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CASE BASED REVIEW

Kawasaki disease and influenza—new lessons from old associations

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Abstract

Kawasaki disease (KD), an enigmatic medium vessel vasculitis, presents as an acute febrile illness predominantly affecting young children. KD appears to be a hyper-inflammatory response elicited by environmental or infectious agents (including respiratory viruses) in genetically predisposed individuals. Numerous reports from the current era of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic have described the occurrence of KD/KD-like illness in close temporal proximity to SARS-CoV-2 infection or exposure. Notably, KD has been reported in association with H_1N_1-pdm09 virus that caused the previous pandemic a decade ago. Non-H_1N_1 influenza infections as well as influenza vaccination have also been reported to trigger KD. Herein, we report a case of H_1N_1-pdm09 influenza who developed KD. We review the published literature on influenza infection or vaccination triggering KD. This may help in a better understanding of the KD/KD-like illness associated with SARS-CoV-2. Besides, we also evaluate the safety of aspirin in influenza-triggered KD as aspirin administration in children with influenza is associated with the risk of development of Reye syndrome.

Keywords Aspirin · Coronavirus · COVID-19 · Influenza · Kawasaki disease · SARS-CoV-2 · Vaccine

Abbreviations

CAAs	Coronary artery abnormalities
CPAP	Continuous positive airway pressure
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
FiO_2	Fraction of inspired oxygen
H_1N_1-pdm09	Influenza A (H_1N_1) virus responsible for 2009 pandemic
H_1N_1-KD	Kawasaki disease associated with H_1N_1 influenza infection
IVIg	Intravenous immunoglobulin
KD	Kawasaki disease
KDSS	KD shock syndrome
NT-proBNP	N-terminal pro-B-type natriuretic peptide
PCR	Polymerase chain reaction
RT-PCR	Reverse-transcription polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SpO_2	Oxygen saturation on pulse oximetry

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Introduction

Kawasaki disease (KD) is an acute febrile vasculitic disorder of childhood predominantly affecting medium size arteries with a predilection for coronary arteries. KD is now the leading cause of acquired heart disease in children worldwide [1]. The illness was first reported by Dr. Tomisaku Kawasaki, a Japanese pediatrician, in 1967 when he reported a series of 50 patients [2]. Classic or 'complete' KD clinically presents with fever for at least 5 days with four of the following clinical

manifestations: edema of hands and feet in the acute stage and/or subacute periungual skin peeling of fingers and toes, polymorphous exanthematous rash, non-exudative bilateral bulbar conjunctival injection, orolabial changes, and cervical lymphadenopathy. 'Incomplete' KD is diagnosed when the full diagnostic criteria of KD are not met [3]. The most dreaded complication in KD is cardiac involvement leading to development of coronary artery abnormalities (CAAs). KD shock syndrome (KDSS) is a condition in which patients present with diminished left ventricular function due to myocarditis. KDSS is often accompanied by CAAs [4].

The exact etiology of KD remains unknown. It appears that KD is a hyper-inflammatory response in a genetically predisposed individual that is possibly triggered by several environmental factors or infectious agents including respiratory viruses [5]. In the current novel coronavirus (SARS-CoV-2) pandemic, KD/KD-like illness has been strongly associated with SARS-CoV-2 infection or exposure in children [6–8]. Similar to KD, evidence suggests that KD-like illness (post-SARS-CoV-2) to be a result of aberrant immune reaction rather than the direct effect of viral infection [6–8]. This finding has renewed research interest into the role played by infections, especially respiratory viruses, in triggering anomalous inflammatory responses.

Interestingly, KD has also been reported in association with the H_1N_1-pdm09 virus that was responsible for the previous pandemic a decade ago [9–12]. Besides, there are reports of KD in association with non-H_1N_1 influenza infections [13–21] and also influenza vaccination [22–24]. We report herein a case of H_1N_1-pdm09 influenza who developed KD (H_1N_1-KD). We also review the published literature on the subject. Additionally, we highlight the similarities and dissimilarities between KD triggered by influenza infection and KD/KD-like illness triggered by SARS-CoV-2. This may help in a better understanding of this illness in particular and KD in general.

