid bilateral cervical lymphadenopathy, which had not been apparent on physical examination, with additional abnormal splenic uptake (*Figures 1a–c*). Histopathological examination of a cervical lymph node excision biopsy showed histiocytic necrotizing lymphadenitis diagnostic of Kikuchi–Fujimoto disease (*Figure 2*).

He was managed conservatively and subsequently discharged. He remained completely well at 12-month follow up.

Figure 2. Excision-biopsy specimen of excised cervical lymph node showing histiocytic necrotizing lymphadenitis characterized by crescentic histiocytes (arrows) with abundant necrosis and karyorrhectic debris (arrowhead) (haematoxylin and eosin, × 40).



a diagnosis. ^{18}F-FDG positron emission tomography with computed tomography is increasingly used in these patients. It is reported in studies as being both sensitive and specific (Keidar et al, 2008) and having a high negative predictive value (Ferda et al, 2010).

Kikuchi–Fujimoto disease is a benign self-limiting disorder of unknown aetiology with a typical age of onset between the second and third decades of life (Kang et al, 2016). Presenting symptoms usually include pyrexia and cervical lymphadenopathy, which is often unilateral but can involve multiple sites. Extra-nodal involvement is rare, but in a large retrospective analysis hepatosplenomegaly was found in 3% of cases (Kucukardali et al, 2007). In this case, ^{18}F-FDG positron emission tomography with computed tomography showed splenic ^{18}F-FDG avidity, suggestive of extra-nodal splenic involvement.

Patients with Kikuchi–Fujimoto disease usually have normal haematological indices, and normocytic anaemia, thrombocytopenia and leukopenia are rare (Smith et al, 1992). A definitive diagnosis is made on histopathological examination of a lymph node, which demonstrates effacement of normal lymph node architecture by paracortical expansion composed of necrotic foci surrounded by a histiocytic infiltrate (Hutchinson and Wang, 2010). Often there are numerous, atypical lymphocytes, which on a background of necrosis can give the appearance of a lymphoma. Clinicopathological correlation between physicians and the histopathologist is key in avoiding an erroneous diagnosis.

Prognosis of Kikuchi–Fujimoto disease is excellent and symptoms typically resolve without treatment and very rarely recur (Smith et al, 1992). Long-term follow up is advised to ensure remission. Overall, this patient had a good clinical outcome and remained asymptomatic at 12-month follow up. **BJHM**

LEARNING POINTS

- Meticulous diagnostic work up and consideration of a wide differential diagnosis is key in cases of pyrexia of unknown origin.
- When approaching patients with lymphadenopathy, clinicopathological correlation is essential in avoiding an erroneous diagnosis (e.g. lymphoma).
- For patients with pyrexia of unknown origin ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography is an important diagnostic tool.

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