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Lymph-Node-First Presentation of Kawasaki Disease Compared with Bacterial Cervical Adenitis and Typical Kawasaki Disease

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Abstract

Objective—To identify characteristics differentiating the node-first presentation of Kawasaki disease (NFKD) from bacterial cervical lymphadenitis (BCL) and typical Kawasaki disease (KD).

Study design—From our prospectively collected database, we compared clinical, laboratory, and imaging characteristics of NFKD and BCL cohorts and performed multivariable logistic regression to identify variables that distinguish NFKD from BCL. We then compared outcomes of NFKD and patients with typical KD treated during the same period.

Results—Over 7 years, 57 patients were hospitalized for NFKD, 78 for BCL, and 287 for typical KD. Patients with NFKD were older and had more medical encounters and longer duration of illness prior to correct diagnosis than patients with BCL. Of patients with NFKD, 33% had an admission diagnosis of bacterial adenitis or abscess. Compared with patients with BCL, patients with NFKD had lower leukocyte (WBC), hemoglobin, and platelet counts and higher absolute band counts (ABC), C-reactive protein (CRP), alanine transaminase and γ -glutamyl transpeptidase levels, and erythrocyte sedimentation rates. In the multivariable analysis, smaller nodes, lower WBC, and higher ABC and CRP were independently associated with NFKD. Patients with NFKD had multiple enlarged solid nodes and comparable rates of retropharyngeal edema. Compared with patients with typical KD, patients with NFKD were older, had more severe

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inflammation, and had similar rates of coronary artery abnormalities and resistance to intravenous immune globulin.

Conclusions—High ABC and CRP values and multiple enlarged solid nodes in febrile patients with cervical adenopathy should prompt consideration of NFKD to prevent delayed diagnosis of KD. Retropharyngeal edema on radiography should not dissuade from the diagnosis of NFKD.

Keywords

Kawasaki disease; cervical adenopathy; computed tomography; bacterial lymphadenitis

Cervical lymphadenitis with fever is common in children. Symptoms usually resolve with empiric antibiotics, and diagnostic tests are unnecessary. Kawasaki disease (KD) typically manifests with fever followed by rash, conjunctival injection, cervical adenopathy, and changes of mucous membrane and extremities. Of the principal diagnostic criteria, cervical adenopathy is the least common, noted in 50%–75% of Japanese cases,¹ 42% to 52% of US cases,^{2,3} and 24% of Chinese cases.⁴ On occasion, KD manifests with fever and cervical adenopathy before other clinical signs appear.^{5–7} In others, adenopathy dominates the presentation even when other signs are present.⁸ Such presentations may be misdiagnosed as bacterial cervical lymphadenitis (BCL), potentially delaying definitive treatment for KD and leading to serious cardiac sequelae. In the absence of specific diagnostic tests, the diagnosis of node-first KD (NFKD) remains obscure until other clinical features have appeared or an echocardiogram demonstrates characteristic coronary artery changes.

NFKD is not well-known among clinicians who treat febrile children, and, even for clinicians familiar with this presentation, the differentiation of NFKD from other forms of cervical adenitis is challenging. Previous reports have compared NFKD with typical KD.^{9,10} Others have described radiologic features¹¹ and laboratory values¹² that could distinguish NFKD from BCL. Our KD Research Center's extensive database afforded the unique opportunity to describe and compare NFKD, typical KD, and BCL from a single center. We sought to identify clinical, laboratory, and imaging features that distinguish patients with BCL and NFKD. We also sought to determine whether patients with NFKD have more frequent or severe complications than those with typical KD.

