Mysterious Diseases: Kikuchi Fujimoto Disease

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Abstract

Kikuchi-Fujimoto Disease (KFD) is very uncommon diseases in the population and also called by alternative name as Histiocytic Necrotizing Lymphadenitis.

Its show the symptoms like cancer as benign and create the confusion in the detection and also shows self-limiting auto-immune disease, systemic lupus erythematosus and tuberculosis. It has symptoms such as cervical lymphadenopathy (enlargement of lymph nodes), low fever, headache, fatigue, night sweats and muscles pain. It typically affects young females under the age of 20-35 years and it mostly affects Asian populations. The accurate diagnosis of KFD is characterized by Fine Needle Aspiration Cytology (FNAC) by taking blood sample from the swelled lymph node.

Diagnosis is also possible with Fine Needle Aspiration Biopsy (FNAB). Treatment for this disease has not been established. Non-steroidal Anti-Inflammatory Drugs (NSAIDS) or steroids are used to alleviate lymph node tenderness and fever.

Keywords:

Kikuchi Fujimoto Disease, Cervical Lymphadenopathy, Histiocytic Necrotizing Lymphadenitis, Systemic Lupus Erythematosus, Lympho-histiocytic and Non- Hodgin Lymphoma.

Introduction

Kikuchi-Fujimoto (KFD) is firstly manuscripted by Japanese in 1972 by Kikuchi and Fujimoto and the name of disease were kept on the name of discoverer. This disease cause destruction of their own body cells by their own immune system considered an auto immune diseases. The basic mechanism of this disease is not discovered yet and other information like symptoms, problems based on the case study. Observation describes that it is gender bias and mainly females are more sufferer comparative to males. Even in the female, Asian descent between the ages of 20-35 years are mostly affected by this disease. It has a male: female ratio of 1:2; more than persons of other places. It has been reported in various countries but 80% of cases taken place in Japan. [1].

The onset of adenopathy and systemic B symptoms in KFD has mostly led to misdiagnosis of malignant lymphoma although modern diagnosis techniques led to misdiagnosis less likely. Morphologic examination

of the swollen lymph nodes is the main path of the correct diagnosis in KFD, however, the recognition by morphology is a challenge to many pathologists, even to hemato-pathologists, because of its features simulating non-Hodgin lymphoma or reactive lymphadenopathy of other causes [2].

The typical presenting features of KFD such as lymphadenopathy, fever, muscles pain lead to its often being mistaken for mild infection or malignancy [3].

Symptoms [4]

- Lymphdenitis (Painful Lymph Nodes with swelling).
- Lymph Node non-tender and rubbery.
- Mild shortness of breath.
- Night sweats, fatigue, nausea and vomiting.
- High Fever (Continuous).
- Muscles pain, headache and weight loss.

Clinical Features

Clinical features are shown by the presence of cervical lymphadenopathy in more than 90% of cases, which is usually present in the trapezius and carotid lymph nodes and observed in patients. Lymph nodes become swell, sometimes very large measuring 2 to 6 cm in diameter, mobile and painful. Systemic signs include fever, muscle pain and nausea etc were also present in patients and have been reported in 30% to 50% of cases. They often led to misdiagnosis as malignancy or cancer. A pseudo-urticarial rash, hepatosplenomegaly, arthralgia, weight loss or deep lymph nodes (mediastinal, retroperitoneal) may also be present [5].

The fever is usually lasts for upto 2 months in rare cases. It weakens the immune system. Disease lasts for 1 year, 6 months or more. Patients recover with very long time [6].

Cause and Pathogenesis:

Cause and Pathogenesis of this disease has not been found clearly. It has been in doubt whether it is a viral or autoimmune disease. Some researchers suggested it is caused due to virus but some as auto-immune disease. Kikuchi Fujimoto Disease is an uncommon and very rare disease. The causes and pathogenesis of the disease remain unclear. Nevertheless, on the basis of clinical presentation infectious causes have been hypothesized particularly as viruses due to the clinical features [7].

Numerous inciting agents have been proposed such as Epstein-Barr Virus, human Herpes virus, but failed to confirm the causative link between these infectious agents and KFD [8].

Based on clinical presentation, laboratory research and histo-pathologic features, it has been hypothesized that KFD might represent T cell mediated hyper-response to certain antigen stimuli in genetically susceptible individuals. But some studies have shown that the primary cells are the CD8+ T lymphocytes, which induce apoptosis, some indicates that levels of inflammatory mediators, such as interleukin 6 support an immune-mediated etiology [9].

Case Report of KFD: (India, 2016)

In 2016, a 23 year old girl was presented in Holy Family Hospital, New Delhi. She was suffering from three week fever, and losing weight and 4 enlarged lymph nodes. There was no previous history of such symptoms and girl was healthy and fine and not taking any type of medicine. On examination, significant findings were as lymphadenopathy, posterior auricular and cervical. There was found 2cm smooth, tender lymph node lumps near the left ear.

