CASE REPORT

Kikuchi-Fujimoto disease and acute appendicitis

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SUMMARY

A 29-year-old Japanese man developed fever, nausea, vomiting, diarrhoea, right lower quadrant abdominal pain and rebound tenderness. With the clinical suspicion of appendicitis, an abdominal CT scan was performed, which revealed mesenteric lymphadenitis. The patient was hospitalised and treated with antibiotics, but was ultimately found to have Kikuchi-Fujimoto disease (KFD). This diagnosis was facilitated by the use of positron emission tomography scan that identified an accessible inguinal lymph node for biopsy and histopathological evaluation. Invasive abdominal surgery was thereby averted and the patient made a complete recovery on subsequent follow-up. Review of the published literature reveals that pseudoappendicitis due to KFD is a rare occurrence that has generally required abdominal surgery to establish the diagnosis, thus supporting the potential value of the approach taken here.

BACKGROUND

In 1972, Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotising lymphadenitis, was first described in Japan separately and independently by Kikuchi and Fujimoto.^{1 2} It is a rare, benign condition with no known definitive cause, although a variety of infectious agents have been sought and postulated to play a pathogenetic role. Clinically, KFD is characterised by cervical lymphadenopathy and fever. However, occasional cases of KFD have been reported with axillary, mesenteric and inguinal lymphadenopathy involvement.³ KFD that affects the mesenteric lymph nodes can present as acute appendicitis. Over the 30 years since its discovery, only 15 such cases to our knowledge have been reported in the literature.^{4–15} We present an example of KFD with mesenteric lymphadenitis mimicking acute appendicitis, accompanied by high fever and relative bradycardia. In this instance, abdominal surgery was avoided with the use of positron emission tomography (PET) scan to

identify an optimally accessible biopsy site for definitive diagnosis.

CASE PRESENTATION

A 29-year-old Japanese man presented to his primary care physician with fever for 3–4 weeks, associated with rigours, night sweats and myalgia. His symptoms progressively worsened, and he reported a 10-pound weight loss. He denied any animal, travel or unusual dietary exposures. Empiric outpatient treatment with levofloxacin for 1 week yielded no response. The patient additionally noted the onset of right lower quadrant pain with nausea, vomiting and non-bloody diarrhoea. CT of the abdomen and pelvis revealed prominent mesenteric lymph nodes compatible with mesenteric lymphadenitis.

Physical examination on admission to the hospital revealed a temperature of 39.9°C with rigours, pulse of 76 bpm, right lower quadrant tenderness on deep palpation and moderate rebound tenderness. A tender 1 cm lymph node was palpated in the left inguinal region. The peripheral white cell count was 3.7×10^3 cells/mm³ (38% lymphocytes; 60% neutrophils) and platelet count was 145×10^3 /mm³. Serum electrolyte determinations were unremarkable. The patient was thought clinically to have acute appendicitis, but because the CT scan was non-confirmatory, he was observed and treated conservatively with only intravenous fluids, ceftriaxone and metronidazole.

He continued to have daily high spiking fever, rigours, relative bradycardia and abdominal pain 4 days into admission. Laboratory testing included C reactive protein of 4.8 mg/dL, erythrocyte sedimentation rate 26 mm/h, serum lactate dehydrogenase 1142 U/L; routine blood, urine and stool cultures yielded no growth; *Clostridium difficile* stool toxin assay was negative. Fungal and acid-fast blood cultures yielded no growth. Serologies for *Brucella*, *Ehrlichia*, *Coxiella*, *Salmonella*, *Bartonella* and *Toxoplasma gondii* were all negative. Viral cultures

Figure 1 Abdominal CT scan with contrast (A) and ¹⁸F-fluorodeoxyglucose positron emission tomography (¹⁸F-FDG PET) scan of mesenteric lymph nodes (B) cluster of hypermetabolic lymph nodes seen in the bowel mesentery along the right colic distribution of the superior mesenteric artery to the level of the caecum.

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Figure 2 CT scan with contrast (A) and ^{18}F -fluorodeoxyglucose positron emission tomography (^{18}F -FDG PET) scan (B) of left inguinal node—left inguinal node seen on CT scan is identified as hypermetabolic on PET scan.

were negative as were serologies for hepatitis C virus, cytomegalovirus and Epstein-Barr virus (EBV). The patient was a known chronic carrier of HBV, with a positive maternal history and positive test for hepatitis B surface antigen (HBsAg), and negative tests for hepatitis B surface antibody (HBsAb) and hepatitis B core antibody (HBcAb IgM). Serum HIV-1 antibody level was negative and plasma HIV-1 RNA concentration was undetectable. To establish a diagnosis, laparoscopic abdominal surgery was being considered. Although it was noted that the patient had an accessible inguinal lymph node, its relationship to the present illness, and hence diagnostic value, was uncertain. To help resolve this question, a PET scan was performed to determine and compare the reactivity of the involved lymph nodes.

PET scan revealed numerous hypermetabolic lymph nodes in the neck, chest, abdomen, pelvis and inguinal region. The largest cluster of hypermetabolic nodes was seen in the bowel mesentery along the right colic distribution of the superior mesenteric artery to the level of the caecum (figure 1). The largest node in the mesentery measured at 2.2×1.3 cm with a maximum Standard Uptake Value (SUV) of 16.0. The palpable left inguinal node (1.1×0.8 cm) was also identified as hypermetabolic (maximum SUV 10.7; figure 2). On biopsy, this node demonstrated the characteristic histological pattern of KFD: necrotising non-granulomatous inflammation without polymorphonuclear cells, together with CD68 staining for histiocytes (figure 3). Bacterial, viral, fungal and acid-fast bacilli cultures of the lymph node were all negative. Antibiotics were discontinued after 7 days, and the patient was discharged on hospital day 8. He was not treated with any other therapies such as corticosteroids or other anti-inflammatory medications. On subsequent follow-up, he made an uneventful recovery.