METHODS

Our KD Research Center maintains a database of standardized, prospectively collected information for patients treated for KD at this free-standing children's hospital which is the principal pediatric inpatient facility for a population of approximately 3 million. From this database, we identified all patients with acute KD treated during the 7-year period from March 2003 to March 2010 who had fever ≥ 3 days but < 10 days and who fulfilled at least 4 of 5 diagnostic criteria (rash, conjunctival injection, cervical lymphadenopathy, oral mucosal changes, and peripheral extremity changes), 3 criteria plus coronary artery abnormalities documented by echocardiography, or 2 to 3 criteria with elevation of inflammatory indices and 3 supplemental laboratory criteria.¹³ We defined NFKD as acute KD presenting at the first medical encounter with fever and cervical adenopathy prior to the appearance of other clinical criteria. To capture the full spectrum of disease, we included 4 additional patients with NFKD who were diagnosed after 10 days of fever. The remaining patients with KD formed the typical KD comparison group. The Institutional Review Board of the University of California San Diego approved this study and granted a waiver of informed consent.

We retrospectively identified patients with acute lymphadenitis by computerized search (International Classification of Diseases, Ninth Revision code 683) discharged from the inpatient ward during the same time period. We excluded patients with mycobacterial

lymphadenitis, chronic lymphadenitis, or adenopathy not associated with fever. The BCL group consisted of febrile patients with a unilateral nodal mass > 1.5 cm confined to the neck who had purulent or culture- or gram stain-positive material obtained by aspirate, surgical drainage, or biopsy or whose fever improved following appropriate antibiotic therapy.

For all patients with KD, we analyzed the following data prospectively collected during the hospital admission leading to the final diagnosis: clinical and demographic data (age, sex, and number of calendar days of fever at diagnosis); laboratory values obtained prior to the administration of intravenous immune globulin (IVIG); response to IVIG; and echocardiographic data. We abstracted laboratory data from hospital admission for patients with BCL. For both patients with BCL and patients with NFKD, we abstracted the number and timing of clinic, office, and ED visits, the number of prior hospital admissions, the use and duration of antibiotics, admission diagnoses, and surgical consultations and procedures. For patients with NFKD, we also abstracted the earliest available laboratory results. We converted percentage neutrophil and band counts to absolute neutrophil (ANC) and band counts (ABC) and hemoglobin values to age-adjusted Z-scores.¹⁴ For laboratory values outside the range of the test, we used the maximum or minimum value detected in the assay.

Two attending pediatric radiologists, blinded to the original radiographic interpretations and the final diagnoses, interpreted computed tomographic (CT) and ultrasound (US) images for subjects with NFKD and BCL. For CT studies, they recorded the anatomic region containing the majority of the nodal mass, grouping of nodes, the degree of suppuration, the presence of adjacent inflammation, and the presence of retropharyngeal edema. For US studies, they recorded only grouping, suppuration, and adjacent inflammation. We defined grouping by 1 of 3 morphologic descriptions: multiple homogeneously-sized nodes consistent with the previously described “cluster of grapes,”¹ multiple heterogeneously-sized nodes, or a single dominant mass or conglomeration of nodes radiographically inseparable due to anatomic continuity or interposed inflammation. The spectrum of suppuration included solid nodes, phlegmon, and abscess. On CT, phlegmon was a low attenuation mass without rim enhancement, and abscess was a fluid density collection with peripheral enhancement. On US, phlegmon and abscesses were hypoechoic structures with and without internal vascular flow, respectively.

We compared the NFKD and typical KD groups with regard to age, illness day at diagnosis, laboratory values, coronary artery measurements, and IVIG resistance. We converted internal diameters of left anterior descending (LAD) and right coronary arteries (RCA) to Z-scores, normalized for body surface area.^{15, 16} Abnormal coronary Z-scores were those > 2.5. We defined coronary Z-worst as the worst-ever Z-score for either the RCA or LAD on any echocardiogram following diagnosis. IVIG resistance was defined as persistent or recrudescent fever (temperature ≥ 38.0°C) ≥ 36 hours following completion of IVIG infusion (2 g/kg). Forty patients with KD (including 9 with NFKD) participated in a randomized, placebo-controlled, double-blind trial of adjunctive infliximab for initial treatment (NCT00760435 in the ClinicalTrials.gov registry) and were excluded from analyses of IVIG response and coronary artery measurement.