In this review, we also evaluate the safety of aspirin in influenza-triggered KD. Given the risk of development of Reye syndrome, when aspirin is administered in children with influenza, this assessment is of crucial clinical significance.

Search strategy

Two authors (AZB and AM) independently retrieved articles on influenza and KD. Both influenza A (H_1N_1 and non-H_1N_1) and influenza B infections were included. Besides, articles describing KD as an adverse event following influenza immunization were also included in the analysis. Literature search was performed using PubMed/Medline and Google Scholar databases. Keywords included in the search were 'Kawasaki disease' and 'influenza'; 'Kawasaki disease' and 'H1N1'; 'Kawasaki disease' and 'virus'; 'Kawasaki disease' and 'vaccine'; 'Kawasaki disease' and 'pandemic'; and 'vasculitis' and 'vaccine'. All English language articles were included. Articles in other languages with English language abstracts or titles were also included. References of the articles included were also checked to obtain additional articles. Reports describing infections or vaccinations associated with KD were also searched for data regarding influenza infection and vaccination.

Details of our patient and data obtained from the literature search were entered into a predesigned Excel spreadsheet (Microsoft Office 2010) to perform a combined analysis. Data regarding age, gender, clinical features (relating to KD), duration of fever before presentation and intravenous immunoglobulin (IVIg) treatment, laboratory investigations, coronary echocardiography, and treatment outcome were included.

Data on H_1N_1 and KD, influenza (A or B or unspecified) and KD, and influenza vaccination and KD were analyzed separately to derive the results. Values of parameters have been expressed as mean (range) [y_a] or percentages [$n \times 100$], with 'n' used to denote the number of cases (x) out of the cohort examined (y) [$n = x/y$]. The subscript 'a' in [y_a] denotes the cohort included for analysis where $a = 1$ for H_1N_1 and KD, $a = i$ for influenza and KD, and $a = v$ for influenza vaccination and KD.

Case presentation

In February 2019, a 9-year-old girl presented with fever for 7 days (maximum up to 104 °F). She developed a non-productive cough on day 2 of illness and fast breathing on day 3 of illness. She was treated with oral antimicrobials at a local healthcare facility. However, she persisted to have fever and respiratory distress for which she was referred to our institute.

On examination, she had pallor, tachypnea (respiratory rate of 44 per minute), chest wall retractions, bilateral coarse crepitations, and hypoxia (SpO_2—88% on room air). Investigations showed leukopenia (total leucocyte count of 1.8×10^9/L) and thrombocytopenia (platelet count 87×10^9/L ($150–400 \times 10^9$/L)). Chest radiograph revealed patchy consolidation predominantly involving the right middle and lower lobes (Fig. 1a). Nasopharyngeal swab showed H_1N_1-pdm09 virus on reverse-transcription polymerase chain reaction (RT-PCR) test. She required respiratory support in the form of non-invasive continuous positive airway pressure (CPAP) therapy (initial pressure: 6 cm of water, initial FiO_2: 60%). She was treated with oral oseltamivir (60 mg twice daily for 5 days). This resulted in improvement of respiratory distress and weaning off from CPAP/O_2 therapy. The leukocyte count and platelet count also normalized (Fig. 1c).

