Clinical Case Report

Medicine®

OPEN

A case of Kawasaki disease presenting with parotitis

A case report and literature review

Yanchun Li, MD, Qingran Yang, MS, Xiuhua Yu, MD, Hongmei Qiao, MD*

Abstract

Rationale: Kawasaki disease affects multiple organ systems. Its typical symptoms include fever, rash, oropharyngeal mucosal erythema, bilateral non-exudative conjunctivitis, cervical lymphadenopathy, extremity changes, and membranous desquamation of the fingers and toes. In severe cases, cardiovascular, respiratory, musculoskeletal, gastrointestinal, neurological, and genitourinary complications may occur. In the early stage, Kawasaki disease is often manifested by uncommon symptoms, such as pyuria, meningitis, shock, and retropharyngeal or parapharyngeal abscess, which may delay diagnosis and treatment. We have reported a case of Kawasaki disease presenting with mumps and reviewed the clinical features of 14 other similar cases, in order to facilitate the early diagnosis and treatment of this unusual presentation of Kawasaki disease.

Patient concerns: A 10-year-old boy presented with persistent fever and parotitis and was diagnosed with suppurative parotitis. After antibiotic therapy, the parotid swelling reduced, but the fever persisted and other typical symptoms of Kawasaki disease appeared, including bilateral conjunctival hyperaemia, cervical lymphadenopathy, oropharyngeal mucosal erythema, membranous desquamation of the fingers, and left coronary artery widening.

Diagnoses: The patient was diagnosed with Kawasaki disease 12 days after the onset of fever.

Interventions: The patient was administered γ-globulin 1.0 g/kg·d for 2 consecutive days and oral aspirin 5 mg/kg·d.

Outcomes: The left coronary artery returned to a width of 3.8 mm after 1 month and of 3.1 mm after 3 months. The dose of aspirin was reduced to 3 mg/kg·d after 2 months and to 1.5 mg/kg·d after 3 months.

Lessons: Physicians should be aware that Kawasaki disease may develop after parotitis.

Abbreviations: CRP = C-reactive protein, ESR = erythrocyte-sedimentation rate.

Keywords: Kawasaki disease, literature review, parotitis

1. Introduction

Kawasaki disease is a type of systemic vasculitis presenting with fever, rash, bilateral nonexudative conjunctivitis, erythema of the oral and pharyngeal mucosa, cervical lymphadenopathy, and extremity changes. However, some patients present with less-common symptoms such as pyuria, meningitis, shock, and retropharyngeal or parapharyngeal abscess[1] instead of the above typical symptoms. These unusual presentations often result in a delay in the diagnosis. One such unusual presentation of Kawasaki disease is parotitis.

Thus far, 2 cases of Kawasaki disease presenting with mumps have been reported in the United States (1987, 2008),[2,3] 1 in South Korea (2009),[4] 1 in Japan (2017),[5] and 10 in China (2009, 2011, 2013, 2017).[6–9] However, most of these articles only reported the symptoms without discussing the relationship between mumps and Kawasaki disease. It has been proposed that parotitis may present as the first symptom of Kawasaki disease since it has been hypothesized that infectious agents associated with Kawasaki disease trigger a complex and incompletely understood cascade of inflammation in susceptible children.[5] Furthermore, the mumps virus was identified using serological tests in 1 patient with Kawasaki disease.[4] Moreover, intra-salivary gland arteritis in one-third of the patients and periductal and interacinar infiltration of lymphocytes and mononuclear cells in the salivary gland in 81% was described in a series of 37 autopsies in patients with Kawasaki disease in Japan by Amano et al. Salivary gland fibrosis was identified in those who died long after the onset of the disease.[10] Pathological studies have suggested that small-vessel vasculitis lesions of Kawasaki disease

Editor: N/A.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Written informed consent was obtained from the patient's parents for the publication of this case report and the accompanying images.

The authors declare that they have no conflict of interest.

Department of Pediatric Respiratory Medicine, The First Hospital of Jilin University, Changchun, Jilin Province, China.

* Correspondence: Hongmei Qiao, Department of Pediatric Respiratory Medicine, The First Hospital of Jilin University, Changchun 130021, Jilin Province, China (e-mail: 2670132366@qq.com).