Statistical analyses

To identify opportunities for early diagnosis, we used the earliest available laboratory data for the comparison of NFKD and BCL groups. To compare severity among KD subtypes at the time of diagnosis, we used the laboratory values obtained closest in time prior to the administration of IVIG.

We compared demographic, clinical, and laboratory measurements between groups using the Wilcoxon rank sum test for continuous variables and Fisher exact test for categorical variables. Using Spearman rho square, we calculated univariate correlations between each potential predictor and the diagnostic outcome. Multivariable logistic regression was used to evaluate whether the continuous variables of age, illness duration, clinically measured node size, white blood cell (WBC) count, ABC, age-adjusted hemoglobin, and C-reactive protein (CRP) could differentiate NFKD from BCL. No adjustments were made for multiple comparisons, and p-values < 0.05 were considered statistically significant. All statistical analyses were performed using R, version 2.10.0 (cran.r-project.org/).

RESULTS

During the study period, 340 patients, including 53 with NFKD, were treated for acute KD by the tenth day of illness. Four additional patients with NFKD were treated after the tenth day of illness. The 57 patients with NFKD were older than the 78 patients with BCL (Table I). Although times to initial presentation were similar, patients with NFKD experienced more outpatient visits, hospital admissions, total health care encounters, and days of illness prior to diagnosis. Approximately 80% of both groups received preadmission antibiotic therapy (most often β -lactam agents, clindamycin, and clindamycin-cephalosporin combinations).

One-third of patients with NFKD had an admission diagnosis of bacterial adenitis or abscess and received initial antibiotic therapy (Table I). Compared with patients with BCL, patients with NFKD had lower WBC, age-adjusted hemoglobin, and platelet counts and higher ABC, erythrocyte sedimentation rate (ESR), CRP, alanine transaminase (ALT), and γ -glutamyl transpeptidase (GGT) levels (Table II). The multivariable logistic regression revealed that smaller lymph node size (adjusted odds ratio [AOR]: 0.41; 95% confidence interval [CI]: 0.25–0.67), lower WBC (AOR: 0.81; 95% CI: 0.69–0.96), higher ABC (AOR: 1.001; 95% CI: 1.000–1.001), and higher CRP (AOR: 1.15; 95% CI: 1.02–1.28) retained an independent association with NFKD after adjusting for age and duration of illness.

Twelve patients with NFKD and 44 with BCL underwent imaging studies (Table III). CT revealed predominantly anterior and posterior adenopathy in both groups. Patients with NFKD more commonly had groups of nodes of different sizes (Figure; available at www.jpeds.com). Nodes were solid in most patients with NFKD (91%), whereas the majority of patients with BCL had phlegmon or abscess. Inflammation was confined to the perinodal region in NFKD and was more diffuse and affected parapharyngeal regions in BCL. Retropharyngeal edema was common in NFKD and BCL (Figure). US findings (Table III) loosely paralleled those of CT, revealing predominantly clusters of multiple solid nodes in NFKD and single dominant or coalescent masses in BCL. In contrast to CT, inflammatory changes were absent or equivocal on US in two-thirds of NFKD cases and one-third of BCL. Thus, US permitted superior resolution of individual nodes, which appeared as single dominant or coalescent masses on CT.

In a comparison of patients with NFKD and those with typical KD treated by the tenth day of fever (Table IV; available at www.jpeds.com), patients with NFKD were older (median 4.2 years vs. 2.0 years) and had significantly higher ANC (10.8×10^9 cells per L vs. 8.3×10^9 cells per L), ESR (75 mm/h vs. 58 mm/h), and CRP (13.0 mg/dL vs 7.4 mg/dL), but hemoglobin, total WBC and platelet counts did not differ. Coronary Z-worst scores and rates of IVIG resistance and coronary artery aneurysms did not differ between patients with NFKD and those with typical KD.