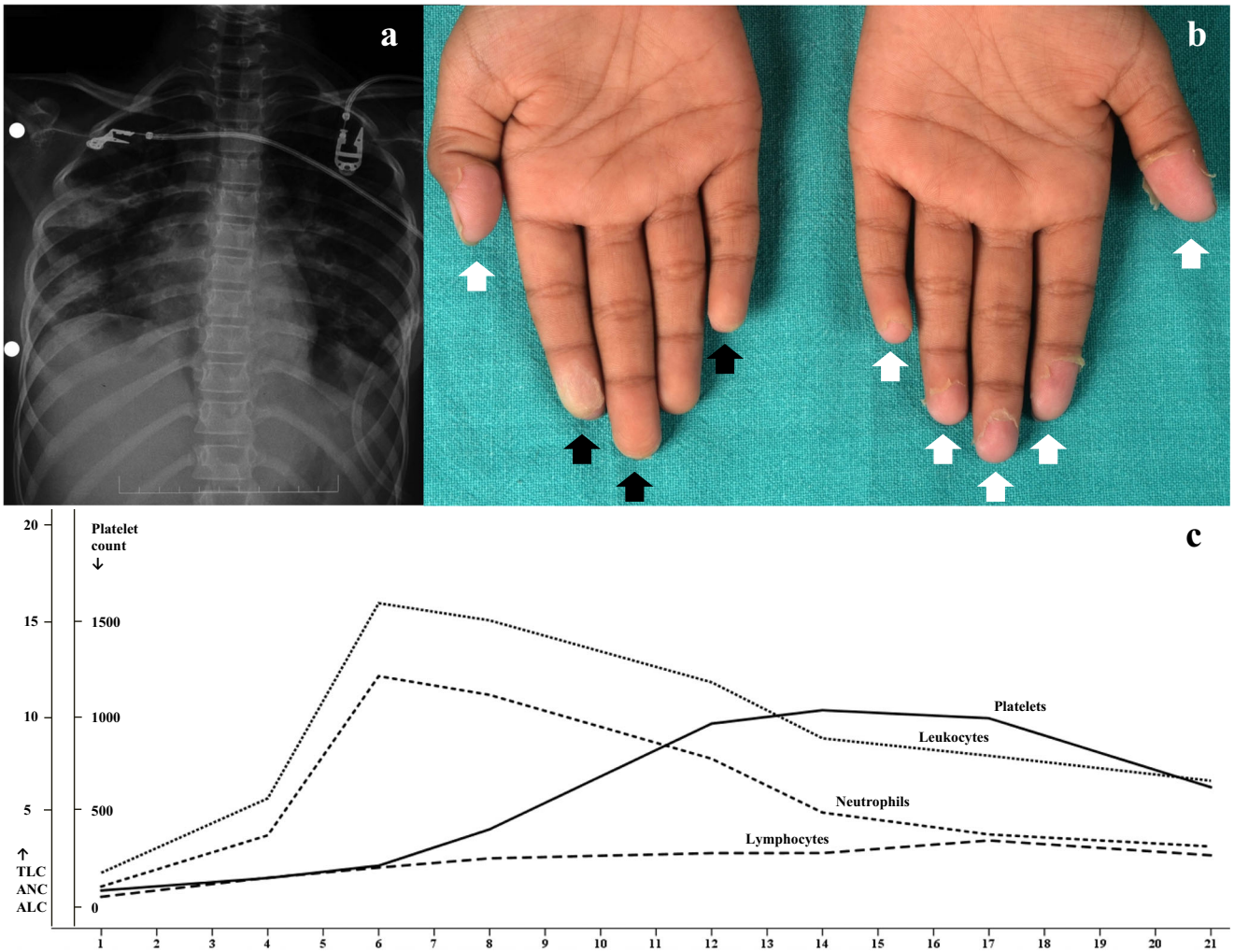

Fig. 1 Kawasaki disease triggered by H_1N_1-pdm09 influenza infection. **a** Chest radiograph showing patchy areas of consolidation in upper, middle, and lower lobes of right lung with collapse of the ipsilateral middle lobe. Left paracardiac infiltrates are also noted. **b** Characteristic periungual peeling (white arrows) noted in both hands; premonitory coarsening of skin of the finger pulps just beginning to peel is also noted (black arrows) [25]. c Trend of parameters on complete blood count in index child (*y*-axis: parameter value ($\times 10^9$/L), *x*-axis: day of hospitalization; abbreviations: TLC: total leukocyte count, ANC: absolute neutrophil count, and ALC: absolute lymphocyte count)