Medicine (2019) 98:22(e15817)

Received: 16 December 2018 / Received in final form: 15 April 2019 / Accepted: 29 April 2019

http://dx.doi.org/10.1097/MD.0000000000015817

can affect the parotid gland, which may be the pathological basis of mumps lesions in Kawasaki disease.[10] Some scholars[2,3] consider that parotitis should be added to the already lengthy list of associated findings in Kawasaki syndrome.

Here, we present another case of Kawasaki disease occurring after parotitis in a 10-year-old child and summarize the features of all cases of Kawasaki disease presenting with mumps that have been reported in the literature. We hope that our findings will provide a basis for clinicians to facilitate early diagnosis and treatment.

2. Case report

A 10-year-old boy was admitted to our hospital because of fever since 5 days and painful swelling of the left ear since 4 days. He did not have a history of mumps exposure. A physical examination revealed a tender swelling of the left ear and the surrounding tissue, limited mobility of the mandible, and elevated body temperature. Enlarged lymph nodes could be palpated on the right side of the neck; they were approximately 1.5 cm wide and were not tender. Other findings included limited mouth opening, throat congestion, and absence of a skin rash or purulent secretions in the parotid duct opening. The respiratory rate was 18 beats/min, and the breath sounds were clear, without any wet or dry rales. The heart rate was 96 beats/min, without any murmurs. The abdomen was soft and without tenderness, rebound tenderness, or muscle tension. A neurological examination revealed no positive signs. Blood examination demonstrated the following: white blood cells, 26.29×10^9/L; neutrophils, 86%; lymphocytes, 5%; erythrocytes, 4.35×10^{12}/L; haemoglobin, 119 g/L; platelets, 336×10^9/L; C-reactive protein (CRP), 87.47 mg/L; erythrocyte-sedimentation rate (ESR), 76 mm/h; and fibrinogen, 8.40 g/L. Liver function, myocardial enzymes, renal function, and lipase, amylase, and procalcitonin levels were normal. Negative results were obtained on 5 Epstein-Barr virus, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* antibody assays. Neck ultrasonography showed changes in the left parotid gland with bilateral enlargement of the submandibular lymph nodes. The patient was diagnosed with suppurative parotitis. He was treated with ceftriaxone sodium at 80 mg/kg·d for 5 days and cefminox at 60 mg/kg·d for 7 days, but developed bilateral conjunctival hyperemia on the next day after hospitalization (6th day after the onset of fever). He was therefore also diagnosed with conjunctivitis at this point. By 5 days after the development of conjunctivitis, the parotid swelling reduced, and color Doppler ultrasonography showed no abnormalities in the parotid gland. However, the patient continued to have fever, and routine blood examination showed the following: white blood cells, 14.88×10^9/L; neutrophils, 72%; lymphocytes, 17%; hemoglobin, 124 g/L; platelets, 412×10^9/L; high-sensitivity-CRP, 127.00 mg/L; ESR, 76 mm/h; and fibrinogen, 7.90 g/L. All the laboratory results have been summarized in Table 1. Antibiotic treatment was therefore continued and the fever was relieved on the 6th day after admission. However, the patient then developed redness of the oral mucosa and dry, chapped lips lip mucosal blush, dry, and chapped, together with mild scaling on the bilateral thumb tips on the 7th day after admission. Colour Doppler ultrasonography indicated mild widening of the left coronary artery (4.2 mm). Therefore, the patient was diagnosed with Kawasaki disease and was administered γ-globulin 1.0 g/kg·d for 2 consecutive days and oral aspirin from 5 mg/kg·d decreased to 3 mg/kg·d after 2 months. The left coronary artery returned to the width of 3.8 mm after 1 month and of 3.1 mm after 3 months. Thus, the amount of aspirin was reduced to 1.5 mg/kg·d.

3. Review of literature

We searched the PubMed and CNKI databases using the keywords "Kawasaki disease" and "parotitis." Articles published since 1980 were included in the search. According to the relevant literature, 14 other cases of Kawasaki disease occurring after parotitis have been reported (Table 2).[2–9] Together with our report, this includes 10 boys and 5 girls with a mean age of 3.3 years (range, 3 months to 10 years). In these 15 patients, the

Table 1

Laboratory results.