DISCUSSION

In the absence of a specific diagnostic test for KD, the differentiation of NFKD from BCL remains challenging. Our study identified older age, elevated markers of systemic and hepatobiliary inflammation, and anemia for age as variables to help recognize NFKD. Among these, ABC and CRP were the most robust variables distinguishing NFKD from BCL. Characteristic radiologic findings included single dominant nodes or conglomerations and suppuration in patients with BCL, limitation of inflammation to the perinodal region in NFKD, and multiple discrete nodes in patients with NFKD. Retropharyngeal edema was unexpectedly common on CT of patients with NFKD. Compared with patients with typical KD, patients with NFKD treated by the tenth day of illness were older and had elevated markers of inflammation (ANC, ESR, and CRP) but did not have more severe outcomes.

Node-first or node-predominant presentations have represented 9% to 23% of smaller series of acute KD admissions.^{1, 9, 10} A Japanese comparison of 14 patients with NFKD and 24 patients with BCL¹² revealed that patients with NFKD, as in our study, were older and had higher CRP levels. In contrast, their patients with NFKD had higher WBC, ANC, and aspartate aminotransferase levels and lacked the relative anemia and thrombocytopenia which we observed. The authors proposed a 4-item scoring system to discriminate NFKD from BCL (age >5.0 years, ANC >10×10⁹ cells/L, CRP >7.0 mg/dL, aspartate aminotransferase level >30 IU/L),¹² which we could not assess due to the lack of aspartate transaminase levels in our database.

Compared with those with typical KD, previously reported patients with NFKD^{9, 10} and patients with KD with cervical adenopathy^{3, 4} were older and ill longer prior to diagnosis and had higher CRP^{9, 10} and ESR values.³ In the largest previous series (16 patients with NFKD and 171 with typical KD), patients with NFKD more often required repeated administration of IVIG and had an increased risk of coronary artery lesions.¹⁰ In contrast, our patients with NFKD and previously reported patients with KD with cervical adenopathy⁴ did not appear to have a greater risk of coronary artery lesions or IVIG resistance. As in our series, antibiotic treatment for presumed BCL is common among patients with KD with adenopathy.³

Previously reported sonographic findings included 5–10 mm nodes resembling a “cluster of grapes” in KD and single well-defined, centrally hypoechoic masses with surrounding normal-sized nodes in BCL.¹ Others report a high frequency of multiple enlarged nodes in both patients with NFKD and patients with BCL.¹² Patients with KD with the CT finding of retropharyngeal edema have greater extension of inflammation into deep neck spaces and more adjacent soft tissue involvement than patients with retropharyngeal edema of infectious etiology.¹¹ Nonetheless, patients with NFKD with retropharyngeal edema commonly experience delayed diagnosis due to the erroneous diagnosis of bacterial infection.^{17, 18} Because CT is unnecessary in typical KD, the overall frequency of retropharyngeal edema in KD is unknown. However, the finding may be more common than previously appreciated and suggests a local inflammatory response to an antigen or infectious agent entering through the upper airway.

We recognize several strengths and limitations to our study. This study reported results of blinded reading of CT images from patients with NFKD and BCL and described characteristic CT and sonographic findings in these patients. Our prospective KD database was assembled by clinical personnel experienced in the evaluation and management of patients with KD and BCL. However, we retrospectively obtained all BCL data, all pre-admission KD clinical features, and additional KD node-related clinical characteristics such as location, mobility, dimensions, skin changes, tenderness, induration, and fluctuance.

