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Cervical Lymphadenitis as the First Presentation of Kawasaki Disease: A Case Report

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ABSTRACT

Background and Objective: While Kawasaki disease (KD) is common in Asia, the incidence of lymph-node-first presentation of Kawasaki disease (NFKD) in infants is unusual. We present the case of a nine-month-old boy with NFKD.

Case Report: A previously healthy nine-month-old boy presented with symptoms including fever, tenderness, erythema, and severe edema. Physical examination revealed neck swelling and restricted mobility due to lymph node enlargement on the left side of his neck. The initial diagnosis of antibiotic-resistant bacterial lymphadenitis was made. Additional signs and symptoms included bilateral non-exudative bulbar conjunctivitis, erythema of the oral and pharyngeal mucosa accompanied by a reddened tongue and lips, erythema of the hands and feet, and the progressive development of a maculopapular rash. Laboratory tests revealed elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). An echocardiogram indicated a coronary artery abnormality. The patient was diagnosed with NFKD after meeting the diagnostic criteria for KD. Treatment was initiated with intravenous immune globulin (IVIG), aspirin and methylprednisolone. Following IVIG administration, his fever subsided and his symptoms improved.

Conclusions: KD should be considered as a differential diagnosis in febrile infants with cervical adenopathy; patients meeting these criteria should be evaluated for this condition.

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Introduction

Kawasaki disease (KD) is a systemic inflammatory disease with a self-limiting course that primarily affects the microvasculature of neonates and infants under five years of age [1]. Clinically, KD is diagnosed based on specific criteria [2]. Incomplete KD, which is difficult to diagnose based on fewer than four clinical features and is increasing in frequency [3, 4]. Fever with cervical lymphadenopathy occurs in 9-23% of cases [5, 6]. Patients whose initial clinical manifestation is cervical lymphadenopathy are classified as node-first Kawasaki disease (NFKD) [7-9]. At the onset of NFKD, pediatric patients are often misdiagnosed with bacterial cervical lymphadenitis (BCL), delaying the diagnosis of KD and the administration of appropriate treatment [5, 9-11]. NFKD in infants is extremely uncommon. This study presents the case of a nine-month-old boy with NFKD, initially treated for cervical lymphadenitis.

Case Report

On June 19, 2022, our center received a referral for a previously healthy nine-month-old boy presenting with erythema, edema, and tenderness on the left side of his neck, along with a fever that had persisted for six days. The swelling caused severe pain and restricted neck mobility. Initially, he was administered antibiotics and antipyretics for three days at the first medical facility, which had diagnosed him with lymphadenitis. However, the antibiotic treatment had no effect on the patient's symptoms; in addition to fever and lymphadenitis, he developed erythema of the lips and conjunctivitis.

He was therefore referred to our hospital on the sixth day of his illness. At the time of admission, he was conscious but appeared ill, noxious, and dehydrated. His respiratory rate was 50 per minute, he had a heart rate of 120 beats per minute, a temperature of 39°C, and an oxygen saturation of 99% on room air. He suffered from severe pain and edema in the left side of his neck, with his head tilted to the right. Additionally, he presented with a generalized maculopapular rash, non-exudative bilateral bulbar conjunctivitis, edema and erythema of the hands and feet, and non-exudative tonsillitis. He also had red lips and a strawberry-colored tongue.

Initial hospital laboratory results indicated an elevated erythrocyte sedimentation rate (ESR) of 100 mm/hour, a C-reactive protein (CRP) level of 3+, and a white blood cell (WBC) count of 17,000. Table 1 displays the laboratory results obtained at the time of admission to our medical facility. The prothrombin time was within the expected range. Urinanalysis was normal.

The detection of SARS-CoV-2 by polymerase chain reaction (PCR) was negative. Blood and urine cultures were also negative. An ultrasound examination of the neck revealed multiple 5–10 mm nodes resembling a "cluster of grapes" with perilesional infiltration. Abdominal ultrasonography was normal.

Treatment was initiated with oral high-dose aspirin (50 mg/kg/day) and intravenous immune globulin (IVIG) at a dose of 2 g/kg. The patient remained on antibiotic therapy for a further 48 hours due to his general appearance until the cultures were negative. During IVIG treatment, the lymphadenitis, pain, tenderness, and other symptoms improved. Echocardiography showed marked perivascular lucency.

Given this finding and the unusual presentation of the illness, we classified the patient as high-risk. Following IVIG, he received a single dose of 30 mg/kg methylprednisolone pulse. Subsequently, he began taking 2 mg/kg oral prednisolone, which was reduced over the course of three weeks. After the patient recovered on the eighth day and his CRP level reached 30, he was discharged from the hospital. After discharge, the patient was treated with low-dose prednisolone and aspirin (5 mg/kg/day) for three weeks. We also recommended the MMR (measles, mumps, and rubella) vaccination for the child at the age of 20 months. Two weeks after discharge, his echocardiogram was normal, platelet count was 480×10^3/mm^3, ESR was 15 mm/h, and CRP was negative. Peeling of the hands and feet occurred in the third week of the illness.

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Table 1. Laboratory results at the time of admission

Test	Result
WBC	15000
Neut	77%
Lymph	22%
Eos	1%
Hb	9.2
Plt	817000
ESR	70
CRP	86
ALT	42
AST	65
Bilirubin	0.9
U/A	Nl
U/C	Neg.
B/C	Neg
Covid PCR	Neg.

