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Recurrent Kawasaki Disease in a Child With Retropharyngeal Involvement

A Case Report and Literature Review

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Abstract: Kawasaki disease (KD) is a multisystemic vasculitic disease. Recurrent KD is rare and generally presents in a similar clinical picture as the first episode, and early diagnosis with prompt treatment is the key point in preventing associated cardiovascular morbidities.

A 9-year-old boy, who was diagnosed with KD when he was 1.5 years' old, was referred to our hospital for surgical drainage of retropharyngeal abscess. He had a 7-day history of high fever, sore throat, left-sided neck swelling, and restricted neck movements. Subsequently, he was diagnosed with recurrent KD and retropharyngeal involvement. He was successfully treated with a single dose of intravenous immunoglobulin (IVIG) and acetyl salicylic acid.

Recurrence is rare and occurs most commonly in children. Atypical presentation, incomplete disease, short duration of fever, and reduced response to IVIG treatment were found to be the risk factors for recurrence. KD can occasionally present with clinical and radiographic findings of deep neck bacterial infection. Unusual presentations in KD may cause delay in diagnosis and increase the risk of life-threatening complications.

We describe a case of recurrent KD presenting with a clinical picture resembling retropharyngeal infection who fully recovered after 1 dose of IVIG instead of surgical drainage and antibiotic use.

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Abbreviations: APR = acute phase reactant, ASA = acetyl salicylic acid, CAA = coronary artery aneurysm, CT = computerized tomography, IVIG = intravenous immunoglobulin, KD = Kawasaki disease, MRI = magnetic resonance imaging.

INTRODUCTION

Kawasaki disease (KD) is a multisystemic vasculitic disease that can affect any organ in the body. Coronary artery aneurysms (CAAs) are the most important life-threatening complications of KD. For the diagnosis of KD, there should be at least 4 of 5 principal clinical criteria (nonpurulent bulbar conjunctivitis, changes in the lips or oral cavity, polymorphous exanthema, erythema with later desquamation of the extremities, at least 1 cervical lymph node >1.5 cm in size) with prolonged ($\geq$5 days) high fever.[1] However, the patients can be diagnosed as having ''incomplete KD'' in the presence of 2 or 3 principal symptoms accompanied by high fever. Incomplete KD is more prevalent in young infants and some authors advocate that it is associated with increased incidence of CAA, especially in Asians and Indians. Although CAA develops in 15% to 25% of the untreated patients, incidence of this complication decreases to $<5\%$ with intravenous immunoglobulin (IVIG) therapy. However, IVIG treatment is most effective within the first 10 days of KD.[1–4] Clinicians should be aware of unusual clinical and laboratory findings of KD for timely treatment.

Deep neck involvement is one of the least common symptoms.[1,2,5] The precise pathophysiology of the association of KD with retroparapharyngeal pathology is unclear. However, inflammation and edema are hypothesized as the main mechanisms.[2,5–9] Recurrent KD is a rare phenomenon that occurs in approximately 3% of all patients diagnosed with KD.[1,2,10–12] We describe a case of recurrent KD presenting with a retropharyngeal edema mimicking an abscess formation of a bacterial deep neck infection. He was fully recovered after a single dose of IVIG instead of surgical drainage.

CASE PRESENTATION

A 9-year-old boy, who was diagnosed with KD when he was 1.5 years' old, presented to an outlying hospital with a 7-day history of high fever, sore throat, and left-sided neck swelling. He had restricted neck movements on physical examination. He had elevated acute phase reactant (APR) and magnetic resonance imaging (MRI) findings suggestive of retropharyngeal abscess. He was started on meropenem and gentamicin and was consulted to Department of ear-nose-throat, Faculty of Medicine, Ankara University, for surgical drainage. Department of Pediatric Infectious Diseases was involved to manage the antibiotic coverage for this patient. Parents reported that he was diagnosed with KD when he was 1.5 years' old and was treated with 1 dose of IVIG followed by acetyl salicylic acid (ASA) for 7 years because of a coronary aneurysm until the aneurysm completely regressed. On physical examination, he was pale and sluggish. He had bilateral nonpurulant conjunctivitis, cracked lips, strawberry tongue, edematous fingers on the hands and feet, scrotal edema, and restriction of neck

