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An Atypical Presentation of Kawasaki Disease and Potential Markers for Diagnosis

Tzu Ning Liu, BS[1*], Abigail C. Kuplicki, BS, BA[1*], and Jocelyn Y. Ang, MD[1,2,3]

Abstract

Cervical lymphadenopathy is seldom the initial symptom of Kawasaki disease (KD), making diagnosis difficult in early node-first Kawasaki disease (NFKD). Early treatment is important to prevent cardiovascular sequelae. This report discusses a case of a 4-year-old African American female with NFKD and retropharyngeal phlegmon who was initially treated with antibiotics for cervical lymphadenitis. She later developed classic symptoms of KD, including mucositis, conjunctivitis, palmar erythema, and truncal rash. KD was then suspected and treated appropriately, with the patient experiencing rapid clinical improvement. Early misdiagnosis of NFKD is not uncommon, but certain indices, such as patient age, elevated absolute neutrophil count, or elevated liver enzymes, may be helpful in increasing clinical suspicion. NFKD and retropharyngeal phlegmon remain a rare presentation of an already known condition. The case presented here emphasizes the need for KD to be a differential diagnosis in cases of cervical lymphadenitis and retropharyngeal abscess refractory to antibiotic treatment.

Keywords

Kawasaki disease, node-first Kawasaki disease, retropharyngeal abscess, bacterial lymphadenitis, cervical lymphadenopathy

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Introduction

Kawasaki disease (KD) is a systemic inflammatory illness of unknown etiology that affects children predominantly under 5 years of age.[1] As there are no specific diagnostic tests for KD, the diagnosis is based on the presence of fever and 4 of 5 principal clinical features: bilateral bulbar conjunctival injection, changes of lips and oral cavity, rash, changes of peripheral extremities, and unilateral non-suppurative cervical lymphadenopathy.[1,2] Although diagnostic symptoms may present in any order during the acute phase, the initial presentation of cervical lymphadenopathy along with retropharyngeal phlegmon/abscess and fever is the least common, termed node-first Kawasaki disease (NFKD).[3-5] This contributes to the increased risks of delayed diagnosis and treatment. Therefore, there is a need for improved diagnostic tools and awareness of this manifestation of KD.

Case Report

Hospital Course

A previously healthy, 4-year-old African American female presented with a 4-day history of fever, nasal congestion, rhinorrhea, non-productive cough, and sore throat. Despite daily over-the-counter anti-pyretic

[1]Wayne State University School of Medicine, Detroit, MI, USA
[2]Division of Infectious Diseases, Department of Pediatrics, Children's Hospital of Michigan, Detroit, MI, USA
[3]Department of Pediatrics, Central Michigan University College of Medicine, Mount Pleasant, MI, USA

*Co-first authors.

Corresponding Author:
Tzu Ning Liu, Wayne State University School of Medicine, 540 East Canfield, Detroit, MI 48201, USA.
Email: tzu.ning.liu@med.wayne.edu

administration, her symptoms continued to worsen, including persistent fevers, along with a new onset of left-sided neck swelling associated with drooling and preferential head deviation toward the right side. The patient also experienced fatigue, sore throat, and decreased oral intake, and she denied any recent travels, ear pain, or shortness of breath.

In the emergency department, she was febrile at 38°C and tachycardic (124 beats/minute). Infectious disease workup was negative for group A Streptococcus pharyngitis, respiratory syncytial virus, influenza A/B, and COVID-19 infections. Her laboratory findings were significant for leukocytosis (white blood cell (WBC) count 19.5×10^9/L), neutrophilia (absolute neutrophil count (ANC) 16.2×10^9/L), elevated C-reactive protein CRP (230.7 mg/L), normocytic anemia (hemoglobin 10.1 g/dL with MCV 82.8 fl), hypoalbuminemia (3.6 g/dL), elevated liver enzyme (aspartate aminotransferase (AST) 45 U/L), and sterile pyuria (urine WBC 5-10 cells/hpf), indicating significant systemic inflammation. Neck computed tomography (CT) revealed a retropharyngeal hypodensity extending from the clivus to approximately the C6 vertebral body, along with left palatine tonsillar enlargement and scattered bilateral posterior triangular lymph nodes that was more prominent on the left compared to the right (Figures 1 and 2). Given this clinical picture, she was admitted to the hospital for treatment of left cervical lymphadenitis and retropharyngeal phlegmon with concerns for an evolving abscess.

After 24 hours of intravenous empiric antibiotic therapy, the patient continued to spike multiple fevers, with temperatures peaking at 39.7°C, in addition to persistent, tender left cervical lymphadenopathy and worsening neck mobility. On day 2 of admission, she had a new onset of a non-pruritic, warm, erythematous, desquamating rash in the anterior diaper area extending into the intertriginous region bilaterally (Figure 3). Later in the day, she developed a raised, circular rash that spread from her anterior neck to the axillary region bilaterally, a sandpaper-like rash on her trunk, and erythema on her palms and soles. Additionally, she had bilateral conjunctivitis with perilimbal sparing as well as dry, cracked lips.