However, she continued to have fever, developed neutrophilic leukocytosis, and progressive thrombocytosis (Fig. 1c). Elevated erythrocyte sedimentation rate (ESR) was 71 mm in the 1st hour (normal < 20) and C-reactive protein (CRP) was 22 mg/L (normal < 6). She was empirically treated with intravenous antimicrobials (ceftriaxone and cloxacillin) considering a possibility of secondary bacterial infection. Fever, however, persisted. Repeat blood and sputum cultures were noncontributory; multiple sputum specimens for acid-fast bacilli staining and mycobacterial cartridge-based nucleic acid amplification test were negative; urine microscopy was normal, and urine culture was sterile. Her biochemical investigations were normal except for mild elevations in alanine and aspartate aminotransferases (110 and 55 U/L, respectively [normal < 45]) (Supplementary Table 1).

On day 11 of hospital stay, she developed characteristic periungual skin peeling (Fig. 1b). Incomplete KD was considered given the findings of persistent fever, periungual peeling, neutrophilic leukocytosis, thrombocytosis, and elevated inflammatory parameters (ESR, CRP) (Fig. 1c). Intravenous immunoglobulin (2 g/kg) was administered and this resulted in resolution of fever. Aspirin (3 mg/kg/day) was given during the acute stage and continued for 6 weeks. 2D transthoracic echocardiography showed normal coronary arteries and myocardial function throughout her illness. N-terminal pro-B-type natriuretic peptide (NT-proBNP) also remained normal (6.81; 19.53 pg/mL [normal < 125]). She is currently well at 1.5 years of follow-up.

Results

We reviewed 16 articles describing influenza infection or vaccination in association with KD. Of these, six were

retrospective studies describing one or more cases and the rest (10) were individual case reports describing a single patient. Complete clinical and laboratory details of patients with influenza infection-associated KD were available in all case reports. However, only one among the retrospective studies had complete details.

H_1N_1 influenza and KD

To date, five case reports (including ours) specifically describe H_1N_1-KD (total patients [y_1] = 5) (Table 1). Mean age at presentation was 41 months (5–108) [y = 5] and 80% [n = 4/5] were males. Excluding our case (who presented at 109 months), mean age at presentation was 24 months. Mean duration of fever before presentation was 7 days (3–9) [y_1 = 5] and IVIg was administered at a mean of 13 days of fever (9–18) [y_1 = 5]. Incomplete KD was diagnosed in 60% [n = 3/5]. All five children had a good response to IVIg. Dilatation of the left main coronary artery developed in 40% [n = 2/5] and it normalized on follow-up. Aspirin in doses varying from 3 to 50 mg/kg/day was used in all five patients; however, Reye syndrome was not documented in any of these cases.

Non-H_1N_1 influenza and KD

Influenza infection and concomitant KD have been reported in about 38 patients to date (4 case reports and 5 retrospective studies)—21 with influenza A and 11 with influenza B, and in the remaining 6, data on type of influenza virus were unavailable (Table 2). Mean age at diagnosis was 24 months (2–48) [y_i = 19] with all cases occurring before 48 months of age. Boys constituted 63% of this cohort (n = 12/19). Incomplete KD was diagnosed in 32% (n = 6/19). Coronary artery dilatations were noted in 50% (n = 9/18). IVIg resistance was noted in 18% (n = 3/17); this was managed with second dose IVIg in one patient [13]. Treatment details of the other two patients were not available [17]. In the influenza infection and KD cohort, two patients did not receive IVIg as the fever resolved spontaneously within 1 week. Aspirin was used in at least 53% of patients (n = 20/38) with dosage details available for five patients. In one patient, aspirin doses of up to 80–100 mg/kg/day were used [15], whereas, the other four received only antiplatelet doses [16]. Reye syndrome was not reported in any of the influenza patients with KD.