Test		4th d	8th d	Reference range
Blood routine	White blood cells	26.29×10^9/L	14.88×10^9/L	$4–10 \times 10^9$/L
	Neutrophils	86%	72%	50%–70%
	Lymphocytes	5%	17%	20%–40%
	Erythrocytes	4.35×10^{12}/L		$3.5–5 \times 10^{12}$/L
	Haemoglobin	119 g/L	124 g/L	110–150 g/L
	Platelets	336×10^9/L	412×10^9/L	$100–300 \times 10^9$/L
C-reactive protein		87.47 mg/L	127.00 mg/L	<3 mg/L
Erythrocyte-sedimentation rate		76 mm/h	76 mm/h	<15 mm/h
Fibrinogen		8.40 g/L	7.90 g/L	2–4 g/L
Etiology	Epstein-Barr virus antibody assay	Negative		
	Mycoplasma pneumoniae antibody assay	Negative		
	Chlamydia pneumoniae antibody assay	Negative		
Liver function		Normal		
Myocardial enzymes		Normal		
Renal function		Normal		
Lipase		Normal		
Amylase		Normal		
Procalcitonin levels		Normal		
Neck ultrasonography		Changes in the left parotid gland with bilateral enlargement of the submandibular lymph nodes		

Table 2

Characteristics of the 15 patients who developed parotitis followed by Kawasaki disease.

Case	Sex	Age, yr	IFPS, d	Side	PD, d	Imaging	History	CKD	WBC, $\times 10^9$/L	Neutrophils (%)	Hb, g/L	PLT, $\times 10^9$/L	CRP, mg/L	ESR, mm/h	CAD	Other complications	γ-Gb dose	Fever subsided	Dx, d
1[†]	M	10	2	L	10	USG		Y	31	0.88	138	325	119	76	L	N	1.0 g/kg × 2	Before γ-Gb treatment	12
2[7]	M	5	3	L/R	*	*	Mumps contact history	Y	20.98	0.9598	122.49	498.6			N	N	*	*	13
3[6]	M	0.25	2	R	6	USG	Purulent secretion in parotid duct	N	16.6	0.451	90	462	239.97	20	R	*Mycoplasma pneumoniae* infection, impaired liver function	2 g/kg × 1	1 d after γ-Gb treatment	12
4[8]	F	1.33	1	*	5	*	*	Y	12.7	0.724	82	160	31.1	55	N	Cholecystitis, bronchopneumonia, impaired liver function	0.5 g/kg × 5	4 d after γ-Gb treatment	6
5[8]	F	5	1	*	9	*	*	Y	16.88	0.76	97	529	2.8	41	N	Cholecystitis, pancreatitis, impaired liver function	0.4 g/kg × 4	1 d after γ-Gb treatment	11
6[9]	M	1.92	2	L	7	USG	*	No	19.2	*	*	372	34.89	61	N	N	1.0 g/kg × 2	2 d after γ-Gb treatment	12
7[9]	M	5	3	L/R	8	USG	*	Y	26.8	*	*	368	52	63	N	Suppurative tonsillitis, pancreatitis	Unused	-	6
8[9]	M	1.25	2	L	7	USG	*	Y	23.2	*	*	321	86	40	L	N	1.0 g/kg × 2	2 d after γ-Gb treatment	10
9[9]	F	5	4	L	10	USG	*	Y	21.7	*	*	320	130	57	N	Adenomesenteritis	1.0 g/kg × 2	Insensitive, hormone therapy was added	6
10[9]	M	7	2	R	8	USG	*	Y	16	*	*	202	21.37	29	L	Suppurative tonsillitis, mycoplasma pneumonia, impaired liver function, cardiac insufficiency	1.0 g/kg × 2	2 d after γ-Gb treatment	7
11[9]	M	0.83	2	L	6	USG	*	N	18.23	*	*	498	62	45	R	No	1.0 g/kg × 2	2 d after γ-Gb treatment	11
12[5]	M	1	1	R	*	CT	Parotitis antibody negative	Y	28.2	0.67	*	*	7.73		N	N	2 g/kg × 1	1 d after γ-Gb treatment	5
13[4]	M	0.25	1	L	*	CT	Parotitis antibody positive	Y	11.82	0.765	97	266	82.7		L	N	1.0 g/kg × 2	Sustained fever	9
14[2]	F	1.67	1	L	*	CT	*	Y	36	0.67	107	637	4	60	N	Pancreatitis	2 g/kg × 1	<1 d after γ-Gb treatment	13
15[3]	F	4	2	L/R	12	*	*	Y	13.7	0.52	108	397	1:08	57	N	Pancreatitis	*	*	*
Average	M:F, 2:1	3.3	1.93		8				20.8673	0.711089	105.1863	382.5429	67.19692	50.33333					9.5

γ-Gb = gamma-globulin dose and number of doses, CAD = coronary artery dilation, CKD = complete Kawasaki disease, CRP = C-reactive protein, CT = computed tomography, Dx = timing of diagnosis measured in days since the onset of fever, ESR = erythrocyte-sedimentation rate, Hb = hemoglobin, IFPS = interval between fever and appearance of parotid swelling, L = left, N = no, PD = timing of parotid detumescence measured in days since the onset of fever, PLT = platelet count, PS = parotid swelling, R = right, USG = ultrasonography, WBC = white blood cell count, Y = yes.

