Lateral rectus palsy as the first presentation of Kikuchi Fujimoto’s disease

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Abstract

Kikuchi Fujimoto’s Disease (KFD) or histiocytic necrotising lymphadenitis is recognised as a disease with a benign and indolent course. The common clinical symptoms of KFD include fever, headache, arthralgia and cervical lymphadenopathy. The diagnosis is based on clinical grounds and histological findings of lymph node biopsy. Kikuchi disease presenting with neurological manifestations is seldom seen. Out of all reported neurological manifestations, aseptic meningitis, brainstem encephalitis and cerebellar ataxia are common. We report a case of a 16 year old girl presenting with right sided lateral rectus palsy as the first presentation of KFD.

Keywords: aseptic meningitis, Kikuchi Fujimoto’s disease, lateral rectus palsy, lymphadenopathy

Introduction

Kikuchi-Fujimoto disease (KFD) is a form of necrotising lymphadenitis that was first described in Japan in 1972. It is most commonly seen in women younger than the age of 30 years. The typical presentation includes cervical lymphadenopathy, headache and fever. Although neurological manifestations are rare, there have been few cases reported worldwide with brainstem encephalitis and aseptic meningitis. The case we are reporting highlights the importance of considering KFD as a differential diagnosis, most importantly in the younger population when the presentation includes features of meningitis, focal neurological signs and lymphadenopathy.

Case presentation

We report a 16-year-old girl with no previous illnesses presenting with sudden onset diplopia on binocular vision and intermittent low grade fever for one month, later diagnosed to have an isolated ipsilateral abducens nerve palsy after cranial nerve examination. The diplopia had worsened over three days. Further questioning revealed a history of a headache which was temporal and throbbing type. She denied any history of recent weight loss, loss of appetite, chronic cough, contact history of tuberculosis or past history of tuberculosis, history of any chronic disease, malignancy, illicit drug use and alcohol abuse.

In the neurological examination, except for the isolated lateral rectus nerve palsy, the cranial nerve examination was normal including visual acuity. Kernig’s sign was negative with no demonstrable neck stiffness. Her respiratory and cardiovascular examinations were unremarkable, with vesicular breathing and normal heart sounds. Her abdomen was soft, non-tender with no organomegaly. The basic haematological and serological investigation profile is shown in table 1.

Upon admission to the ward, the patient was subjected to an non-contrast enhanced computed tomography scan (NCCT). As it did not reveal any cerebral oedema or space occupying lesion, a lumbar puncture (LP) was performed. She was promptly

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Table 1 - Basic haematological and serological investigation profile

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Value</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10⁹/L)</td>
<td>7.27</td>
<td>4.00-10.00</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>14</td>
<td>12-16</td>
</tr>
<tr>
<td>PLT (x10⁹/L)</td>
<td>345</td>
<td>150-450</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>28.4</td>
<td>&lt;50</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>30.9</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Gamma GT</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin (umol/L)</td>
<td>6.92</td>
<td>5-21</td>
</tr>
<tr>
<td>Direct bilirubin (umol/L)</td>
<td>0.97</td>
<td>0-3.4</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>6.7</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Serum creatinine (umol/L)</td>
<td>80</td>
<td>74-110</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>4</td>
<td>2.8-7.2</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>134.8</td>
<td>36-146</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.0</td>
<td>3.5-5.1</td>
</tr>
<tr>
<td>Albumin corrected Calcium (mmol/L)</td>
<td>2.39</td>
<td>2.06-2.60</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>235 later risen to 537</td>
<td>125-243</td>
</tr>
<tr>
<td>ESR (mm/1ˢᵗ hour)</td>
<td>75</td>
<td>0-10</td>
</tr>
<tr>
<td>CPK (U/L)</td>
<td>77</td>
<td>&lt;17</td>
</tr>
<tr>
<td>Blood picture</td>
<td>Red cell changes and anaemia suggestive of acute illness and early iron deficiency.</td>
<td></td>
</tr>
</tbody>
</table>

started on IV ceftriaxone in meningitic doses as an intracranial infection was suspected with the presenting complaint. Cerebrospinal fluid (CSF) examination revealed a CSF sugar of 62.97 mg/dL, red cells - 2/uL, lymphocytes-55/uL, polymorphs - 10/uL and protein 26.4 mg/dL. Random blood sugar level was 110.52 mg/dL with CSF ADA 1.9 U/L and CSF genexpert for tuberculosis (TB) was negative. CSF cultures were negative and HSV PCR was also negative. Although the patient was continued on ceftriaxone at meningitic doses, the patient’s lateral rectus palsy persisted and fever spikes continued. Her blood cultures and urine cultures were negative despite many intermittent fever spikes. A decision was taken to repeat the LP after completing 10 days of IV antibiotics on the twelfth day after the first lumbar puncture. Second LP report revealed; CSF sugar- 69.4 mg/dL, red cells- 9/uL, lymphocytes 2/uL and polymorphs 3/uL, protein 13.4 g/dL. The CSF cultures were repeatedly negative. Due to the young age of the patient along with headache, a space occupying lesion that compresses the sixth nerve was also considered a possibility, however the fundoscopy examination was normal without papilledema while NCCT and MRI brain were normal. As this is a case of mononeuritis with on and off fever, TB meningitis was considered to be the first differential diagnosis because tuberculosis is on rise among young Sri Lankans. But normal CSF proteins, CSF genexpert and CSF ADA being negative and absence of basal exudates in MRI suggested otherwise. The patient being a young female, presenting with mononeuritis, systemic lupus erythematosus (SLE) was also considered a differential diagnosis, but both her ANA and anti dsDNA were negative. Neurosarcoïdosis was excluded as serum ACE level and serum calcium levels were normal. She tested negative for HIV. Though she initially didn't have cervical lymphadenopathy, during the ward stay she
developed shotty cervical lymphadenopathy. There were firm, non-tender, palpable cervical lymph nodes bilaterally, with a maximum size of 7x9x3 mm³.