Therefore, we were unable to determine whether clinicians failed to recognize subtle diagnostic features in our NFKD cohort during preadmission clinical encounters or to identify the clinical nuances that an experienced clinician might use to differentiate the adenopathy of NFKD from that of BCL. Our NFKD definition required neither a specific interval between appearance of adenopathy and that of other clinical criteria⁹ nor the absence of other criteria at time of clinical presentation leading to the diagnosis of KD.^{9, 12} However, we avoided such criteria in order to better inform a wider group of clinicians who encounter patients with NFKD without knowledge of the subsequent evolution. Although we identified significant differences in laboratory characteristics, the values were not available for all patients and are not commonly obtained when KD is not suspected. Therefore, we were unable to analyze other candidate predictors that might distinguish NFKD from BCL (e., ESR, ALT, and GGT). Our selection criteria resulted in a relatively small hospitalized BCL group which may not have represented the spectrum of patients who cause diagnostic dilemma with NFKD in the outpatient setting. However, an inpatient comparison group is more likely to have complete description of clinical presentation, laboratory values and clinical evolution. Among patients with BCL, <30% had culture confirmation of bacterial etiology, but their clinical responses to parenteral antibiotic therapy during inpatient observation made them an appropriate comparison group.

Clinicians who treat febrile children with cervical adenopathy should keep NFKD in the differential diagnosis and should counsel the parents of such patients to return for re-evaluation if mucocutaneous or peripheral extremity changes suggesting KD occur. Clinicians and radiologists should be alert to the occurrence of retropharyngeal edema and multiple solid enlarged nodes NFKD when interpreting CT and US images of nodes to ensure the timely diagnosis of KD.

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Abbreviations

ABC	absolute band count
ALT	alanine transaminase
ANC	absolute neutrophil count
AOR	adjusted odds ratio
BCL	bacterial cervical lymphadenitis
CRP	C-reactive protein
CT	computed tomography/computed tomographic
ESR	erythrocyte sedimentation rate
GGT	γ -glutamyl transpeptidase
IVIG	intravenous immune globulin
KD	Kawasaki disease
NFKD	node-first Kawasaki disease
US	ultrasound

WBC white blood cell/white blood cell count

References

1. Tashiro N, Matsubara T, Uchida M, Katayama K, Ichiyama T, Furukawa S. Ultrasonographic evaluation of cervical lymph nodes in Kawasaki disease. *Pediatrics*. 2002; 109:E77. [PubMed: 11986483]
2. Burns JC, Mason WH, Glode MP, Shulman ST, Melish ME, Meissner C, et al. Clinical and epidemiologic characteristics of patients referred for evaluation of possible Kawasaki disease. United States Multicenter Kawasaki Disease Study Group. *J Pediatr*. 1991; 118:680–6. [PubMed: 2019921]
3. April MM, Burns JC, Newburger JW, Healy GB. Kawasaki disease and cervical adenopathy. *Arch Otolaryngol Head Neck Surg*. 1989; 115:512–4. [PubMed: 2923695]
4. Sung RY, Ng YM, Choi KC, Mok GC, Cheng YW, Ho MH. Lack of association of cervical lymphadenopathy and coronary artery complications in Kawasaki disease. *Pediatr Infect Dis J*. 2006; 25:521–5. [PubMed: 16732150]
5. Waggoner-Fountain LA, Hayden GF, Hendley JO. Kawasaki syndrome masquerading as bacterial lymphadenitis. *Clin Pediatr (Phila)*. 1995; 34:185–9. [PubMed: 7789011]
6. Kao HT, Huang YC, Lin TY. Kawasaki disease presenting as cervical lymphadenitis or deep neck infection. *Otolaryngol Head Neck Surg*. 2001; 124:468–70. [PubMed: 11283510]
7. Park AH, Batchra N, Rowley A, Hotaling A. Patterns of Kawasaki syndrome presentation. *Int J Pediatr Otorhinolaryngol*. 1997; 40:41–50. [PubMed: 9184977]
8. Stamos JK, Corydon K, Donaldson J, Shulman ST. Lymphadenitis as the dominant manifestation of Kawasaki disease. *Pediatrics*. 1994; 93:525–8. [PubMed: 8115224]
9. Kubota M, Usami I, Yamakawa M, Tomita Y, Haruta T. Kawasaki disease with lymphadenopathy and fever as sole initial manifestations. *J Paediatr Child Health*. 2008; 44:359–62. [PubMed: 18476929]
10. Nomura Y, Arata M, Koriyama C, Masuda K, Morita Y, Hazeki D, et al. A severe form of Kawasaki disease presenting with only fever and cervical lymphadenopathy at admission. *J Pediatr*. 2010; 156:786–91. [PubMed: 20097355]
11. Roh K, Lee SW, Yoo J. CT analysis of retropharyngeal abnormality in Kawasaki disease. *Korean J Radiol*. 2011; 12:700–7. [PubMed: 22043152]
12. Yanagi S, Nomura Y, Masuda K, Koriyama C, Sameshima K, Eguchi T, et al. Early diagnosis of Kawasaki disease in patients with cervical lymphadenopathy. *Pediatr Int*. 2008; 50:179–83. [PubMed: 18353055]
13. 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; 110:2747–71. [PubMed: 15505111]
14. Tremoulet AH, Best BM, Song S, Wang S, Corinaldesi E, Eichenfield JR, et al. Resistance to intravenous immunoglobulin in children with Kawasaki disease. *J Pediatr*. 2008; 153:117–21. [PubMed: 18571548]
15. McCrindle BW, Li JS, Minich LL, Colan SD, Atz AM, Takahashi M, et al. Coronary artery involvement in children with Kawasaki disease: risk factors from analysis of serial normalized measurements. *Circulation*. 2007; 116:174–9. [PubMed: 17576863]
16. Manlhiot C, Millar K, Golding F, McCrindle BW. Improved classification of coronary artery abnormalities based only on coronary artery z-scores after Kawasaki disease. *Pediatr Cardiol*. 2010; 31:242–9. [PubMed: 20024653]
17. Langley EW, Kirse DK, Barnes CE, Covitz W, Shetty AK. Retropharyngeal edema: an unusual manifestation of Kawasaki disease. *J Emerg Med*. 2010; 39:181–5. [PubMed: 19150196]

