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Management of Kikuchi's disease using glucocorticoid

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Abstract
Histiocytic necrotizing lymphadenitis, or Kikuchi's disease, is a self-limiting cervical lymphadenitis of unknown origin. Since no specific treatment has been reported for Kikuchi's disease to date, once a diagnosis of Kikuchi's disease has been established, the role of the physician has been limited only to treating the symptoms. Sometimes, however, the clinical manifestations of the disease can be very distressing for the patients. Thus, a more aggressive form of treatment may be required for the patients who suffer from severe and persisting symptoms and recurrence. We present three cases of Kikuchi's disease that benefited significantly from systemic administration of prednisone.

Key words: Glucocorticoids; Histiocytic Necrotizing Lymphadenitis

Introduction

Histiocytic necrotizing lymphadenitis, or Kikuchi's disease, is an increasingly recognized, self-limiting cervical lymphadenitis of unknown origin.[1] The most frequent clinical manifestation consists of fever and painless cervical lymphadenitis. Occasionally, it is associated with more general symptoms and multiorganic involvement.[2]

Since no specific treatment has been reported for Kikuchi's disease to date, once a diagnosis of Kikuchi's disease has been established by biopsy, the role of the physician has been limited only to treating the symptoms. Sometimes, however, the clinical manifestations of the disease can be very distressing to the patients, especially the lingering fever and adenopathy.[3] Moreover, three per cent of the patients experience recurrence,[4] and even fatalities have been reported during the acute phase of the illness.[5,6]

Thus, a more aggressive form of treatment may be required in the particular patients who suffer from severe and persisting symptoms, and frequent recurrence. However, there has not been a report that aimed to develop a new management strategy for this perplexing disease. Due to its potent anti-inflammatory and immunomodulating effects, glucocorticoid has been widely used in various inflammatory conditions. Therefore, we administered prednisone in selected cases of Kikuchi's disease in order to facilitate the symptomatic improvement and recovery from the disease. We present three cases of Kikuchi's disease that benefited significantly from this systemic administration of prednisone.

Case reports

Case 1

A 30-year-old female presented to our otolaryngology department with a three-week history of painful swelling on her left lateral neck, fever, chills, and headache. On admission, physical examination revealed a body temperature of 38°C and a soft, tender, mobile mass (3×3 cm in size) with local inflammation. A laboratory study showed a total leukocyte count of 3.200/mm^3 and an ESR of 27 mm/hour. On serological examination, anti-nuclear antibody was weakly positive, whereas anti-double stranded DNA antibody and anti-smooth muscle antibody was negative. A computed tomography (CT) scan demonstrated multiple enlarged lymph nodes in the left superior jugular, and posterior cervical areas. Under the impression of tuberculous lymphadenitis, an open excisional biopsy was performed on the fifth hospital day. The histopathological features were consistent with Kikuchi's disease.

Despite the symptomatic treatment using antibiotics and acetyl salicylic acid (ASA), tender cervical lymphadenitis, nocturnal fever (up to 39.8°C), general malaise and headache persisted. On the ninth hospital day, oral prednisone was administered in a dosage of 60 mg/day and maintained for five days, and then tapered off for the following 10 days. On the 10th day, fever and other symptoms resolved dramatically and the cervical lymph node swelling began to decrease in size. She was discharged on the 14th hospital day without any notable complication. During the six months of follow-up, she had recurrences of lymphadenitis and fever three times. Each recurrence was successfully managed by prednisone at a dosage of 20 mg/day for five to seven days.

Case 2

A 23-year-old male visited our department with 10-day history of fever and a four-day history of painful swelling on the right lateral neck. On admission, physical examination revealed an acutely ill-looking appearance and a body temperature of 38.3°C. The leukocyte count was 3100/mm^3, and the ESR was 13 mm/h. On serological examination, anti-nuclear antibody, anti-double stranded DNA antibody, and anti-smooth muscle antibody were all negative. A CT scan showed multiple enlarged lymph

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nodes in the jugulodiagastric, posterior cervical, submandibular and submental areas. Kikuchi's disease was suspected and confirmed by open excisional biopsy on the third hospital day.

