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Kikuchi Disease in Elderly: Report of a Rare Disease in an Unusual Age

Elnaz Sahebi[1], Sahar Karimpour Reyhan[2*], Mahsa Abbaszadeh[1], Nasim Khajavi Rad[1]

1. Department of Internal Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
2. Endocrinology and Metabolism Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Kikuchi disease is a benign, self-limited, and rare condition presented mainly by lymphadenopathy and fever. Kikuchi disease is more common in women, especially women under 40. We report a 63-year-old Iranian woman presenting with long-term fever, constitutional symptoms, and cervical lymphadenopathy. A lymph node biopsy was done for her, and the diagnosis of Kikuchi disease was confirmed. Kikuchi disease is a self-limited condition with a good prognosis that can resolve with no specific treatment within a few weeks. Still, some patients are at risk of recurrence and development of SLE and Lymphoma. Our patient was treated with a low dose of glucocorticoids. On 6 month follow-up, she had no signs and symptoms of recurrence and no evidence of SLE development. The interesting point of this case is the clinical picture and her age of presentation.

Introduction

Kikuchi disease or Kikuchi necrotizing lymphadenitis is a benign and rare disease that commonly presents with cervical lymphadenopathy and fever. There is no specific cause to justify the pathogenesis of this disease. Still, there is much evidence in clinical signs and symptoms and histologic changes that favor the immune response of T cells and histiocytes to an infectious agent such as EBV, HHV, HHV8, HIV, or parvovirus B19 [1], as the pathogenesis of this disease.

Kikuchi disease is more common in women, especially those under 40, but this can happen in patients aged 6 to 80 years [2, 3]. One study showed that the ratio of men with Kikuchi to women is 1:4 [4].

Patients with Kikuchi disease almost present cervical lymphadenopathy and low-grade fever for about

*** Corresponding Author:**
Sahar Karimpour Reyhan, PhD.
Address: *Endocrinology and Metabolism Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.*
E-mail: *skarimpour@sina.tums.ac.ir*

a week [4]. Six of patients' most common signs and symptoms are lymphadenopathy, fever, rash, arthritis, fatigue, and hepatosplenomegaly [5]. This disease's less common clinical findings include rigors, myalgia, arthralgia, chest and abdominal pain [4], night sweats, nausea and vomiting, diarrhea, and weight loss [3].

Kikuchi disease usually involves cervical, particularly posterior cervical lymph nodes, which are almost localized [4] and moderately enlarged [6] and are also firm, smooth, discrete, and mobile, often with dull or acute pain. Usually, we expect unilateral cervical lymphadenopathy in patients with Kikuchi disease, and we don't expect mediastinal lymphadenopathy.

Kikuchi disease is associated with the following infections: Adult Still's disease [7], Cryptogenic Organizing Pneumonia (COP) [8], Systemic Lupus Erythematosus (SLE), and Lymphoma [1].

Many laboratory studies can help us diagnose Kikuchi disease and rule out other similar conditions. The complete blood count is normal in most patients [4], but some patients may be leucopenic [5] or thrombocytopenic, pancytopenia, or anemic [1, 5]. The erythrocyte sedimentation rate may be normal. Bone marrow findings include an increase in macrophage count without atypical cells [9]. There may also be a mild abnormality in liver function tests and an increase in serum lactate dehydrogenase [10]. Many viral infections, such as Epstein-Barr virus (EBV), can be involved in the pathogenesis of Kikuchi, so it's reasonable to check the serology of these viruses.

Finally, we need lymph node biopsy, particularly excisional biopsy, to make a definite diagnosis of Kikuchi [1, 3, 4]. Some other conditions may have confused Kikuchi because of similarities in lymph node biopsy pathologic findings such as lymphoma, tuberculous adenitis, lymphogranuloma venerum [11], and Kawasaki disease, but there are some recommendations about using NSAID or Paracetamol for alleviating fever and painful lymphadenopathy or using glucocorticoids or a combination of high dose glucocorticoid with intravenous immunoglobulin in severe or severe or severe or persistent patients [12, 13]. Also, bilateral cervical lymphadenopathy is a common finding [14], but our patient had bilateral and mediastinal lymphadenopathy.