At this time, the patient was diagnosed with Kawasaki Disease, prompting a cardiovascular evaluation. Echocardiogram revealed a trace pericardial effusion without systolic or diastolic dysfunction, while the coronary arteries did not demonstrate ectasis or aneurysms. She was immediately initiated on a daily moderate dose (30 mg/kg/day) of aspirin divided into 4 doses per day and 2 g/kg infusion of intravenous immune globulin (IVIG) treatment.

Within 12 hours of initiating IVIG therapy, the patient exhibited distinct clinical improvement. She was

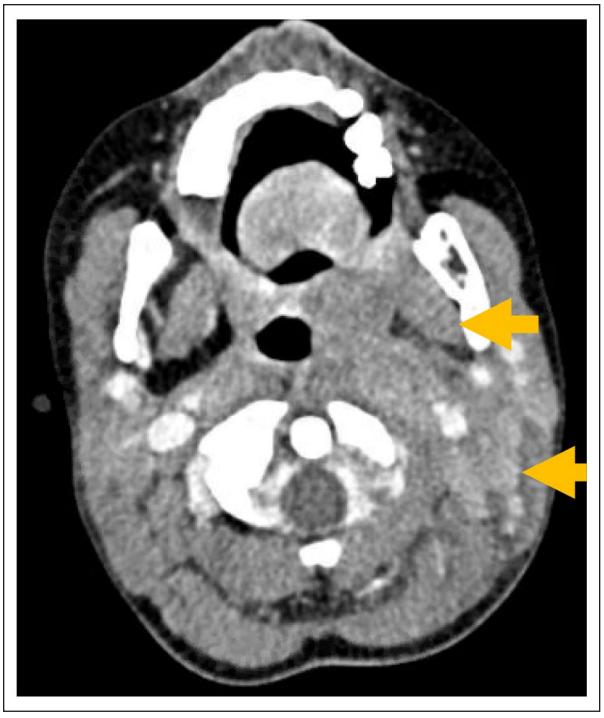

Figure 1. CT taken on admission showing enlargement of the left palatine tonsil and scattered bilateral triangular lymphadenopathy that is more prominent on the left compared to the right.

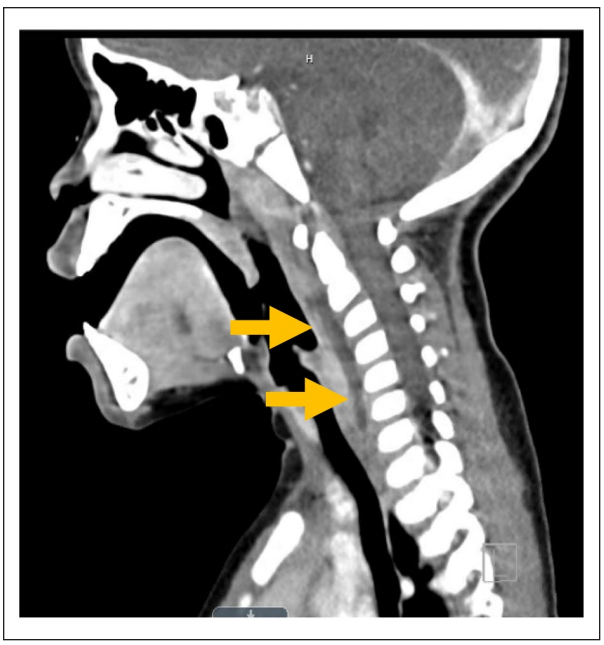

Figure 2. CT taken on admission showing retropharyngeal phlegmon measuring maximum 5 mm in diameter extending from the clivus to approximately the C6 vertebral body.

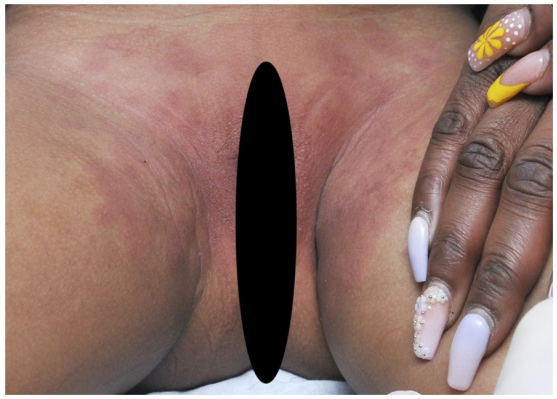

Figure 3. Desquamating rash in the anterior inguinal region that presented on day 2 of admission.

afebrile and had increased energy, appetite, and range of motion of the neck. Physical exam showed resolving left neck swelling, truncal and diaper rashes, conjunctivitis, and erythema in the palms and soles. Her labs showed downtrending CRP (93.2 mg/L), WBC (18.8×10^9/L), and neutrophil levels (ANC 8.5×10^9/L). She was discharged on low-dose aspirin (81 mg) daily.