Discussion

Node-predominant presentation (NFKD) is observed in 9-23% of acute KD (AKD) admissions in smaller series [5, 10, 11]. Comparing 14 patients with NFKD to 24 patients with BCL [8], a 2008 Japanese study found that patients with NFKD were older and had higher CRP serum levels. In contrast, our patient with NFKD was an infant. The authors proposed a 4-point scoring system to differentiate NFKD from BCL (age >5.0 years, ANC >10×109 cells/L, CRP >7.0 mg/dL, aspartate aminotransferase (AST) level >30 IU/L). The presence of three to four KD indices along with fever and lymphadenopathy (KDL) was sufficient to diagnose KD in a patient with 78% sensitivity and 100% specificity [8]. Patients diagnosed with NFKD were older, had a longer duration of disease prior to diagnosis, and had elevated CRP [5, 9-11] and ESR levels [6] compared to those with typical KD. Individuals with NFKD were more likely to require IVIG resistance and repeat administration [5, 6, 10, 11], and also had an increased risk of developing coronary artery lesions [5, 6, 11].

Retropharyngeal edema and multiple enlarged solid nodules were similarly frequently observed in patients with NFKD [6]. Sonographic findings in KD included 5–10 mm nodules resembling a "grape" as in our patient, while solitary, well-defined, centrally hypoechoic masses were seen in BCL, with normal-sized nodules in the vicinity [12].

There are reports of a significant prevalence of multiple enlarged nodules in patients diagnosed with both NFKD and BCL [13]. Individuals diagnosed with NFKD are at high risk of misdiagnosis, unnecessary antibiotic treatment, delayed treatment of KD, and occurrence of coronary artery aneurysm (CAA) [7, 9, 14]. Kao et al. [9] documented 14 patients who were diagnosed with KD and had cervical lymphadenitis or a deep neck infection in their study. After antibiotic treatment, all individuals eventually met the diagnostic criteria for KD after an average duration of illness of 8.2 days. The patient in our case was identified after six days of symptoms. CAA was documented in three patients, representing 21% of the total. The authors concluded that febrile children with fever and an enlarged cervical lymph node should be investigated for KD, while NFKD should be considered in those who do not respond to empirical antibiotics. Four KD criteria were selected to differentiate KDL from controls: Age, neutrophil count, CRP and AST.

The incidence of cervical lymphadenopathy is comparatively higher in older children than in young children diagnosed with KD [8, 10, 13, 15]. The mean age of 6.6 years was significantly greater than that of typical KD patients. Unlike this study, our patient was an infant.

Patients with NFKD had elevated levels of inflammatory markers, including neutrophil count, band cells, CRP and ESR, compared to the control group, which had more localized inflammation [6, 16]. Liver function enzymes [6, 15] are elevated in individuals with KD, and AST [8] is used as a marker to distinguish patients with KD from those with BCL, serving as controls. Seventy-eight percent of the patients studied were diagnosed using these four indices. The use of corticosteroids in the initial treatment of KD is controversial. We reported the clinical diagnosis of NFKD in a nine-month-old neonate after six days of fever. NFKD should be kept in mind in the differential diagnosis of febrile infants with cervical adenopathy. Additionally, clinicians ought to advise parents to seek re-evaluation for KD if any signs and symptoms manifest, including alterations in the peripheral extremities or mucocutaneous tissue. Early

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detection and treatment will enhance the prognosis and prevent coronary aneurysms. The incidence of coronary aneurysms decreases when corticosteroids are added to aspirin-containing therapies, which may or may not include IVIG for the initial treatment of KD, according to a meta-analysis [17]. The findings from four randomized studies involving 447 patients diagnosed with KD demonstrated that the inclusion of corticosteroids in initial treatment reduced the rates of re-treatment with IVIG [18] compared to IVIG alone. An additional meta-analysis revealed that when corticosteroids were combined with IVIG, the incidence of initial treatment failure was reduced by 50% compared to IVIG alone [19, 20]. Initial treatment with corticosteroids and IVIG is significantly more effective than IVIG alone in preventing coronary artery abnormalities and achieving better quality outcomes. This is shown by the results of 16 studies involving 2746 patients [21, 22]. Administeration of a single dose of methylprednisolone was associated with a shortened febrile period, less frequent IVIG re-treatments, and shorter hospitalizations without worsening coronary outcomes. We combined methylprednisolone with IVIG and aspirin because the patient was at high risk due to his age and cardiac abnormality.

Limitations of the study

We encountered some limitations in this study. Unfortunately, due to the advanced age of the echocardiogram, any abnormalities in the coronary arteries are only reported as “perivascular brightness" in our hospital. It is not possible to report more precisely whether it is a dilatation or an aneurysm. Another limitation is that we were unable to obtain a photograph of the patient's lymphadenopathy due to the mother's dissatisfaction.

Conclusion

In this case report, NFKD was clinically diagnosed in a nine-month-old infant after six days of fever. NFKD should be considered in the differential diagnosis for febrile infants with cervical adenopathy. In addition, physicians should advise parents to re-evaluate for KD if signs and symptoms appear, including changes in the peripheral extremities or mucocutaneous tissue. Early detection and treatment will improve prognosis and prevent coronary aneurysms.

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Ethical approval

This study obtained ethics committee approval (Ehical code: IR.BPUMS.REC.1403.010).

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Conflict of interest

There is no conflict of interest.

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