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movements. He had a painful and warm 6 × 6 cm lymphadenopathy on the left side of his neck and restricted neck movements. An erythematous maculopapular rash was observed on the trunk and lower extremities (Figure 1). There was parapharyngeal and retropharyngeal shift on pharyngeal examination. Laboratory evaluation revealed hemoglobin 11.5 g/dL, white blood cell count 19.400 cells/mm^3, platelet count 243,000 cells/mm^3, erythrocyte sedimentation rate 86 mm/h, C-reactive protein 285 mg/L, aspartate aminotransferase 22 U/L, alanine aminotransferase 33 U/L, serum sodium 132 mmol/L, and albumin 3.1 g/dL. Respiratory tract polymerase chain reaction test was negative for viral agents. His immunological test results were normal. Computerized tomography (CT) was performed to rule out retropharyngeal abscess, which revealed a prevertebral hypodense soft tissue compatible with abscess formation, extending from C2 to C5 cervical vertebrae. There was also deep cervical–retropharyngeal necrotic lymphadenopathy left to midline (Figure 2A–C). Initial diagnosis was retroparapharyngeal abscess coexisting with recurrent KD and the patient was started on intravenous ciprofloxacin, clindamycin, and linezolid. IVIG (2 g/kg/12 h) and ASA (100 mg/kg/d) were administered promptly as well. Fever resolved and conjunctivitis regressed within the first hours, whereas the rash and edema disappeared and neck restriction resolved gradually within 6 hours of IVIG treatment. Echocardiography showed no coronary aneurysm. After the literature review for similar cases,[6,8,9] the retropharyngeal findings were interpreted as edema, which could be seen during the course of KD, mimicking a bacterial cause of abscess formation. Thus, antibiotic treatment was stopped after 2 days of use and all signs of retropharyngeal abscess resolved without any further treatment. His clinical picture improved dramatically. APRs returned to normal ranges and thrombocytosis occurred after the first week of treatment. Desquamation of the fingertips and perinea occurred on the 10th day of the illness. ASA was reduced to an antiaggregant dose (5 mg/kg/d). His throat, blood, and urinary cultures remained negative. MRI findings were completely normal in the second week (Figure 2D and E) and he was discharged from the hospital with no sequelae on the 10th day of the illness. Control echocardiogram revealed normal findings and ASA treatment was stopped after the sixth week of the disease. A 6-month follow-up revealed no remarkable additional morbidity and complication regarding with KD.

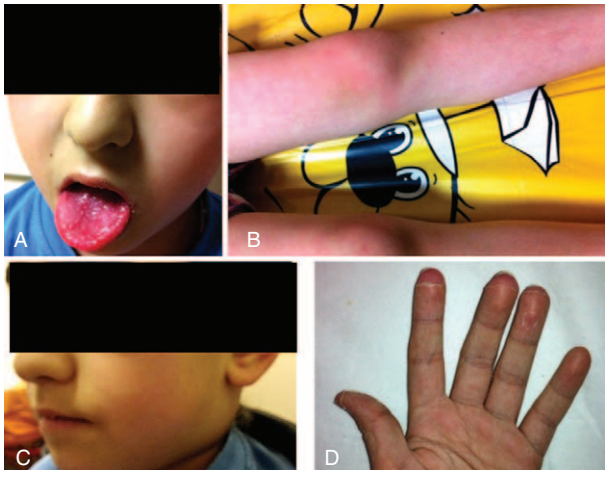

FIGURE 1. Clinical findings of the patient compatible with Kawasaki Disease: bilateral nonpurulant conjunctivitis, cracked lips, and strawberry tongue (A); erythematous maculopapular rash on the lower extremities (B); a large lymphadenopathy on the left of the patient's neck 6 × 6 cm in diameter with restriction of the neck movements (C); desquamation of the fingertips on the 10th day of the illness (D).