During the 2-week follow-up visit, she was back to baseline activity with no evidence of neck swelling or fevers, except for bilateral peeling on her fingers, an expected finding in patients recovering from Kawasaki disease. Echocardiogram showed grossly normal coronary arteries without evidence of pericardial effusion. Finally, at her 6-week follow-up visit, aspirin was discontinued given her normal laboratory (CRP $<$ 5 mg/L; negative complete blood count CBC) and echocardiogram findings.

Discussion

Multiple cases reports have shown that NFKD is often misdiagnosed as bacterial cervical lymphadenitis (BCL) or deep neck infections, as they present similarly with fever, neck swelling, stiffness, tenderness, and dysphagia.[6-10] In addition, the retropharyngeal phlegmon is also a rare presentation of KD. It can be misdiagnosed as a retropharyngeal abscess and has resulted in delayed diagnosis as well as unnecessary needle aspiration and antibiotic therapy.[11] With aspiration, there are absent findings, including scant fluid or negative bacterial cultures, upon needle aspiration of the retropharyngeal space.[4,9,12] Similar to our case, patients are often found unresponsive to antibiotic therapy. Delays in treatment with IVIG and aspirin have resulted in serious cardiovascular sequelae, such as coronary artery aneurysms and thrombosis.[4,13,14] IVIG given within 10 days of fever onset reduces the risk of coronary artery aneurysms from 25% to less than 5%.[15]

Both NFKD and bacterial cervical lymphadenitis patients share similar CT findings, which make these diagnoses difficult to differentiate when other classic KD symptoms are not yet present. Kanegaye et al[16] showed that both groups of patients had comparative rates of retropharyngeal edema on CT, but findings of retropharyngeal phlegmon and abscess were much more common in patients with bacterial cervical lymphadenitis. Our patient was also initially diagnosed with retropharyngeal phlegmon based on a retropharyngeal hypodense region found on CT; however, previous studies[11,17] have suggested that this abscess-like finding is attributable to inflammation rather than an infection.

A retrospective analysis by Yanagi et al[18] proposed 4 indices to differentiate between NFKD and bacterial lymphadenitis, including age, neutrophil counts, CRP, and AST. These indices had a sensitivity of 78% and specificity of 100% for identifying KD patients among patients presenting with fever and lymphadenopathy. The average age of NFKD patients was significantly higher than patients with cervical lymphadenitis (6.6 vs 4.8 years). Higher average neutrophil counts (14.4×10^9/L vs 8.134×10^9/L) and CRP (106 mg/L vs 52 mg/L) in NFKD cases most likely reflected the systemic inflammation of KD as compared to other localized causes of cervical lymphadenopathy. Since transaminitis is a relatively common clinical finding in KD,[5] AST was also elevated in NFKD patients compared to lymphadenitis (143 U/L vs 31 U/L). Consistent with this, Kanegaye et al[16] also found that age, CRP, and alanine aminotransferase (ALT) levels were significantly higher among NFKD patients than those with BCL. Applying these indices in the clinical setting has the potential to increase clinical suspicion and earlier diagnosis of NFKD.

In our case, our laboratory findings were relatively consistent with the indices presented by Yanagi et al.[18] While these indices alone may not be sufficient for the diagnosis of NFKD, increased clinical suspicion for NFKD is warranted in patients with cervical lymphadenopathy, fever, and fulfillment of 3 or 4 of these indices, especially if there is a minimal response to appropriate antimicrobial treatment.

Conclusion

This case depicts an uncommon presentation of KD and provides important lessons for clinicians caring for patients with persistent fevers, cervical lymphadenopathy, and suspected retropharyngeal phlegmon unresolved

with antibiotic therapy. Diagnosis of NFKD was made 6 days after initial fever onset with the development of other classical symptoms of KD, consisting of rash, bilateral conjunctivitis, erythema of palms and feet, and mucosal changes in our patient. IVIG therapy resulted in resolution of fevers and improvement in clinical symptoms. This further emphasizes the importance of early diagnosis to prevent sequelae. Our case shows that NFKD should be one of the differential diagnoses when patients present with findings of cervical lymphadenitis or radiographic findings of retropharyngeal phlegmon/abscess along with significantly elevated CRP, liver transaminases, and fever refractory to antibiotic treatment.

Author Contributions

TNL: Contributed to conception and design; contributed to acquisition; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
ACK: Contributed to conception and design; contributed to acquisition; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
JYA: Contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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Ethical Approval and Informed Consent

Written informed consent was obtained from the patient's parent for the publication of this case report. IRB approval was not required per institutional guidelines.

ORCID iDs

Tzu Ning Liu https://orcid.org/0000-0003-1443-9391
Jocelyn Y. Ang https://orcid.org/0000-0002-3286-5418

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