18. 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:e187–9. [PubMed: 20958860]

Figure.

A, Multiple heterogeneously-sized nodes (arrows) in NFKD demonstrated on axial (left) and coronal (right) CT images. B, Retropharyngeal edema (arrows) in NFKD demonstrated on axial (left) and sagittal (right) CT images.

Table I

Clinical and treatment characteristics of patients with NFKD and BCL

Characteristic	NFKD (n = 57)*	BCL (n = 78)†	P
Age, years, median (IQR)	4.2 (2.7–5.4)	1.6 (1.0–4.9)	<.001
Males, n (%)	31 (54)	40 (51)	.7
Illness day at first presentation, days,‡ median (IQR)	2 (1–3)	2 (1–3)	.2
Outpatient visits prior to diagnosis, median (IQR)	1 (1–2)	1 (0–2)	.001
Patients with prior hospital admissions, n (%)	6 (11)	1 (1)	.04
Prior hospital admissions, median (IQR)	0 (0–0)	0 (0–0)	.02
Total prior medical encounters, median (IQR)	2 (1–2)	1 (0–2)	.0003
Illness day at diagnosis, days,‡ median (IQR)	6 (5–8)	3 (2–6)	<.0001
Size of node, cm, median (IQR)	3 (2–4)	5 (4–6)	<.001
Admission diagnosis, n (%)			<.0001
KD	38 (67)	0 (0)	
Bacterial infection	19 (33)	78 (100)	
Bacterial adenitis	11	69	
Cervical or retropharyngeal abscess/phlegmon	8	9	
Pre-admission antibiotic, n (%)	47 (83)	59 (77)	.5
Oral	34	33	
Parenteral with or without oral	13	26	
Duration of pre-admission antibiotic therapy, d	2 (1–4)	1 (0.5–3)	.07
Inpatient antibiotic, n (%)	17 (30)	77 (99)	<.0001
Duration of inpatient antibiotic therapy, d, median (IQR)	0 (0–1)	2.5 (2–3.5)	<.0001
Surgical consultation, n (%)	15 (26)	53 (68)	<.0001
Surgical procedures, n (%)§	1 (2)	22 (28)	.0001

* Data availability for NFKD group: day of first presentation, 55; duration of pre-admission antibiotic therapy, 55; node size, 48.