After confirming the diagnosis, the patient was managed using aspirin and adequate hydration. But the painful lymphadenopathy and fever persisted. Administration of oral prednisone was started on the fifth hospital day at a dosage of 60 mg/day, maintained for three days, and then tapered over seven days. By the next day, his body temperature returned to normal and myalgia improved dramatically. The patient was discharged without any remarkable symptoms on the 11th hospital day. He has not had a recurrence during the eight months of follow-up period.

Case 3

A 14-year-old male patient came to our otolaryngology department with two-week history of painful lymphadenopathy and spiking fever up to 38.4°C. A magnetic resonance image (MRI) of the neck showed multiple enlarged lymph nodes in the left posterior cervical, upper jugular, and jugulodigastric areas. Kikuchi's disease was suspected and confirmed by open excisional biopsy on the third hospital day. His symptoms resolved only with the use of acetaminophen. Six days after admission, he was discharged without any annoying symptoms.

On the 20th day after discharge, he had recurrent fever and tender cervical lymphadenopathy. His symptoms were controlled with four days use of acetaminophen. Two months after discharge, he presented again with tender neck masses and fever. His symptoms were unresponsive to the previously used acetaminophen. Under the presumptive diagnosis of recurrent Kikuchi's disease, prednisone in a dosage of 30 mg/day was given orally for seven days. His fever and myalgia improved significantly from the third day of the use of prednisone. He did not experience recurrence during 10 months of follow-up.

Discussion

The cause of Kikuchi's disease is unknown. A viral or post-viral hyperimmune reaction has been proposed as its aetiology.[3] A possible link between Kikuchi's disease and systemic lupus erythematosus (SLE)[7] and a nonspecific hyperimmune reaction to a variety of infectious, chemical, physical, and neoplastic agents has also been proposed as its pathogenesis.[4] Apoptosis mediated by cytolytic lymphocytes, and an autoimmune pathogenesis has also been suggested.[8] The diagnosis is usually confirmed by a lymph node biopsy, that shows the typical pathology of this disease that permits differentiation from lymphoma, SLE and infectious lymphadenopathies[3] – some foci of necrosis, which contained plasmacytoides cells and atypical lymphocytes. Except for cervical adenopathy, findings in blood tests, viral serology and radiological imaging are unremarkable.[9] In our three cases, the diagnosis was confirmed by an early excisional biopsy. We would emphasize that excisional biopsy in our three cases served as an important basic step for making a correct diagnosis without delay. Until recently, once Kikuchi's disease was diagnosed by open excisional biopsy, the mainstay of the management was usually a symptomatic treatment using aspirin or NSAIDs and letting the disease run its course.[4]

The use of immunosuppressants or glucocorticoid, as suggested in our study, in the management of Kikuchi's disease has been reported very rarely. In the previous literature, the use of glucocorticoid was limited only to complicated cases of Kikuchi's disease with brachial plexus neuritis[10] and two cases of Kikuchi's disease associated with SLE.[11] In these previous reports, the patients responded favorably to the glucocorticoid. In contrast to the previously reported cases of Kikuchi's disease which had been treated with steroid, our cases did not manifest with complications such as neuritis and were not associated with SLE. We administered prednisone in our series when the patient had prolonged fever and annoying symptoms lasting more than two weeks despite symptomatic treatment using aspirin or NSAID (*Case 1*), the patient having recurrent disease (*Case 3*), and when the patient strongly demanded a prompt return to his job by achieving early symptomatic improvement (*Case 2*). Thus in our series, we broadened the indications of the steroid treatment, and the outcome was satisfactory. In *Case 1* and *Case 2*, fever disappeared after the initiation of the treatment using prednisone, and other symptoms and lymphadenopathy resolved completely within a week. *Case 1* experienced several bouts of recurrence after the initial remission. However, each bout of recurrence was easily manageable with a reduced dosage of prednisone on an out-patient base. In the recurrent case (*Case 3*), the response to prednisone was not prompt, and this might have been due to the lower dosage of the prednisone administered.

In conclusion, we would suggest that in patients with Kikuchi's disease who were diagnosed by excisional biopsy and unresponsive to initial use of aspirin or NSAID, a glucocorticoid such as oral prednisone could be used as an effective option that could result in an early recovery from the disease process.

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