She was referred to the surgical team for excisional cervical lymph node biopsy. The biopsy was obtained from the posterior cervical lymph nodes. The elevated LDH levels along with lymphadenopathy further raised the suspicion of a lymphoma. Therefore excision of the lymph node and tracing the biopsy was prioritised. The lymph node biopsy revealed a lymph node with preserved architecture, reactive follicles with secondary germinal centre formation and sheets of histiocytes. (figure1). This prompted the diagnosis of KFD. As the CSF cultures were persistently sterile, the patient was diagnosed to have aseptic meningitis and was started on prednisolone 30 mg daily which was tailed off gradually over 2 weeks. Over the course of 2 months, the patient's lateral rectus palsy resolved markedly suggesting the indolent and self-limiting nature of KFD. Her cervical lymph nodes gradually decreased in size. She is still being followed up and she remains healthy and asymptomatic 6 months after the discharge.

Discussion

Most common KFD manifestations include fever, lymphadenopathy, anorexia, generalised malaise and hepatomegaly. Overall, the disease course is benign. Spontaneous self-resolution tends to occur within weeks to months and the recurrence rate is low as 3-4%. Long-term follow up of patients with KFD is recommended, because of the risk of recurrence and due to its postulated association as a precursor to autoimmune diseases like SLE. Reported neurological manifestations of KFD are rare, but literature published so far has explained cases of aseptic meningitis, acute cerebellar ataxia and acute brachial neuritis and brain stem encephalitis.(4) Total incidence of neurological manifestations is 11%.(5) Since KFD was not identified as a well-known cause for cranial nerve palsies, several differential diagnoses associated with such presentation were first suspected in this patient. Therefore our patient was thoroughly investigated for alternative more plausible pathologies which are more prevalent such as TB, in these parts of the world. Having excluded all possible aetiologies such as TB, lymphoma and SLE, the team involved in the management was in a great diagnostic dilemma. The lymph node biopsy report was instrumental in reaching the diagnosis.

Central nervous system (CNS) involvement is rarely reported as the first symptom of this disease. A study by Huang et al from China summarises the clinical features of patients diagnosed with KFD combined with the involvement of the central system, at Children's Hospital of Chongqing Medical University (CHCMU). There sixteen patients had been diagnosed with aseptic meningitis while headache (78.9%) was the most common symptom among them.(6) Kucukardali et al. have analysed 244 published cases of KFD since 1991 and reported that neurological involvement was observed in only 4.5% of the patients.

A case published in Japan by Hidenori Kido has
highlighted a case of a 19-year-old boy who was managed for encephalitis associated with KFD further highlighting CNS manifestations, although rare.(7) Nalika et al from Sri Lanka have reported a case of recurrent aseptic meningitis and further highlighted the familial occurrence of the disease.(8) Another case published in India by Jasti et al has shown KFD presenting as brainstem encephalitis with secondary blepharospasm. Aseptic lymphocytic meningitis was described in 9.8% cases in Japan. Our patient also exhibited a lymphocytic predominance in CSF. Cerebellar ataxia, diplopia, and confusion have also been described in a few cases. Furthermore F Rocher et al have reported a case of a 10-year-old girl with third nerve palsy with papilledema and highlights the importance of considering KFD in children with ocular manifestations, lymphadenopathy and fever.(9) A case report from Pakistan published by Hashmat et al has revealed a young girl with KFD having aseptic meningitis developing lateral rectus palsy subsequently during the course of the illness.(9) In Sri Lanka there was only one case which highlighted the neurological complications in Kikuchi-Fujimoto disease.(8) The unusual and rare feature of our case report is that it is the first to be reported about a patient presenting with acute onset lateral rectus palsy as the first presentation of KFD along with aseptic meningitis.

KFD management involves supportive as well as a specific treatment. In KFD, spontaneous resolution is typical(10), and treatment is warranted in certain conditions. Symptomatic treatment is the most effective treatment strategy for KFD. Supportive measures include nonsteroidal anti-inflammatory drugs and antipyretics to relieve fever, lymph nodal tenderness, malaise, and arthralgia. Corticosteroids are reserved for severe cases or where supportive measures fail to control symptoms.(11) However, an optimal method of treatment has not been established yet. Our patient was prescribed a course of steroids as there was evidence to support the use of steroids in many cases with CNS manifestations.(8)

**Conclusion**

Though neurological complications of KFD are rare, it’s important to consider KFD as a differential diagnosis in young patients presenting with focal neurological signs, fever, lymphadenopathy and headache, as that would help in avoiding unnecessary and excessive treatment. Since the disease can be mistaken clinically and histologically for SLE, lymphoma or TB, it is of utmost importance to differentiate it from these conditions. Our case also emphasises the importance of recognising KFD as the culprit in young patients presenting with lymphadenopathy, meningitis and focal neurological signs.

**Declarations**

**Conflicts of interest**

The authors declare that they have no conflicts of interest

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**References**


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