Influenza vaccination and KD

Influenza vaccination has been reported to trigger KD in 2 case reports (1 case each), in addition to a large multicentric retrospective study reporting approximately 20 cases [24]. The two cases (reported in the two case reports) developed KD after 1 and 8 days of influenza vaccination, respectively; however, data regarding temporal correlation of KD with vaccination or the clinical/laboratory details of individual patients were not available in the large multicentric study. Incomplete KD or CAAs were not reported in these patients. However, one of the patients had myocarditis (low ejection fraction and elevated NT-proBNP) with IVIg resistance that was successfully managed with a second dose of IVIg. Both patients had neutrophilia and elevated CRP (~ 150 mg/L) and received aspirin in doses of up to 30 and 50 mg/kg/day, respectively (Table 3).

Discussion

Kawasaki disease is a systemic inflammatory disease of unknown etiology; however, an infectious trigger has been incriminated in etiopathogenesis of this condition. Positive respiratory virus PCR for influenza, parainfluenza, adenovirus, rhinovirus, enterovirus, human bocavirus, and human metapneumovirus has been reported in children with KD [19, 26]. Autopsy studies have also implicated a specific RNA respiratory virus in pathogenesis of KD. Role of respiratory viruses in triggering KD has generated much interest recently due to KD/KD-like as being reported in association with the current SARS-CoV-2 pandemic.

We report a child with an uncommon association of H_1N_1 influenza being complicated with KD. The index child was diagnosed as H_1N_1-influenza at admission (day 1 of hospitalization) and, subsequently, KD was diagnosed on day 11 of hospital stay. The diagnostic procedures (summarized in Supplementary Table 1) performed in index child, although not exhaustive, could not identify any other potential trigger. Based on the close temporal proximity and absence of a suitable alternative explanation, a final diagnosis of influenza (H_1N_1)-triggered KD was proffered [27].

We also performed a detailed literature review of available reports of KD triggered by influenza infection or vaccination. From an epidemiological perspective, influenza infection in context of KD has been reported from North America, Europe, and East Asia—our report is the first from South Asia. Reports from Japan on influenza infection or vaccination triggering KD are sparse (two case reports describing one case each) [14, 22]. This is in stark contrast to the fact that Japan has the highest incidence of KD in the world [28]. In fact, epidemiological studies from Japan have described a suppressive effect of influenza outbreaks on incidence of KD [29]. Genetic influences may seem to be the most logical explanation; however, it is still a work in progress.

Mean age of onset for influenza-KD is 2 years and this is similar to KD as a whole. Index child with H_1N_1-KD was 9 years old at presentation and is among the very few influenza-KD cases that have been reported in children above 5. As many as 50% patients with influenza-KD develop CAAs. This could be due to the fact that influenza-KD is often

Table 1 H_1N_1 influenza infection and Kawasaki disease—clinico-laboratory features, echocardiographic findings, and treatment profile of patients reported till date

Authors, country [reference]	Strain, age (months), gender	Investigations at admission			Day of admission, IVIg therapy	Clinical features		Coronary artery status on echocardiography, (comments)	Aspirin max. dose (mg/kg/day)
		WCC (ANC/ALC)	Platelet (max.)	ESR (CRP)		Criteria[a]	Non-criteria		
Joshi et al., UK [9]	pdm09, 60, male	16.1 (13.2/2.0)	191 (478)	134 (148)	9, 11	All	Nil	Normal	22.5
Ortigado et al., Spain [10]	pdm09, 11, male	18.72 (NA)	366 (655)	74 (225.7)	5, 9	All except LAP	Echo+	Dilated LMCA, normalized on follow-up	3
Celis et al., Spain [11]	NA, 5, male	10.8 (NA)	NA (720)	57 (200.5)	3, 11	Rash	Perianal peeling	Normal, (concomitant rotavirus infection)	20
Wang et al., China [12]	pdm09, 19, male	11.15 (5.5/3.8)	195 (483)	NA (44.77)	9, 16	Edema	Echo+	Dilated LMCA, normalized on follow-up	30–50
Banday et al., India [present case]	pdm09, 109, female	5.69 (3.8/1.5)	152 (1030)	71 (22.1)	7, 18	Edema	Nil	Normal	3

