The Neglected Diagnosis in Retropharyngeal Abnormalities: Kawasaki Disease

Changyun Kwon, MD and Jeong Hwan Choi, MD

Department of Otorhinolaryngology—Head and Neck Surgery, Sanggye Paik Hospital, College of Medicine, Inje University, Seoul, Korea

ABSTRACT

Background and Objectives: In patients with Kawasaki disease, retropharyngeal involvements (KDWRPI) is a rare complication. Most reported cases were diagnosed lately because those were often misdiagnosed as bacterial retropharyngeal abscess (BRA). The purpose of this study was to differentiate KDWRPI from BRA in advance. Materials and Methods: We performed a retrospective study comparing children with KDWRPI to those with BRA hospitalized at the university teaching hospital between January 2008 and September 2013. From our retrospectively collected database, we compared clinical, laboratory, and imaging characteristics of KDWRPI and BRA. Results: The study include 11 patients with retropharyngeal involvement on neck computerized tomography (CT) which were divided into two groups. Group A was classified as KDWRPI (n=6) and group B was classified as BRA (n=5). Compared with group B, patients with KDWRPI had lower sodium and albumin (p=0.0176 and 0.0828, respectively). Conclusions: Careful attention to manifestations and close analyses of laboratory findings and CT images may allow otorhinolaryngologists to differentiate KDWRPI from BRA. In the case of retropharyngeal edema on CT, the diagnosis of KDWRPI should not be neglected. (J Clinical Otolaryngol 2017;28:211–218)

KEY WORDS: Kawasaki disease · Retropharyngeal edema · Lymphadenitis · Retropharyngeal abscess.

Introduction

Kawasaki disease (KD) which was first described in 1967, also known as an acute febrile mucocutaneous lymph node syndrome, is a systemic vasculitis of unknown etiology. KD is notorious for serious complications of the coronary artery aneurysm (CAA), acute myocardial infarction, and even sudden cardiac failure. Because treatment with high-dose intravenous immunoglobulin (IVIG) with aspirin in the acute stage can effectively reduce the incidence of coronary artery involvement, it is very important to get an early diagnosis of KD. However, due to the lack of a specific diagnostic test, diagnosis is only based on a symptom pattern, that includes high fever, polymorphous skin rash, conjunctival injection, erythema of the lips and oral mucosa, cervical lymphadenopathy, and changes in the extremities like desquamation of hands and feet. Furthermore, due to variable presentation of the disease, the diagnosis is often incorrect initially. Therefore, only 40% of KD patients met the diagnostic criteria. Approximately 20% of KD cases with atypical presentations are diagnosed delayed or missed.

Of these symptoms, the most infrequent symptom which appears in less than half of case, is cervical lymphadenopathy, while the others occur in 90% of the case. KD with only lymphadenopathy is considered to have an atypical presentation with unfavorable outcome. Reports of KD presenting as a retro-
pharyngeal involvement such as cellulitis or abscess are rare.\(^4,^6,^10-13^\) Neck computerized tomography (CT) of the neck is not a routine diagnostic modality for KD patients, just in case of severe cervical lymphadenopathy implying deep-neck infections. Thus, we could not know the true incidence of retropharyngeal space involvement in the overall KD cohort. One study reported the retropharyngeal low-density lesions were identified by Neck CT in 3.6% of the KD patients.\(^14^\) Moreover, radiological reports suggested that the retropharyngeal low-density lesions were not abscesses, but rather were due to soft-tissue reactions that improved, as do other KD symptoms, after treatment. Those diagnostic delay and inappropriate treatment may cause the development of CAA finally.\(^15^\) Thus, early diagnosis and differentiation of KDWRPI from bacterial retropharyngeal abscess (BRA) is essential to avoid disastrous consequence.

To the best of my knowledge, the clinical and radiological differences between KDWRPI and BRA have not been thoroughly studied.\(^13^\) The object of this study was to compare the clinical characteristics, laboratory results of patients with KDWRPI to those with BRA.