† Data availability for bacterial adenitis group: day of first presentation, 75; prior medical care, 77; administration of pre-admission antibiotic therapy, 77; duration of pre-admission antibiotic therapy, 73; node size, 69; pre-admission antibiotic, 77.

‡ Illness day 1, first calendar day of fever.

§ NFKD culture results: no growth (1). BCL cultures (from 22 acute and 1 delayed procedures): methicillin-susceptible (13) and methicillin-resistant (5) *Staphylococcus aureus*, group A streptococci (2), and no growth but surgical findings consistent with infection (3). The remaining 55, treated based on clinical and radiologic findings, had favorable clinical responses to antibiotic therapy.

Table II

Laboratory values at initial presentation in patients with NFKD and BCL

Laboratory test	NFKD (n = 57)*	BCL (n = 78)†	P
WBC, $\times 10^9$ cells per L, median (IQR)	16.4 (12.4–18.8)	19.0 (14.0–24.3)	.01
ANC, $\times 10^9$ cells per L, median (IQR)	12.5 (9.1–15.6)	12.5 (8.9–16.4)	.8
ABC, $\times 10^9$ cells per L, median (IQR)	1.9 (0.7–3.1)	0.8 (0.2–1.8)	.002
Hemoglobin Z-score, SD units, median (IQR)	−1.1 (−2.1 to −0.3)	−0.7 (−1.4 to 0.4)	.02
Platelet count, $\times 10^9$ cells per L, median (IQR)	383 (301–460)	433 (336–558)	.02
ESR, mm/h, median (IQR)	79 (64–112)	48 (31–69)	.0001
CRP level, mg/dL, median (IQR)	13.7 (7.1–21.8)	6.1 (3.1–12.1)	.0001
ALT level, U/L, median (IQR)	27 (19–76)	15 (9–21)	.0001
GGT level, U/L, median (IQR)	29 (21–133)	22 (19–24)	.047

WBC, white blood cell; ANC, absolute neutrophil count; ABC, absolute band count; SD, standard deviation; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ALT, alanine aminotransferase; GGT, γ -glutamyl transpeptidase.

* Data availability for NFKD group: band counts, 51; ESR, 53; CRP, 55; ALT, 49; GGT, 45.

† Data availability for bacterial adenitis group: WBC, 74; neutrophil counts, 73; band counts, 56; hemoglobin, 74; platelets, 73; ESR, 34; CRP, 52; ALT, 19; GGT, 9.

Table III

Radiographic findings^{*} in NFKD and BCL based on blinded readings by 2 radiologists

Radiologic finding	NFKD	BCL	P
<i>Computed tomography</i>	11	39	
Location, n (%)			.3
Anterior cervical	6 (55)	18 (46)	
Posterior triangle	3 (27)	12 (31)	
Submental/mandibular	0	7 (18)	
Other [†]	2 (18)	2 (5)	
Grouping of node(s), n (%)			
Dominant mass	5 (46)	31 (79)	.05
Clustered nodes	6 (54)	8 (21)	
Homogenous	1	1	
Heterogenous	5	7	
Degree of suppuration, n (%)			
Solid	10 (91)	11 (28)	.003
Suppurative	1 (9)	28 (72)	
Phlegmon	1	14	
Abscess	0	14	
Adjacent inflammation, n (%)	10 (91)	37 (95)	.5
Retropharyngeal edema, n (%)	7 (64)	13 (33)	.09
<i>Ultrasonography</i>	6	11	
Grouping of node(s), n (%)			
Dominant mass	1 (17)	8 (73)	.05
Clustered nodes	5 (83)	3 (27)	
Homogenous	2	0	
Heterogenous	3	3	
Degree of suppuration, n (%)			
Solid	5 (83)	6 (55)	.3
Phlegmon	1 (17)	5 (45)	

^{*} Imaging studies: CT alone in 6 patients with NFKD and 33 patients with BCL, US alone in 1 patient with NFKD and 5 patients with BCL, and both CT and US in 5 patients with NFKD and 6 patients with BCL.