Microscopic examination of lymph node biopsy shows single or multiple paracortical necrotic foci, and a histiocytic cellular infiltrate. The capsule may be implanted, and perinodal inflammation is also standard [2].

We will introduce a 63-year-old woman who presented to our hospital with 3 weeks of fever and constitutional symptoms, cervical and mediastinal lymphadenopathy, and splenomegaly.

Case presentation

A 63-year-old woman was admitted to our hospital with a complaint of fever, chills, and productive cough 20 days ago. She also had dizziness, myalgia, abdominal pain, and a 5 Kg weight loss during the last three weeks. A physician visited her, and her doctor managed her a common cold. But the patient had no improvement in her symptoms. After 10 days of having fever and chills, she experienced non-bloody diarrhea, and her productive cough continued. At this time, antibiotics were started for the patient, but only the diarrhea was improved.

Then, she was referred to our hospital because of the continuation of her symptoms. On the admission day, she was ill. She had a fever, O_2 saturation was 87%, the temperature was 38°C on her physical examination, hepatosplenomegaly was found, and both lungs had coarse crackles.

After admission, antibiotics were started for her with the diagnosis of pneumonia, and laboratory tests, abdominal ultrasonography, and chest x-ray was done for her. Laboratory tests are summarized in Table 1. There was only pancytopenia in her CBC (WBC:2700/mm^3, Hb:10.7 g/dl, Plt:103000/mm^3), while other lab findings were normal.

Abdominopelvic ultrasonography reported splenomegaly (170 mm) with normal parenchyma. Her liver size was 137 mm with a standard echo, and other findings were normal. Her chest x-ray revealed consolidation in favor of pneumonia.

In Neck ultrasonography, there were multiple suspicious lymph nodes on both sides of the neck with a maximum size of 10*23 mm in zone 1 on the right side and a full measure of 7*26 mm in zone 2 on the right side. There was no evidence of axillary lymphadenopathy. Because of neck lymphadenopathy and long-standing fever, and constitutional symptoms, we performed a lymph node excisional biopsy to rule out lymphoma.

A spiral chest CT scan reported bilateral patchy air space consolidation, favoring active infection. Multiple mediastinal lymphadenopathies with a maximum size of 11 mm were seen in the peritracheal region. Because

Table 1. Patient's lab data

Blood Parameters		Value	Reference Range
White blood cell (per mm^3)		2500	4000-10000
Differential count	Neutrophils (%)	51	-
	Lymphocytes (%)	36.9	-
Hemoglobin (g/dl)		9.3	12-16
Platelet count (per mm^3)		108000	150000-400000
Mean corpuscular volume (fl)		71	77-94
Creatinine (mg/dl)		0.9	Female:0.6-1.3
Urea nitrogen (mg/dl)		20	Adult:15-44
Erythrocyte sedimentation rate (mm/h)		68	Female 51-85 years: <30
C-Reactive protein (mg/lit)		47	Adult:<10
Fe/Iron (ug/dl)		55	50-170
TIBC (ug/dl)		197	250-450
Ferritin (ug/l)		95	Adult Female: 10-120
Na (meq/L)		143	135-145
k (meq/L)		4	3.5-5
Mg (mg/dl)		2.3	Adult:1.6-2.6
Pro-calcitonin (ng/ml)		5	>2 high risk for sever sepsis
Calcium (mg/dl)		8.2	8.6-10.2
Albumin (g/dl)		3.2	Adult:3.5-5.2
LDH		531	-
Retic count (%)		0.7	-
Corrected retic (%)		0.5	-
HBS Ag		Nonreactive	-
Anti-HCV Anti body		Nonreactive	-
HIV Ag/Ab		Nonreactive	-
ANA (U/ml)		2.9	Negative:<10
Anti-ds DNA (IU/ml)		2.45	Negative:<100
EBV IgG Ab		2.8	Positive:>1.2
EBV IgM Ab		0.1	Positive:>1.2
Blood culture		Negative	-
Urine culture		Negative	-
Beta-2 Microglobulin (mg/l)		3.53	0-0.15

of these findings in her chest CT scan, bronchoscopy was done for her to rule out malignancy, but there was no endobronchial lesion.