WCC white cell count ($\times 10^9$ /L), *ANC* absolute neutrophil count ($\times 10^9$ /L), *ALC* absolute lymphocyte count ($\times 10^9$ /L), *Platelet (max.)* platelet count on admission and maximum platelet count ($\times 10^9$ /L), *ESR* erythrocyte sedimentation rate (mm in 1st hour), *CRP* C-reactive protein (mg/L), *IVIg* intravenous immunoglobulin, *pdm09* pandemic 2009, *NA* not available, *LAP* lymphadenopathy, *LMCA* left main coronary artery, *Echo+* coronary artery changes on echocardiography

[a] Criteria manifestations include conjunctival injection, dry cracked lips and/or strawberry tongue, cervical lymphadenopathy, polymorphous skin rash, and extremity changes (edema of hands and feet or periungual peeling) as included in the AHA-2004 criteria for diagnosis of KD

Table 2 Non-H_1N_1 influenza infection and Kawasaki disease—summary of the clinical features, laboratory investigations, and anti-platelet medications employed until date

Authors, country [reference]	Agent (no. of patients), gender	Investigations	Day of IVIg therapy	Clinical features (number)		Coronary artery status on echocardiography (comments)	Anti-platelet therapy given
		WCC (ANC/ALC), *Plat. Ct.*, ESR/CRP		Criteria[a]	Non-criteria		
Sheiko et al., USA [13]	Influenza A (1), male	8.1 [23% bands], *NA*, NA/125	7	All except CI	Echo+	RCA and LAD dilated (IVIg resistance)	Clopidogrel
Asano et al., Japan [14]	Influenza A (1), male	NA	NA	Typical KD	NA	(pancreatitis)	NA
Benseler et al., Canada [15]	Influenza (1), NA	NA	NA	Typical KD	NA	129 KD patients, 42 had concomitant infection	Aspirin
Chang et al., China [16]	Influenza A (2) and B (2), NA	NA	NA	Typical KD in all	NA	226 KD patients, 119 had concomitant infection	Aspirin (LD)
Huang et al., Taiwan [17]	Influenza A (11) and B (4), 9 males	12.35 (6.85/4.31), *402*, 49.79/74.23 {values in mean}	6 (median)	Incomplete KD (6)	Perianal peeling (7), BCG changes (2)	8 patients had CAAs (IVIg resistance in 2)	Aspirin
Jordan-Villegas et al., USA [18]	Influenza A/B (5), NA	NA	NA	NA	NA	251 KD patients, 22 had concomitant infection	NA
Turnier et al., USA [19]	Influenza A (6) and B (3), NA	NA	NA	NA	NA	192 KD patients, 93 had concomitant infection	NA
Jackson et al., USA [20]	Influenza B (1), female	4.8 (2.2/2.2), *NA*, 18/NA	Nil	All except edema	Perianal peeling	Normal (fever for 7 days only, IVIg not given)	Not given
Zahouani et al., USA [21]	Influenza B (1), male	6 (4.5/0.9), *NA*, NA/17.5	Nil	All except LAP	Nil	Normal (fever for 5 days only, IVIg not given)	Not given

