CASE REPORT

Kikuchi-Fujimoto disease: an unusual cause of neck swelling in pregnancy

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SUMMARY

Kikuchi-Fujimoto disease (KFD) is an unusual cause of lymphadenopathy and fever. Pregnancy associated with KFD presents as a diagnostic dilemma for clinicians. The diagnosis can be confirmed with invasive biopsies or non-invasive gene analysis. We report a case of a 24-year-old woman at 18 weeks' gestation with a neck lump and histologically confirmed KFD.

BACKGROUND

Kikuchi-Fujimoto disease (KFD) is a rare cause of acute lymphadenitis in pregnancy. It is reported to be self-limiting with unilateral cervical lymphadenopathy.^{1 2} The presentation commonly raises suspicion for lymphoma, tuberculosis and systemic lupus erythematosus (SLE). Diagnosis is confirmed by excision biopsy, which shows histiocytic necrotising lymphadenitis. Only nine cases of histologically confirmed KFD are reported in pregnancy so far. We present a case of a pregnant woman with histologically confirmed KFD.

CASE PRESENTATION

A 24-year-old woman at 18 weeks' gestation presented to the ear, nose and throat (ENT) clinic with a 3-week history of progressively enlarging and tender right anterior triangle neck swelling and associated intermittent fever. She had no significant medical history. Physical examination revealed a firm 3×2 cm neck swelling suspicious for lymphadenopathy at level II of the right neck. The site was erythematous and tender on palpation. No other area with lymphadenopathy was noted. Cardiovascular and abdominal examinations were unremarkable. The patient's vital signs were within normal limits.

INVESTIGATIONS

Initial investigation contained full blood count, urea and electrolytes, liver function tests, serum lactate dehydrogenase and C reactive protein, which were all normal. A monospot test was carried out and was negative. Erythrocyte sedimentation rate was raised at 29 mm/h.

Ig G and Ig M antibodies for cytomegalovirus (CMV) were positive but CMV IgG avidity was high and also the CMV viral load was negative. Toxoplasma IgG was positive and IgM was negative. Urine and blood cultures showed no growth after 48 h. An intradermal Mantoux test was negative. HIV screen was performed on the patient and it was negative.

Ultrasound scan of the neck confirmed the presence of a 3 cm single lymph node in the right side of the neck. The thyroid and parathyroid glands were normal. Chest X-ray (with abdominal shield) showed normal cardiopulmonary markings.

Fine-needle aspirate of the lymph node showed non-specific acute-on-chronic inflammatory cells. At high power, a single necrotic cell noted was suspicious for lymphoma (figure 1). Microscopy and culture were negative for bacteria, including for acid-fast bacilli.

As lymphoma was a possible differential diagnosis, the case was discussed in a multidisciplinary meeting and it was decided to perform an urgent open biopsy.

Final histological studies showed numerous apoptotic bodies in the background of histiocytes. No granuloma or inclusion bodies were seen. Immunohistochemistry studies showed a prominent T-lymphocytic background with occasional B lymphocytes. CD68 stain confirmed a histiocyte-rich background. EBER stain for Epstein-Barr virus (EBV) was negative. Overall features suggested histiocytic necrotising lymphadenitis, which was compatible with Kikuchi lymphadenitis (figure 2).

DIFFERENTIAL DIAGNOSIS

- Hodgkin's Lymphoma
- Tuberculosis
- Toxoplasmosis
- Sarcoidosis
- SLE

TREATMENT

Empirical antibiotic treatment with penicillin was dispensed. The patient also received paracetamol for fever and pain. During the course of her hospital stay, the obstetricians regularly assessed fetal well-being.

OUTCOME AND FOLLOW-UP

The patient was discharged on paracetamol treatment. She was seen 2 weeks later in the ENT outpatient department and the swelling had abated. Obstetricians had also followed her up and the patient recently had a normal delivery of a healthy baby with no complications.