DISCUSSION

Although KD is a self-limiting vasculitis, diagnostic and therapeutic delays can cause life-threatening complications such as CAAs. The clinical diversities of KD increase the difficulty of diagnosis. Although exact etiology of KD is still unknown, an infectious or toxic triggering agent is suspected by some authors. In addition to increased physician awareness in all over the world, a real increase in incidence of disease has been shown in recent studies.[1–4]

Lymphadenopathy is the least common symptom in patients with KD occurring with an incidence of 50% to 75%. It occurs as the initial presenting symptom in only 12% of the patients.[1,2,5,7] There are several reports of KD with retropharyngeal edema and enlarged cervical adenopathy as a result of increased use of CT.[5–9] Some KD patients may have complaints resembling other kinds of deep neck infections (peritonsillar abscess, peritonsillar or deep neck cellulitis, and retropharyngeal cellulitis or mass).[5–9,13] Our patient had a remarkable cervical lymphadenopathy in addition to significant restriction of neck movements, torticollis, and parapharyngeal and retropharyngeal shifting. Also, CT was compatible with retropharyngeal abscess. Homicz et al[6] reported a 6-year-old patient presenting with fever, torticollis, and odynophagia. As he was initially diagnosed with retropharyngeal abscess, a surgical drainage was performed. However, there were no

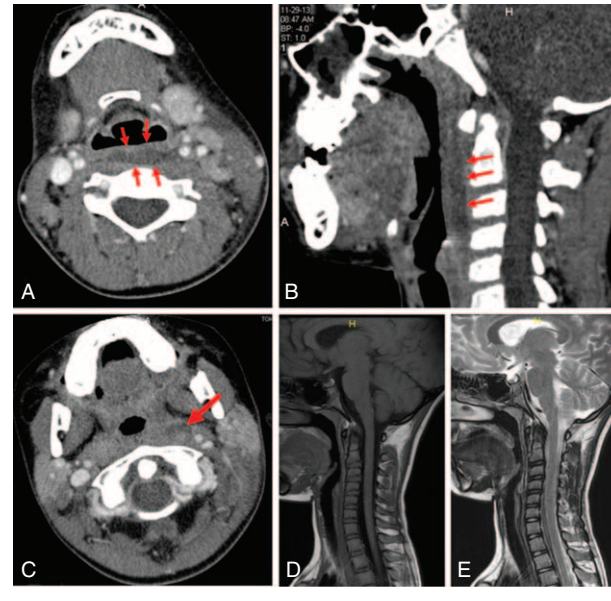

FIGURE 2. (A) Contrast-enhanced CT examination of the neck in axial plane shows hypodense retropharyngeal collection (arrows). Sagittal reformatted CT image (B) better shows the craniocaudal extension of the abscess (arrows). A necrotic lymph node (arrow in C) is also seen on the left of the neck. Follow-up MRI examination, T1-(D) and T2-weighted (E) sagittal plane images reveal that the lesion was completely resolved after IVIG treatment. CT = computed tomography, IVIG = intravenous immunoglobulin, MRI = magnetic resonance imaging.

findings of abscess formation on the back wall of the pharynx by needle aspiration. Thus, the patient was diagnosed as having KD and completely recovered after IVIG and ASA treatment. In a study of Kanegaye et al,[5] 12 patients with KD who presented with lymphadenopathy were evaluated retrospectively. Eleven of them had neck CT done and none of them showed abscess formation. Retropharyngeal edema was found in 7 of these cases.

Yoskovitch et al[7] reported a retrospective study on 155 patients with proven KD. Five percent of patients presented with some form of deep neck infection, 6% with torticollis, and 65% with cervical lymphadenopathy. Cervical lymphadenopathy was detected higher in the patients with classical form of KD than those with atypical forms of KD. In 12% of the patients, presenting symptom is cervical lymphadenopathy and adenopathy can be massive.