WCC white cell count ($\times 10^9$/L), *ANC* absolute neutrophil count ($\times 10^9$/L), *ALC* absolute lymphocyte count ($\times 10^9$/L), *Plat. Ct.* platelet count on admission and maximum platelet count ($\times 10^9$/L), *ESR* erythrocyte sedimentation rate (mm in 1st hour), *CRP* C-reactive protein (mg/L), *CI* conjunctival injection, *Echo+* coronary artery changes on echocardiography, *RCA* right coronary artery, *LD* low dose, *LAD* left anterior descending, *IVIg* intravenous immunoglobulin, *NA* not available, *LAP* lymphadenopathy

[a] Criteria manifestations include conjunctival injection, dry cracked lips and/or strawberry tongue, cervical lymphadenopathy, polymorphous skin rash, and extremity changes (edema of hands and feet or periungual peeling) as included in the AHA-2004 criteria for diagnosis of KD

Table 3 Clinical profile of patients with influenza immunization and Kawasaki disease

Authors, country [reference]	Disease onset after vaccination	Investigations			Day of IVIg therapy	Clinical features		Coronary artery status on echocardiography (comments, no. of cases)	Aspirin max. dose (mg/kg/day)
		WCC (ANC)	Plat. (max)	ESR (CRP)		Criteria[a]	Non-criteria		
Shimada et al., Japan [22]	8 days	24.5 (NA)	NA	NA (145)	~ 5	All	Nil	Normal (−, 1 (female))	30
Jeong et al., South Korea [23]	1 day	12.1 (7.9)	344 (625)	70 (151)	6	All except LAP	BCG site changes, decreased EF	Normal (IVIg resistance, 1 (male))	50
Felicetti et al., multicentric [24]	NA	NA			NA	NA	NA	NA (8% vaccine-related KD due to influenza, ~ 20)	NA

WCC white cell count ($\times 10^9$ /L), *ANC* absolute neutrophil count ($\times 10^9$ /L), *Plat. (max)* platelet count on admission and maximum platelet count ($\times 10^9$ /L), *ESR* erythrocyte sedimentation rate (mm in 1st hour), *CRP* C-reactive protein (mg/L), *LAP* lymphadenopathy, *EF* ejection fraction (cardiac), *IVIg* intravenous immunoglobulin, *NA* not available

[a] Criteria manifestations include conjunctival injection, dry cracked lips and/or strawberry tongue, cervical lymphadenopathy, polymorphous skin rash, and extremity changes (edema of hands and feet or periungual peeling) as included in the AHA-2004 criteria for diagnosis of KD

incomplete. As a result, delays in diagnosis and institution of therapy are understandable, as was the case in our patient as well. Nonetheless, giant aneurysms have not been reported in influenza-KD, and treatment with IVIg has been reported to result in resolution of coronary artery dilatations seen in such cases. Biologics (infliximab, anakinra, and etanercept) and immunosuppressive medications (steroids and ciclosporin) have not been used in patients with influenza-KD.

The American Heart Association 2017 Guidelines have suggested that alternatives to aspirin should be considered in children with influenza and KD. Children on prolonged high-dose aspirin therapy are at risk of Reye syndrome [3]. Majority of patients with influenza-KD reported to date have received aspirin (including doses as high as 80–100 mg/kg/day for a few days) without Reye syndrome being reported. In our case, aspirin in antiplatelet doses was administered. Based on these findings, at least low-moderate doses of aspirin appear to be safe in children with influenza-KD, especially when used for a short duration. However, more data are needed to formulate evidence-based recommendations regarding administration of aspirin in influenza-KD.

A comprehensive summary of the available literature on the intriguing association of influenza with KD including a description on the safety of aspirin in influenza-triggered KD are the important strengths of our case-based review. However, non-systematic literature search limited to PubMed and Google Scholar databases is an important limitation of our study.