DISCUSSION

KFD was initially described in Japan by two separate authors, Kikuchi and Fujimoto, at almost the same period in 1972. The aetiology of this disease is unknown. It is a self-limiting lymphadenitis predominantly affecting the cervical lymph nodes.³

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Figure 1 Fine-needle aspiration cytology showing necrotic cell in the background of lymphocytes.

It was initially believed to be more common in the Asian female population, but current evidence states that the male to female ratio is reported at 1:1.⁴ A recently published case report and review of published work on nine cases of KFD in pregnancy has shown a better outcome in maternal as well as fetal health. So far, there are 10 KFD cases associated with pregnancy published. The common clinical manifestation was fever with isolated cervical lymphadenopathy noted in seven of the 10 case reports. Others had fever with isolated sub maxillary, supraclavicular and mesenteric lymphadenopathy.⁵

Diagnosing KFD is a challenging task, particularly in a pregnant patient. Radiological imaging and empirical treatments such as with antibiotics, steroids and immunoglobulin are restricted due to pregnancy. CMV IgG and IgM were found to be positive in this patient, however, perinatal studies have showed that the CMV avidity test does not necessarily correlate with CMV in the amniotic fluid.⁶ Tests for SLE (eg, antinuclear antibody) were not performed in this patient. The latest series from Taiwan supports this, as it has shown that only 1% of 195 cases were associated with SLE.⁷

The comprehensive review on KFD published in the *American Journal for Clinical Pathology* has discussed in detail, about the cause and pathogenesis of KFD. The positive serology with *Yersinia enterocolitica* and *Toxoplasma gondii* are not sufficient to confirm the association of these diseases with KFD. The histological lymphadenitis presented with these infections is different from KFD. In addition, the article also discusses and

Figure 2 Histology shows histiocytic necrotising lymphadenitis.

draws the conclusion that there is no convincing laboratory evidence associating KFD with EBV, human herpesvirus 6 (HHV-6), HHV-8, human T-lymphotropic virus type 1, parvovirus B19, herpes simplex or CMV.³

There are reports on upcoming non-invasive diagnostic methods for KFD, such as the use of microarray analysis of peripheral blood mononuclear cells (PBMCs), which entails a study of peripheral mononuclear cell genes specifically expressed in these patients by examining the whole transcriptome using PBMC microarray analysis.⁸ However, the definitive diagnosis of KFD is still confirmed mainly by histological examination of lymph node biopsy.

There are cases reported regarding intravenous immunoglobulin treatment with a combination of corticosteroids in case of airway compromise in severe KFD.⁹ Dubois *et al*¹⁰ reported that KFD has shown no impact on pregnancy, delivery or infancy.

It is worth noting that the differential diagnosis includes lymphoma, so early diagnosis is essential, especially taking into account the gestational age, as this can affect the treatment options available to the patient, such as option for early delivery or for radiotherapy with abdominal shield. As our patient was in the second trimester of pregnancy, another option may have been to postpone the chemotherapy until induction of labour.^{11 12}

From our experience, we found that antibiotic therapy did not improve the outcome. However, supportive therapy with fluids and antifevers provided symptomatic relief to the patient. Full diagnostic work up to exclude other possible differential diagnoses and multidisciplinary team input, as were provided in this case, can assist in diagnosing KFD in such a patient.

A multidisciplinary approach in management is crucial in ensuring prompt and appropriate diagnosis for these patients.

Patient's perspective

We were initially anxious and concerned about the swelling in the neck with fever during our early part of the pregnancy. As all other young couples do, we searched the internet and the results were even more worrying, such as it could be a lymphoma. After all the investigations and explanations from the doctors we were a bit relieved. However, until she delivered the baby we were very cautious. The overall outcome was good from our perspective; however, waiting for the biopsy and investigation results were extremely stressful times for the pregnant patient and our family.

Learning points

- ▶ Kikuchi-Fujimoto disease is an innocuous cause for an isolated, unilateral neck swelling.
- ▶ Neck swelling in pregnancy warrants early investigations.
- ▶ Histological assessment is vital to rule out serious causes.

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