DISCUSSION

KFD can present acutely or subacutely evolving over weeks to months. Fever is observed in 30–50% of KFD cases; it is usually low grade and may or may not be accompanied by respiratory

symptoms.^{16 17} Cervical lymphadenopathy, especially in women, is the hallmark of this disease, although systemic symptoms may also include any of the following: night sweats, rigours, nausea, vomiting, diarrhoea, myalgias, abdominal pain, splenomegaly, hepatomegaly and abdominal/mesenteric lymphadenopathy. The lymph nodes are usually tender and resolution can take 3–6 months.^{3 16–19}

KFD presenting with primarily abdominal findings and involvement of mesenteric lymph nodes is uncommon. In a recent case report and literature review, Vijayaraghavan *et al*¹⁴ identified 17 cases of KFD and mesenteric lymphadenopathy, 5 of which presented as acute appendicitis similar to our patient.^{4 8 9 12} The constellation referred to as pseudoappendicitis includes the classic signs of right lower quadrant abdominal pain, positive McBurney's sign and rebound tenderness and may be found in KFD when mesenteric lymphadenitis is exceptionally prominent. In addition to our case, we have identified only 15 other cases in the literature with this presentation; these include the 5 cases identified by Vijayaraghavan *et al*, as well as the patient they reported on.^{4–15} Differential diagnosis includes EBV, *Yersinia enterocolitica*, *Salmonella*, tuberculosis, autoimmune disease, lymphoma and other malignancies.¹⁴

The diagnosis of KFD is made by histological examination of an excised lymph node.¹⁶ When presenting with symptomatic mesenteric lymphadenitis, KFD may be difficult to distinguish from an acute surgical abdomen and lead to surgical exploration on clinical grounds. Even if KFD is suspected clinically, abdominal surgery may be necessary to obtain a biopsy sample. Indeed, of the 15 reported cases presenting as acute appendicitis, abdominal surgery was performed in 14: via laparoscopy (3 cases)^{10 14} or laparotomy (11 cases).^{4–9 13 15} In one instance, the patient declined surgery and underwent a percutaneous transabdominal lymph node biopsy.¹¹ CT scan imaging, known to be performed preoperatively in 11 of the 15 cases, demonstrated isolated mesenteric lymphadenopathy^{5–10 13 14}; none of the patients had PET scan imaging.

Figure 3 H&E staining/CD68 immunohistochemical staining of excised lymph node. (A) Inguinal lymph node (H&E; $\times 2$). Necrotising changes are centred in the subcapsular regions. They appear focal and well circumscribed. (B) Inguinal lymph node (H&E $\times 40$). Crescentic histiocytes (yellow arrow) with areas of wide cytoplasm, others with eccentric nuclei (green arrow). (C) Lymph node CD68 immunohistochemical staining. The histiocytes in the karyorrhectic foci are positive for the CD68 antigen.

The lymph nodes in KFD have been reported to show a high ^{18}F -fluorodeoxyglucose (^{18}F -FDG) uptake relative to size when evaluated by PET scan.²⁰ In our case, an inguinal lymph node proved to be hypermetabolic on PET scan, to a similar extent as the involved mesenteric lymph nodes. Biopsy of the inguinal node thus spared the patient an abdominal surgical procedure.

Clinically, our patient displayed another feature that might be a clue to the diagnosis of KFD, namely relative bradycardia. With severe abdominal pain, rebound tenderness, high temperature (39.9°C) and rigours, his pulse was only 76 bpm, in the absence of any other reason or medication to account for bradycardia. With this degree of fever alone, his heart rate would be expected to be between 120 and 130 bpm.²¹ As pulses were only infrequently reported in the cases we reviewed and medication histories and other contributing factors were often not included, we cannot reliably confirm this observation in the literature, but it would not be unexpected in KFD, given the similarity to other non-infectious, inflammatory and neoplastic conditions known to cause fever and bradycardia.²¹

In conclusion, although KFD is considered a benign disease, the fact that it can mimic malignancies, severe infectious processes and even an acute surgical abdomen, makes it truly 'a sheep in wolf's clothing' as proposed by Rammohan *et al.*¹⁷ It is here worth emphasising that the diagnostic evaluations and/or therapeutic interventions carried out before or in the attempt to make a definitive diagnosis could themselves lead to important medical consequences. Our case illustrates the potential value of PET scan to facilitate diagnosis of KFD by helping to identify an accessible node for biopsy. The case also points to the possibility that, if confirmed, KFD may be added to the list of conditions manifested by fever and relative bradycardia, which in turn could provide a useful bedside clue to the diagnosis.

Learning points

- ▶ Kikuchi-Fujimoto Disease (KFD) presenting with mesenteric lymphadenitis is rare and diagnosis may be difficult to distinguish from acute appendicitis.
- ▶ If clinically suspected, positron emission tomography scan may be a useful tool in identifying accessible lymph nodes for biopsy, therefore avoiding abdominal surgical intervention as illustrated in our case.
- ▶ KFD may be accompanied by fever and relative bradycardia, which in turn could provide a useful bedside clue to the diagnosis.

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Contributors All the authors contributed to conception and design of the report, drafting and revising the article, and final approval of the submitted manuscript.

Competing interests None.

Patient consent Obtained.

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