Materials and Methods

Study design

We performed a retrospective study comparing children with KDWRPI to those with BRP hospitalized at the university teaching hospital between January 2008 and September 2013. We reviewed the radiology reports using the search term “retropharyngeal abscess”, “retropharyngeal edema”, and “retropharyngeal low density area” in those groups. Cases with neck CT showed specific retropharyngeal lesions suggesting other diagnoses were excluded. All of 11 patients had complete medical records insuring the correct diagnosis. The 11 patients with retropharyngeal lesion on neck CT were categorized into two groups: group A was classified as KDWRPI and group B as BRA. KDWRPI (group A) was diagnosed when patients fulfilled the diagnostic criteria of KD.\(^16^\)

We compared the group A and group B with regard to clinical and demographic data (age, sex), physical findings, the earliest available laboratory data prospectively collected during the hospital admission and neck CT findings. Laboratory test results included white blood cell (WBC) counts, hemoglobin concentrations (Hgb), platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum levels of alanine aminotransferase (ALT) level, albumin, and sodium (Na).

The Institutional Review Board of our university hospital approved this study and granted a waiver of informed consent. The approval included viewing images and medical records of the patients.

Statistical analysis

Data are expressed as median and interquartile range (IQR, 25%ile–75%ile). Because of nonnormality of some variables, the Mann-Whitney U test was used for comparison between groups. \(p\) values <0.05 were considered statistically significant. All statistical analyses were performed using MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium).

Results

We identified 6 patients in group A (KDWRPI) and 5 patients in group B (BRA). Group A patients were all in the febrile conditions with retropharyngeal swelling or edema (Fig. 1). All the patients were initially treated with antibiotics but were not responsive and one of them even underwent unproductive, culture-negative surgical drainage of the retropharyngeal space. Following the diagnosis of KD, all patients received high dose IVIG with aspirin. Group B patients who did not fulfill the criteria for KD following neck CT (Fig. 2), were diagnosed as having BRA and treated with antibiotic therapy and/or surgical intervention. Neck CT of both groups demonstrated low-attenuation area without contrast rim enhancement at the retropharyngeal space (Fig. 1, 2).
The clinical characteristics and laboratory data of both groups are shown in Table 1. There were no significant differences in sex ratio between the two groups. In a comparison of two groups, group A patients had low serum sodium level (135.0 vs. 139.0 mEq/L) with statistical significance (p=0.0176). Albumin level was also lower in group A (3.75 vs. 4.00 g/dL), but statistically less significance (p=0.0828). However, WBC, ANC, platelet counts, ESR, and ALT level did not differ between the two groups statistically (Fig. 3).

**Discussion**

KD is often difficult to diagnose because of lack of specific laboratory test for this disease, and furthermore, symptoms that match the diagnostic criteria for KD might not be present at the same time, but rather can appear in random pattern. As both KD and retropharyngeal abscess can be fatal if an appropriate treatment is not applied. When otolaryngologists are consulted for the Image of retropharyngeal low-density area, we pay special attention to this condition. Because these findings are often observed in the cases of retropharyngeal abscess and edema usually associated to incoming lethal condition such as airway obstruction, mediastinitis, and sepsis, if not appropriately treated. So we prefer treating it with prompt surgical intervention. But, in the case of KD, some reports of KD patients with retropharyngeal lesions
revealed drainage or aspiration findings failing the present of fluid or bacterial infection.  

In the absence of a definite diagnostic test for KD, the differentiation of KDWRPI from BRA remains challenging. In such cases, clinicians should pay attention to other clinical or laboratory findings not included in the diagnostic criteria that are useful in corroborating the diagnosis. Because KD sometimes manifests with only fever and cervical adenopathy before other clinical signs and symptoms appear.