[*] Not mentioned in the reference.

[†] Present study.

parotid swelling developed on average 1.93 (1–4) days after the onset of fever. The swelling was bilateral in 3 patients, right-sided in 3 patients, and left-sided in 7 patients; the laterality was not mentioned in 2 cases. One patient had a history of mumps contact, and another had purulent secretions in the parotid duct opening. One child tested positive for the mumps antibody. In most children, the parotid swelling subsided within 6 to 12 days (mean, 8 days) after antibiotic treatment, but the fever continued unabated and the symptoms of Kawasaki disease appeared. According to the diagnostic criteria,[1] 3 patients had incomplete Kawasaki disease, while the rest had complete Kawasaki disease. The mean time from onset to the definite diagnosis of Kawasaki disease was 9.5 days (range, 5–13 days). Nine patients had no coronary artery dilation, 2 exhibited right-sided dilation, and 4 exhibited left-sided dilation. Other complications included 2 cases of *M pneumoniae* infection, 1 case of bronchopneumonia, 4 cases of hepatic injury, 2 cases of cholecystitis, 4 cases of pancreatitis, 2 cases of purulent tonsillitis, 1 case of mesenteric lymphadenitis, and 1 case of cardiac insufficiency. In 2 patients, the fever was relieved on the 9th and 10th day without γ-globulin treatment. The remaining children received γ-globulin treatment after the diagnosis. Two of these patients still got fever after γ-globulin treatment; 1 patient, the fever was relieved after 4 days of γ-globulin treatment (500 mg/kg·d γ-globulin for 5 days); the other 10 patients, the fever was relieved within 2 days of γ-globulin treatment (most of them received 1 g/kg·d for 2 days or 2 g/kg·d for 1 day).

4. Discussion

The etiology of Kawasaki disease is unknown. The condition is associated with diverse clinical features. The diagnosis of "classic" Kawasaki disease is based on the presence of fever for ≥5 days along with the presence of at least 4 of the 5 principal clinical features:

(1) erythema and cracking of the lips, strawberry tongue, and/or erythema of the oral and pharyngeal mucosa,
(2) bilateral bulbar conjunctival injection without exudate,
(3) rash,
(4) erythema and edema of the hands and feet in the acute phase and/or periungual desquamation in the subacute phase, and
(5) cervical lymphadenopathy (≥1.5 cm in diameter), usually unilateral.[1]

Patients who meet the above diagnostic criteria are said to have complete Kawasaki disease (also referred to as typical or classic Kawasaki disease). Patients who do not have sufficient principal clinical findings may be diagnosed with incomplete Kawasaki disease (also referred to as atypical Kawasaki disease).[1] In certain cases, the onset of Kawasaki disease is heralded by a completely different systemic clinical manifestation such as shock,[11] ventricular arrhythmia,[12] pyuria, or meningitis,[1] which is followed by the development of more typical symptoms such as rash, red eyes, and red lips. However, these symptoms are often attributed to an antibiotic reaction, and this may lead to the diagnosis of Kawasaki disease being missed or delayed. Therefore, a summary of such atypical presentations of Kawasaki disease will be helpful to increase physicians' awareness of Kawasaki disease and to avoid delayed diagnoses. In this article, we report a case of Kawasaki disease occurring after parotitis in a 10-year-old child and summarize the clinical features of 14 similar cases reported previously in order to increase awareness of the fact that Kawasaki disease could develop after parotitis.