Finally, the result of pathology revealed atypical lymphoproliferative disorder with necrosis. IHC results showed CD20 positive in the residue of lymphoid follicles, CD3 positive in expanded interfollicular lymphocytes, CD68 positive in many atypical cells, and CD15 positive in a few sinus histiocytes. That was in favor of Kikuchi lymphadenitis.

Discussion

Kikuchi disease is a rare, benign, and self-limited disease [1] that is also more common in young women and more common in Japanese and Asian populations [1, 14]. But our patient was an old woman who presented with Kikuchi disease signs and symptoms.

The patient presented with long-term fever as a common symptom, but she also had abdominal pain and myalgia and constitutional symptoms like weight loss and night sweating which are not common presentations of Kikuchi disease. We considered working up for lymphoma because of the chest, neck, hepatosplenomegaly, and pancytopenia lymphadenopathy.

We tested antibodies against EBV, CMV, and HIV in our patient to find the potential pathogens related to Kikuchi, but all of these tests were negative. FANA and anti-dsDNA were also negative.

Laboratory findings are normal in most patients, but some nonspecific findings in laboratory tests of patients with Kikuchi disease include anemia, leukopenia, high CRP level, high Lactate dehydrogenase level, and elevated immunoglobulin [15], and mildly abnormality in liver function tests [10]. Our patient only had pancytopenia with all other normal lab tests. So laboratory findings cannot be helpful in the definitive diagnosis of underlying disease.

It is necessary to distinguish between Kikuchi and other diseases with excisional lymph node biopsy and histological examination of the specimens [1]. The pathological finding can also help us determine between the diagnosis of Kikuchi disease and other sinister conditions such as lymphoma and tuberculosis [4]. Biopsy specimens of Kikuchi involved lymph nodes present patchy areas of coagulative necrosis in macroscopy examination and paracortical foci with histiocytic infiltrate in microscopic findings [15].

In some cases, immunophenotyping may help differentiate Kikuchi from other sinister conditions such as SLE and high-grade lymphoma, similar histopathological findings. Our patient's pathology report of neck lymph node excisional biopsy was atypical lymphoproliferative disorder with necrosis, so IHC was done to confirm the diagnosis; IHC result was CD20 and CD3 and CD68 CD15 positive, which all of these findings were in favor of Kikuchi lymphadenitis.

Kikuchi disease is a benign and self-limited condition that can resolve with no specific treatment over one to four weeks [1, 14]. It's essential for patients diagnosed and treated with Kikuchi disease to be followed up for a few years because 3-4% of patients may experience recurrence of the disease, and sometimes there may be an association between Kikuchi and the development of SLE [15]. On a six-month follow-up, our patient had no signs and symptoms of recurrence and no evidence of developing another disease such as SLE and lymphoma.

Conclusion

Kikuchi disease is a benign, self-limited, and uncommon disorder that can mimic clinical features of other conditions like SLE, lymphoma, and TB. Early diagnosis is essential to prevent more excessive evaluation and unnecessary treatment. Kikuchi-Fujimoto is more common in young women, but it can occur at any age, such as our patient, and we should be aware of this condition in elderly patients and should be kept in our mind. Follow-up for at least a Few years is recommended in patients with Kikuchi disease because of the risk of recurrence end development of SLE and lymphoma.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Conflict of interest

The authors declared no conflict of interest.

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