As KD is mainly diagnosed and treated by pediatricians, these children are extremely rarely seen by an otorhinolaryngologist. However, as many of the manifestations occur in the head and neck, an otorhinolaryngologist may be the first medical professional to see a patient with KD. KD may begin with fever and cervical adenopathy with other clinical signs appearing later.

Otolaryngologists should be considered a rare symptom of KD in dealing with the patients, especially children with cervical lymphadenopathy, retropharyngeal edema, and the presence of low-density lesions in the retropharyngeal space observed by neck CT. Furthermore, when the febrile patient with leukocytosis, lymphadenopathy, and edema of the retropharyngeal space visit clinic, retropharyngeal infection might be initially suspected, but retropharyngeal abnormalities as atypical manifestations of KD should also be considered.

The posterior pharyngeal wall adenitis symptoms such as fever, neck pain, torticollis, and cervical lymphadenopathy are all shared with Kawasaki disease.

Fig. 2. Neck CT with contrast enhancement of group B patients (bacterial retropharyngeal abscess (BRA)) shows cervical lymph node enlargement with retropharyngeal swelling.
Thus it is not surprising that Kawasaki disease can be misdiagnosed as retropharyngeal abscess.

More than half of KD patients have atypical presentations that often result in erroneous or delayed diagnosis and appropriate treatment.\(^6,7\) Furthermore, due to the slow and variable evolution of the disease, the initial diagnosis is often incorrect.\(^5\) Such erroneous or delayed diagnosis can lead to increased development of CAA that have been reportedly to occur in 20% of KD patients with up to 2% of overall mortality.\(^18,32\)

With regards to the diagnosis of a retropharyngeal abscess, CT may be a sensitive tool for the detection of deep neck lesions.\(^6\) CT scan provides the most accurate information on the extent and exact anatomical location of the lesion.\(^23\) In the presence of acute febrile illness, lymph nodes in the retropharyngeal space can become enlarged and have enhancing surrounding with a hypodense core on CT scan which could be interpreted as an abscess.\(^23\)

Thus, a hypoa-
tenuating rim-enhancing retropharyngeal collection on CT scan is predictive, but not diagnostic of abscess.  

The lack of enhancement around the fluid collection in the KDWRPI may be helpful to distinguish the BRA. However, if the fluid collection is accompanied by necrotic lymphadenopathy, it is difficult to distinguish KDWRPI and BRA.

Both the pathogenesis of KD and the etiology of retropharyngeal low-density lesions remain unclear. However, considering the operative findings of unproductive surgical drainage, negative culture results for drainage specimens and the responses to immunoglobulin, inflammation and edema are considered as one of the pathogenesis. KD starts with vasculitis increasing microvascular permeability, causing extravascular albumin leakage and edema. Vasculitis of microvessels with tissue edema and inflammation is hypothesized to cause extensive KDWRPI. During the acute phase of KD, mucosal immune system produce inflammatory cytokines. Retropharyngeal lesions in KD might be explained by this mechanism. RPE formation could be a risk factor for developing CAA. The retropharyngeal space consists of lymphatic vessels and adipose tissue. This space was surrounded by alar and prevertebral fascia. Besides retropharyngeal abscess, retropharyngeal hypodense lesion in the CT can be observed in various pathogenesis related with cervical lymph node swelling. Thus, this lesion on CT might be a type of nonsuppurative inflammation rather than an infection as proved by my surgical cases.

Laboratory tests can be performed to help with the diagnosis. Blood test may show leukocytosis and elevated acute-phase reactants, such as CPR, ESR, normocytic normochromic anemia, thrombocytosis. Other findings include elevated liver enzymes (ALT), decreased cholesterol and high-density lipoprotein levels, increased triglycerides level, hypoalbuminemia, hyponatremia, and more rarely hyperbilirubinemia. Urinalysis may reveal sterile pyuria, whereas the analysis of cerebrospinal fluid shows evidence of aseptic meningitis. Our study identified lower sodium level in serum was the most reliable variables distinguishing KDWRPI from BRA. Lower serum albumin level also was taken into consideration. Unnecessary pharyngeal exploration or unproductive surgical drainage for patients with KDWRPI can be avoided.