CBC (Complete Blood Count) Test was performed which was found negative. Other ANA (Anti-Nuclear Antibody) Test was performed to evaluate the patient for autoimmune disorders that are systemic (affect the many tissues and organs throughout the body) but all was negative. During this period, she was given the **Augmentin Antibiotic** until it was diagnosed.

Doctors of Holy Family Hospital suspected for tuberculosis and patient undergone for Mantoux Tuberculin Skin Test. But no virus of tuberculosis was found. In chest X-ray, infection was found. This case was become very critical and serious.

At last, doctors suggested for FNAC (Fine Needle Aspiration Cytology) test. On examination reactive lymphadenopathy was found. Then, this case was misdiagnosis as cancer but before the biopsy doctors had meeting with the senior doctors in which it was diagnosed as Kikuchi Fujimoto.

Discussion:

In India, it was the very rare case of kikuchi Fujimoto. Patient became very weak and the infection in the form of lumps was spread in her neck. After diagnosis, she had under medication and regular check-ups because of the swelled lymph nodes for 1 year [10].

Medication Available:

Dose of **Wysolone tablet** a type of corticosteroids was given to the patient. Dose was increased from 5mg to 15mg for induction therapy. She had taken for 6 months. This steroid has various side effects like patient undergone through various behavioral disturbances such as anxiety, depression and sleeplessness and others like weight gain, muscle and bone aches and pains etc.

Other drugs like **Pantocid 40** used to treat gastric problems and D3 sol to prevent the deficiency of vitamin D as to prevent the deficiency other vitamins in the patient's body.

At last with all these medication within 1 year of time she got healed of this disease but the side effects remain for more 1 year [11].

Diagnosis: Advanced Techniques:

Lymph Node Biopsy:

Fine-Needle Aspiration Biopsy (FNAB) is a valuable tool for the diagnosis of some infectious lymph-node disorders; excisional biopsy is the preferred diagnostic tool in patients which are presenting with new adenopathy and swelled lymph nodes. Some of the scientists has been analyzed approximately 44 cases of patients with confirmed KFD with the help of FNAB technique [12].

In this, lymph node is removed for examination under a microscope. When an infection is present in the lymph nodes, they swell. Lymph nodes are the small glands that make white blood cells (lymphocytes) which fight against the infection, and it related to immune system [13-14].

FNAC:

Fine Needle Aspiration Cytology (FNAC) of the lymph node is a very simple diagnostic tool to diagnose the KFD and to make it clear whether it is malignancy or not. In this, a thin 23-25 gauge, a hollow needle is inserted into the mass or lump present in the neck for sampling of cells that, after being stained, and it will be examined under a microscope. It is a most powerful technique to diagnose Kikuchi and by this technique there are less chances of misdiagnosis [15-16].

Treatment:

Treatment for this disease has not been established, and recommendations are based or depend upon the case reports and expert opinion alone. Due to the rare and self limiting disease it is important to observe the symptoms which can be quite serious. High dose glucocorticoids with intravenous immunoglobulin have been shown some benefits in the severe symptoms.

Non-steroidal Anti-Inflammatory Drugs (NSAIDS) or steroids used to alleviate the tenderness of the lymph node and fever.

The use of corticosteroids, such as prednisone, has been recommended in severe extranodal or generalized kikuchi disease. In some critical and complicated conditions, hydroxychloroquine can be used [17-18].

Conclusion

Kikuchi Fujimoto Disease is an extremely rare, more or less worldwide, and often under-diagnosed condition; predominantly involving the posterior cervical lymph nodes.Kikuchi's disease seems to be more spread in

Japanese and Asian individuals. Few cases reported in India in 2016. Histopathologic features support its cause being viral but it is not proved. In some cases, it is not recognized earlier which become the cause for severe condition. Hence, early recognition of this disease is very important to prevent the patient from misdiagnosis of malignancy. In order to avoid misdiagnosis, awareness of this disease in the whole world is very necessary especially for the clinician as well as for the pathologists. KFD in some cases treated with the lymph node biopsy technique. Earlier, FNAC is also used for its diagnosis. Nowadays, there is no proper treatment found for it except the steroids, which would have various side effects. Albeit was identified more than forty years ago and remain less popular among the population due to this the main cause was not identified and so no proper cure available. Infectious or autoimmune processes were proposed but have been definitely confirmed. Clinical presentation with symptoms such as systemic and fever led to it and create misperception and wrongly associate with other disease symptoms.

There is requirement to diagnose correctly and on the time which will end the current procedure of regular checks up due to their increased risk of Systemic Lupus Erythematosus. Even now this disease is very rare and no proper treatment is found. Its mild effect is over immune system.

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