Thus far, a total of 15 cases of parotitis followed by Kawasaki disease have been reported. In these 15 patients, the parotid swelling disappeared after antibiotic treatment. However, the fever was sustained in most patients, and the symptoms of Kawasaki disease, such as conjunctival hyperemia, chapped red lips, perianal desquamation, and hand and foot sclerosis, appeared later. Laboratory examination demonstrated continued elevated white blood cell count and CRP level, suggesting that local parotid inflammation can be controlled, but the vasculitis is gradually and progressively aggravated. Some children also developed other common complications, such as pancreatitis, cholecystitis, and impaired liver function. The clinical and epidemiological characteristics of Kawasaki disease suggest a potential infectious cause.[13] It is hypothesized that infectious agents related to Kawasaki disease trigger an incompletely understood cascade of inflammation in susceptible children.[14] Owing to the lack of awareness of the possibility of Kawasaki disease developing after parotitis, the average diagnosis time was 9.5 days. Therefore, when children with parotitis present symptoms of Kawasaki disease, the possibility of Kawasaki disease should be considered, and cardiac echocardiography should be performed to reduce the delay in diagnosis.

Among the 15 cases of parotitis complicated by Kawasaki disease, we found no specific clinical features that were characteristic of Kawasaki disease and common to all patients. The sex ratio of Kawasaki disease in the general population is 1.5:1, with an average age at onset of 3 years.[1] In our cohort of parotitis patients, there were more male children than female children, and the sex ratio was 2:1. Kawasaki disease can be divided into complete and incomplete types based on the clinical manifestations. The incidence of coronary artery dilation was 40%, which is similar to that observed in other Kawasaki disease patients.[1] Other complications included pancreatitis (26.7%), liver damage (26.7%), bronchial pneumonia (20%), cholecystitis (13.3%), purulent tonsillitis (13.3%), mesenteric lymphadenitis (6.7%), and cardiac insufficiency (6.7%). In our review, 13.3% children did not respond to γ-globulin, which is similar to the data from other Kawasaki disease patients.[14] Most children became afebrile within 2 days after γ-globulin treatment.

In conclusion, physicians should be aware that Kawasaki disease may develop after parotitis.

Author contributions

Data curation: Qingran Yang.
Formal analysis: Xiuhua Yu.
Project administration: Hongmei Qiao.
Writing – original draft: Yanchun Li.
Writing – review and editing: Hongmei Qiao.
Yanchun Li orcid: 0000-0001-7491-9982.

References

[1] McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation 2017;135:e927–99.
[2] Douvoyiannis M, Belamarich PF, Litman N. Parotitis and Kawasaki disease in a child with Noonan syndrome. Pediatr Infect Dis J 2008;27:89–90.

[3] Seyedabadi KS, Howes RF, Yazdi M. Parotitis associated with Kawasaki syndrome. Pediatr Infect Dis J 1987;6:223.
[4] Do HJ, Baek JG, Kim HJ, et al. Kawasaki disease presenting as parotitis in a 3-month-old infant. Korean Circ J 2009;39:502–4.
[5] Yokoyama K. Parotitis as an initial symptom of Kawasaki disease. Case Rep Paediatr 2017;2017:5937276.
[6] Han D, Chen W. A 3-month-old baby presented with Kawasaki disease, acute suppurative parotitis and pneumonia. Clin Res 2017;25:125.
[7] Chen K. A case with Kawasaki disease was misdiagnosed as mumps. Chin Commun Physician 2011;34:245.
[8] Zhang L. Two cases with Kawasaki disease was misdiagnosed as parotitis, cholecystitis and septicemia. Heilongiiang Med J 2009;22: 913–4.
[9] Qian W, Yan W, Lu H, et al. Six cases with Kawasaki disease and parotitis. J Clin Pediatr 2013;31:393–4.
[10] Amano S, Hazama F, Kubagawa H, et al. General pathology of Kawasaki disease. Acta Pathol Jpn 1980;30:681–94.
[11] Gamez-Gonzalez LB, Moribe-Quintero I, Cisneros-Castolo M, et al. Kawasaki disease shock syndrome: Unique and severe subtype of Kawasaki disease. Pediatr Int 2018;60:781–90.
[12] Hu F, Shi X, Li Y, et al. Ventricular arrhythmia as an initial sign in acute Kawasaki disease: a case report. Medicine (Baltimore) 2018;97:e0641.
[13] Shulman ST, Rowley AH. Kawasaki disease: insights into pathogenesis and approaches to treatment. Nat Rev Rheumatol 2015;11:475–82.
[14] Benseler SM, McCrindle BW, Silverman ED, et al. Infections and Kawasaki disease: implications for coronary artery outcome. Pediatrics 2005;116:e760–6.