This is the first study that has compared the clinical characteristics of patients of KDWRPI with patients of BRA with significant different laboratory findings unlike previous study. Distinguishing patients with KDWRPI from patients with BRA in the early phase is difficult. However, our study showed that KDWRPI and BRA could be distinguished by careful evaluation of clinical manifestations serially.
Our study had some limitations. A sample size was too small for conclusions and generalizations to be representative of all patients. However, this may be a starting point for further research seeking variables significantly leading to proper patient management and preventing unnecessary surgical intervention. Furthermore, we diagnosed KD and BRA clinically. Thus, there was no definitive diagnostic standard for BRA. Further research is needed to eliminate these limitations.

Conclusion

KD sometimes presents with symptoms first in the head and neck region and the patient may initially be admitted to ORL ward. The other symptoms leading to diagnosis of KD may appear only after several days. The diagnosis requires a high level of awareness. The possibility of KD should be kept in mind, at least prior to surgery, in pediatric patients with suspicion of retropharyngeal infections. Clinicians who treat febrile children with cervical adenopathy should keep KD-WRPI in the differential diagnosis. Clinicians should be alert to the occurrence of retropharyngeal edema and multiple solid enlarged nodes KDWRPI when interpreting CT of nodes to ensure the timely diagnosis of KD. Prompt diagnosis of KD and appropriate treatment with IVIG can lead to proper patient management and prevent unnecessary surgical intervention as well as serious cardiac complications.

This work was supported by Grant from Inje University, 2008.

REFERENCES

1) Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Aervrgi 1967;16:178-222.
2) Newburger JW, Takahashi M, Burns JC, Beiser AS, Chung KJ, Duffy CE, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med 1986;315 (6):341-7.
3) Dajani AS, Taubert KA, Gerber MA, Shulman ST, Ferrieri P, Freed M, et al. Diagnosis and therapy of Kawasaki disease in children. Circulation 1993;87(5):1776-80.
4) Hung M, Wu K, Hwang B, Lee P, Meng CL. Kawasaki disease resembling a retropharyngeal abscess-case report and literature review. Int J Cardiol 2007;115(2):e94-6.
5) Murrant N, Cook J, Murch S. Acute ENT admission in Kawasaki disease. J Laryngol Otol 1990;104(7):581-4.
6) Park AH, Batchra N, Rowley A, Hotaling A. Patterns of Kawasaki syndrome presentation. Int J Pediatr Otorhinolaryngol 1997;40(4):41-50.
7) Manhiot C, Christie E, McCrinkle BW, Rosenberg H, Chahal N, Yeung RS. Complete and incomplete Kawasaki disease: two sides of the same coin. Eur J Pediatr 2012;171(4):657-62.
8) Burgner D, Festa M, Isaacs D. Delayed diagnosis of Kawasaki disease with massive lymphadenopathy and airway obstruction. BMJ 1996;312(7044):1471-2.
9) Nomura Y, Arata M, Koriyama C, Masuda K, Morita Y, Hazeke D, et al. A severe form of Kawasaki disease presenting with only fever and cervical lymphadenopathy at admission. J Pediatr 2010;156(5):786-91.
10) Kritsaneeapaiboon S, Tanaanantarak P, Roymance S, Lee EY. Atypical presentation of Kawasaki disease in young infants mimicking a retropharyngeal abscess. Emerg Radiol 2012;19(2):159-63.
11) Rooks VJ, Burton BS, Catalan JN, Syms MJ. Kawasaki disease presenting as a retropharyngeal phlegmon. Pediatr Radiol 1999;29(11):875-6.
12) Kim JS, Kwon SH. Atypical Kawasaki disease presenting as a retropharyngeal abscess. Braz J Otorhinolaryngol 2016;82(4):484-6.
13) Nomura O, Hashimoto N, Ishiguro A, Miyasaka M, Nosaka S, Oana S, et al. Comparison of patients with Kawasaki disease with retropharyngeal edema and patients with retropharyngeal abscess. Eur J Pediatr 2014;173(3):381-6.
14) Tona R, Shinohara S, Fujiwara K, Kikuchi M, Kanazawa Y, Kishimoto I, et al. Risk factors for retropharyngeal cellulitis in Kawasaki disease. Auris Nasus Larynx 2014;41 (5):455-8.
15) Muta H, Ishii M, Yashiro M, Uehara R, Nakamura Y. Late intravenous immunoglobulin treatment in patients with Kawasaki disease. Pediatrics 2012;129(2):e291-7.
16) Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, Burns JC, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004;110(17):2747-71.
17) Craig FW, Schunk JE. Retropharyngeal abscess in children: clinical presentation, utility of imaging, and current management. Pediatrics 2003;111(6 Pt 1):1394-8.
18) Homicz MR, Carvalho D, Kears DB, Edmonds J. An atypical presentation of Kawasaki disease resembling a retropharyngeal abscess. Int J Pediatr Otorhinolaryngol 2000;54(1):45-9.
19) Pontell J, Rosenfeld RM, Kohn B. Kawasaki disease mim-
Gross M, Eliashar R, Attal P, Sichel JY. Radiology quiz case 2: Kawasaki disease (KD) mimicking a retropharyngeal abscess. Arch Otolaryngol Head Neck Surg 2001;127(12):1507-1508-9.