[†] Other NFKD locations: anterior plus posterior (1) and para- or retropharyngeal (1) adenopathy. Three patients with NFKD with predominantly anterior adenopathy had posterior cervical involvement. Other BCL locations: anterior and posterior (1) and anterior, posterior, and lateral retropharyngeal (1) adenopathy. One patient with BCL and anterior adenopathy had co-existing submandibular involvement.

Table IV

Comparison of demographic characteristics and laboratory values obtained prior to IVIG treatment in subjects with NFKD and typical KD treated by tenth day of illness

Clinical and laboratory characteristics	NFKD, (n = 53) [*]	Typical KD (n = 287) [†]	P
Age, years, median (IQR)	4.2 (2.7–5.4)	2.0 (0.9–3.8)	<.0001
Males, n (%)	30 (57)	182 (63)	.4
Illness day at diagnosis, days, [‡] median (IQR)	6 (5–7.5)	5 (4–7)	.1
WBC count, ×10 ⁹ cells per L, median (IQR)	14.5 (11.7–17.6)	13.4 (10.4–17.3)	.2
ANC, ×10 ⁹ cells per L, median (IQR)	10.8 (8.4–13.7)	8.3 (6.3–11.3)	<.0001
ABC, ×10 ⁹ cells per L, median (IQR)	1.7 (0.6–2.7)	1.7 (0.8–2.9)	1.0
Hemoglobin Z-score, SD units, median (IQR)	−1.6 (−2.3 to −0.4)	−1.2 (−2.1 to −0.3)	.1
Platelet count, ×10 ⁹ cells per L, median (IQR)	385 (293–487)	396 (307–476)	.7
ESR, mm/h, median (IQR)	75 (60–116)	58 (40–74)	<.0001
CRP level, mg/dL, median (IQR)	13.0 (7.1–21.9)	7.4 (4.5–14.4)	.001
ALT level, U/L, median (IQR)	30 (19–94)	39 (21–113)	.4
GGT level, U/L, median (IQR)	44 (23–119)	43 (18–130)	.7
Albumin level, g/dL, median (IQR)	3.7 (3.3–3.9)	3.8 (3.4–4.1)	.2
Urinary WBC, cells/mcL, median (IQR)	31 (13–63)	19 (8–78)	.1
Coronary Z-worst, SD units, median (IQR)	1.6 (1.0–2.3)	1.6 (1.1–2.8)	.4
Coronary artery lesion, n (%)	10/44 (23)	77/253 (30)	.4
IVIG resistance, n (%)	8/43 (19)	51/238 (21)	.8

WBC, white blood cell; ANC, absolute neutrophil count; ABC, absolute band count; SD, standard deviation; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ALT, alanine transaminase; GGT, γ -glutamyl transpeptidase; IVIG, intravenous immune globulin.

^{*}Data availability for NFKD group (total diagnosed at illness day 10, 53): ANC, 52; ABC, 49; ESR, 50; ALT, 50; GGT, 51; albumin 34; urinary WBC, 46; coronary Z-worst and abnormality, 44; IVIG resistance, 43.

[†]Data availability for typical KD group (total diagnosed at illness day 10, 287): WBC, 283; ANC, 282; ABC, 267; hemoglobin, 283; platelets, 283; ESR, 277; CRP, 279; ALT, 264; GGT, 271; albumin 96; urinary WBC, 253; coronary Z-worst and abnormality, 253; IVIG resistance, 238.

[‡]Illness day 1, first calendar day of fever.