Influenza-KD—a sequitur

Besides secondary bacterial infection, KD should also be considered in children with influenza who have persistent fever despite antiviral therapy. Laboratory findings of progressive neutrophilic leukocytosis or thrombocytosis or marked elevations of CRP may be pointers towards KD. Assessment of coronary artery dimensions by 2D echocardiography is crucial, as about half of the patients with influenza-KD may develop CAAs. Anti-platelet doses (3–5 mg/kg/day) of aspirin, used for periods up to 6 weeks, appear to be safe in children with influenza-KD. Even moderate (30–50 mg/kg/day) to

Table 4 Important contrasting features of KD/KD-like illness seen in association with SARS-CoV-2 as compared with influenza infection-triggered KD

Characteristic of KD/KD-like illness	H_1N_1 infection	Influenza infection	SARS-CoV-2[a]
Median age at diagnosis (years)	1.6	2	8–10
Median illness duration prior to diagnosis (days)	11	6	21–25
Male/female ratio	4:1	~ 2:1	~ 3:2
Coronary artery abnormalities (percentage (%))	40	50	6–9
Myocarditis/decreased ejection fraction (%)	0	0	38–66
Treatment with IVIg (%)	100	95	54–77
Mortality (%)	0	0	2–3

[a] Data calculated from references [6–8]

high (80–100 mg/kg/day) doses of aspirin may be safe in children with influenza-KD when used for few days only; however, data in this regard are still sparse.

New insights

Similar to the relative paucity of reports regarding association of KD with influenza from Japan, reports of SARS-CoV-2 and KD-like illness are also scarce from Japan [30]. While influenza-KD is primarily seen in children < 5, KD-like illness in context of SARS-CoV-2 is a disease of older children (median age ~ 9–10 years) [7, 8]. On the other hand, both illnesses have male predilection [6, 8]. While influenza-KD has been reported to occur within 3 weeks of antecedent influenza infection or vaccination, KD-like clinical features in association with SARS-CoV-2 often occur after 3 weeks of initial illness [6, 8].

Myocarditis, elevated NTpro-BNP, and decreased ejection fraction have been reported in an 18-month-old girl with KD following influenza vaccination; however, myocardial involvement has not been reported in any child with influenza infection and KD. Influenza and SARS-CoV-2 appear to have a different pattern of cardiac involvement when these viruses result in KD/KD-like illness—predominantly myocardial involvement in SARS-CoV-2 and CAAs in influenza (Table 4) [6–8].

The hyper-inflammatory response associated with SARS-CoV-2 may be a manifestation of dysregulated immune response. Novelty of this coronavirus or lack of vaccination for related coronaviruses may be contributing factors. It would be interesting to see how the KD-like illness associated with SARS-CoV-2 evolves when vaccines for the novel coronavirus are used in children.

Conclusion

KD triggered by influenza infection seems to be distinct from KD/KD-like illness associated with SARS-CoV-2. While influenza-triggered KD peaks at 2 years of age and occurs within 3 weeks of the onset of influenza, KD/KD-like illness post-SARS-CoV-2 peaks at 8–10 years, and often occurs more than 3 weeks of the antecedent illness. Influenza-triggered KD commonly affects coronaries whereas KD/KD-like illness post-SARS-CoV-2 predominantly affects the myocardium.

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Authors' contributions AZB: patient management and follow-up, inception of idea, writing of initial draft of manuscript, editing and revision of manuscript at all stages of its production, review of literature, and final approval.

AR: patient management and follow-up, inception of idea, writing of initial draft of the manuscript, contributed to editing of manuscript, review of literature, and final approval.

PV: patient management and follow-up, editing of manuscript, critical revision of the manuscript at all stages of production, and final approval.

MPS/KG: performed virological investigations of index child, contributed to editing of manuscript, and final approval.

SS: patient management and follow-up, contributed to editing of manuscript, revision of the manuscript, and its final approval.

Data availability Relevant data included in Tables 1, 2, and 3.

Compliance with ethical standards

Disclosures None.

Ethical approval and informed consent As this manuscript pertains only to a case-based review, specific ethics approval is not mandated.

Consent Informed consent has been obtained from parents of the case reported here.

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