Kanegaye JT, Van Cott E, Tremoulet AH, Salgado A, Shimizu C, Kruk P, et al. Lymph-node-first presentation of Kawasaki disease compared with bacterial cervical adenitis and typical Kawasaki disease. J Pediatr 2013;162(6):1259-63. e1-2.

Vural C, Gungor A, Comerci S. Accuracy of computerized tomography in deep neck infections in the pediatric population. Am J Otolaryngol 2003;24(3):143-8.

Boucher C, Dorion D, Fisch C. Retropharyngeal abscesses: a clinical and radiologic correlation. J Otolaryngol 1999;28(3):134-7.

Stone ME, Walner DL, Koch BL, Egelhoff JC, Myer CM. Correlation between computed tomography and surgical findings in retropharyngeal inflammatory processes in children. Int J Pediatr Otorhinolaryngol 1999;49(2):121-5.

Tomita H, Yamashiro T, Ikeda H, Fujikawa A, Kurihara Y, Nakajima Y. Fluid collection in the retropharyngeal space: a wide spectrum of various emergency diseases. Eur J Radiol 2016;85(7):1247-56.

Langley EW, Kirse DK, Barnes CE, Covitz W, Shetty AK. Retropharyngeal edema: an unusual manifestation of Kawasaki disease. J Emerg Med 2010;39(2):181-5.

Ueda Y, Saita Y, Matsuzawa T, Wada T, Kanai N, Kobayashi I. Six patients with Kawasaki disease showing retropharyngeal low-density areas on computed tomography. Pediatr Int 2010;52(4):e187-9.

Roh K, Lee SW, Yoo J. CT analysis of retropharyngeal abnormality in Kawasaki disease. Korean J Radiol 2011;12(6):700-7.

Abe J. Immunological aspects of Kawasaki disease. Nihon Rinsho 2008;66(2):267-71.

Philpott C, Selvadurai D, Banerjee A. Paediatric retropharyngeal abscess. J Laryngol Otol 2004;118(12):919-26.

Chiang A, Hwang B, Shaw G, Lee B, Lu J, Meng C, et al. Changes in plasma levels of lipids and lipoprotein composition in patients with Kawasaki disease. Clin Chim Acta 1997;260(1):15-26.

Moon JH, Ahn HY, Chang MK, Cha CI. Cervical lymphadenopathy as the initial manifestation of Kawasaki disease. J Clinical Otolaryngol 2002;13(2):229-33.