In a review by Hung et al,[8] a 29-month-old male patient who was admitted with complaints of neck swelling, restricted neck movements, and fever was reported and compared with other cases in the literature. The patient's CT imaging showed a hypodense lesion in the retropharyngeal area without contrast enhancement. In this review study, similar to our case, there was no abscess formation in any of the cases. None of these 6 patients who presented with retropharyngeal findings responded to antibiotherapy and they showed complete improvement after IVIG and ASA. Machaira et al[15] reported a case of incomplete KD who presented with clinical picture resembling abscess formation. In this case, the pathological examination of surgical biopsy specimens showed necrotizing vasculitis and myositis findings.

A 3-year-old male patient who presented with fever and neck swelling on the right side was reported by Langley et al[9] CT findings of this case identified the right lymphadenopathy and retropharyngeal edema. Patient was diagnosed with KD on the seventh day of the disease and clinical findings regressed after IVIG treatment. In this review,[9] 11 patients were evaluated and 10 of them were presented with retropharyngeal findings. It was pointed out that none of them had benefit from antibiotic treatment. All these patients responded to IVIG treatment dramatically. Five of 11 patients had delayed diagnosis, and there was pericardial effusion in 1 case, coronary artery dilatation or ectasia in 3 patients, and CAAs in 3 patients. Surgical drainage was performed in 5 of them and none had a positive culture of the inflammatory material. Only 1 case was reported to have a repeat radiological imaging after IVIG treatment in this study. In our case, control MRI findings revealed total regression of the retropharyngeal enlargement after 3 weeks from IVIG treatment.

Almost all cases in the literature who presented with deep neck infection findings were referred to otorhinolaryngologist and received antibiotic treatment initially.[5–10,13–16] To date, no study has reported KD accompanied with a proven retropharyngeal abscess formation. Therefore, it is hypothesized that the retropharyngeal space widening and edematous changes are clinical presentations of inflammation in KD. Fang et al[13] reported a case of KD (3-year-old girl) presenting with retropharyngeal edema and shock syndrome. She had open surgical exploration and cultures were found to be sterile in this case report. Similar to our case and a case that was reported by Kao et al,[14] extensive involvement in retropharyngeal space and airway compression regressed after IVIG treatment on repeat imaging. The authors criticized this study that they could have avoided unnecessary surgeries, if they were familiar with retropharyngeal findings in the course of KD before. In this respect, with timely literature search after KD was diagnosed in our case, an unnecessary surgical drainage was avoided.

Recurrence is rare and occurs most commonly in children. There are few case reports that include recurrences of KD in adulthood in the literature.[11,17,18] As in our case, See et al[10] reported a recurrent KD case, which was presented with retropharyngeal phlegmon. Similarly, this case was diagnosed at 2 years of age and was treated with 1 dose of IVIG and ASA. It was stated that a mild dilatation was detected on the left and right coronary arteries. Two years later, she was admitted with signs of fever, torticollis, and massive swelling on the left side of the neck. Retropharyngeal edema was detected on the CT imaging. Initially surgical drainage was planned, but on the follow-up, the patient was diagnosed with recurrent KD with all clinical manifestations of the disease. After the diagnosis, the patient was treated with a single dose of IVIG and ASA. In this case report, authors pointed out that recurrence is more common in Asian people. Also, in this report, it is mentioned that factors such as having initially cardiac sequelae and first attack at the age of around 1 to 2 years are associated with high risk of recurrence. In a similar manner, our patient was diagnosed with KD at 1.5 years of age, coronary aneurysm was detected at that time, and a single dose of IVIG was administered. Besides, in this article, recurrence has been found to be associated with atypical presentation, incomplete disease, short duration of fever, and reduced response to IVIG treatment. However, in our case, the duration of fever was not short; he had typical findings at the recurrence and had a good response to the first dose of IVIG.

In conclusion, current case report and short review of the literature emphasize that clinicians should be alert to head and neck manifestations that show a poor response to initial intravenous antibiotics, as they could be early presentations of KD. KD should be considered in children who presented with cervical adenopathy unresponsive to antibiotic therapy, and in the patients with deep neck infection findings. Thus, with a prompt diagnosis, coronary complications could be reduced and unnecessary surgical drainage could be avoided.

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