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PIMS-TS, an artful masquerader - Geographical clustering in the second wave of the COVID-19 pandemic

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Abstract

Background: Paediatric Multisystem Inflammatory Syndrome (PIMS-TS) temporally associated with SARS-CoV-2 was described in April 2020. The incidence of PIMS-TS is rare and the overall risk to children in the UK is considered to be low. We report a cluster of children presenting with PIMS-TS and Kawasaki disease to an Emergency Department (ED) in an NHS trust in London from 17th January 2021 to 28th February 2021.

Methods: This is a single centre retrospective observational study describing an unusual clustering of 12 children with PIMS-TS and 2 children with Kawasaki disease/Kawasaki on PIMS-TS spectrum. The time period of the distribution of cases was compared to the preceding published laboratory confirmed regional SARS-CoV-2 infection rates in the population in this geographical area.

Results: The peak in the number of PIMS-TS/Kawasaki cases in this centre followed the regional peak in the number of cases of laboratory-confirmed SARS-CoV-2 positive cases in the hospital and the community by four weeks. There was a significant spike in SARS-CoV-2 positive cases in adults and children in the hospital and community in December 2020 and January 2021. The clinical features described in these children showed significant overlap between Kawasaki disease and Toxic shock syndrome.

Conclusion: Children with PIMS-TS presented four weeks after the peak in the number of cases of laboratory confirmed SARS-CoV-2 infection in adults and children in the hospital and the community in this region. This illustrates the geographical and temporal relationship of PIMS-TS with SARS-CoV-2. The cases reported in this study provide evidence of a wide spectrum of illness and highlight the challenges in identification of these children presenting to the Emergency Department.

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Introduction

PIMS-TS shares features with Kawasaki disease and Toxic shock syndrome [1]. The incidence is low, reported as 2 per 100,000 persons younger than 21 years of age [2]. Afro-Caribbean children were over represented in the children diagnosed with PIMS-TS in the first wave of the pandemic [3]. PIMS-TS is an artful masquerader. Prompt diagnosis is not easy due to the heterogeneity of the disease presentation. Children can present with fluid refractory shock or with partial Kawasaki features of rash and conjunctivitis. It can also present as an acute abdomen mimicking appendicitis [4]. Clinical acumen is key in identifying children presenting to ED with PIMS-TS.

Kawasaki disease is a rare acute paediatric vasculitis, the diagnosis is based on clinical and laboratory criteria. A cluster of ten cases of Kawasaki-like disease was reported from Bergamo, Italy, at the peak of the first wave of the pandemic. The incidence was 30-fold higher than observed for Kawasaki disease across the previous five years [5] Two of the ten children had a positive SARS-CoV-2 PCR swab and eight of ten had a SARS-CoV-2-Positive serology test which raised the question as to whether this cluster was Kawasaki disease with SARS-CoV-2 as the triggering agent or represented an emerging Kawasaki-like disease characterised by multisystem inflammation [6].

Methods

The distribution of PIMS-TS cases was compared to the published regional SARS-CoV-2 infection rates in the population. Data of the number of children with laboratory-confirmed SARS-CoV-2 infection from the hospital done as part of universal admission screening was extracted. A descriptive analysis that summarized the clinical presentation to ED was carried out. An example of the range of clinical features is highlighted in Table 1

Results

There was a significant spike in SARS-CoV-2 positive cases in the hospital and community in December 2020. (Figure 1). There was also a spike in admission rates for adults with COVID-19 to this hospital (Figure 2). This was mirrored by a corresponding spike in children testing positive for SARS-CoV-2 on NPA/NS RT PCR done as a part of the universal screening for all admitted children (Figure 3) There was no significant rise in the admission or acuity of children presenting to this ED in December 2020 and January 2021. Four children who presented with PIMS-TS had a parent or sibling who tested positive for SARS-CoV-2 on NPA/NS RT- PCR in December 2020, two children tested positive for SARS-CoV-2 on NPA/NS RT- PCR in January 2021.

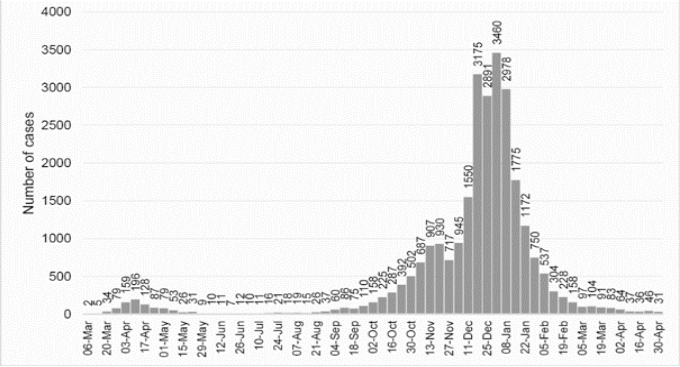

Figure 1: Spike in laboratory confirmed SARS-CoV-2 positive cases in the hospital and the community in this geographical area, Office of National Statistics

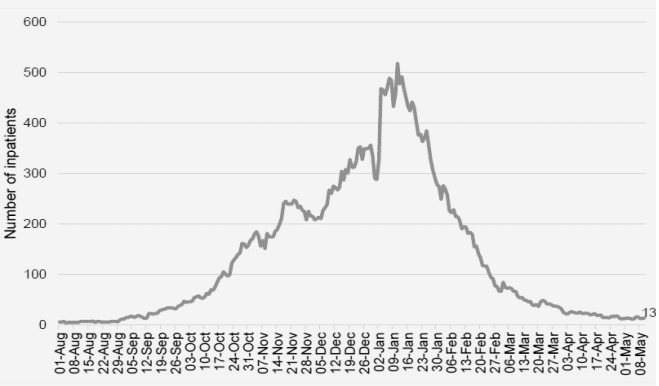

Figure 2: Spike in admission rates for adults with COVID-19 to the hospital, Office of National Statistics

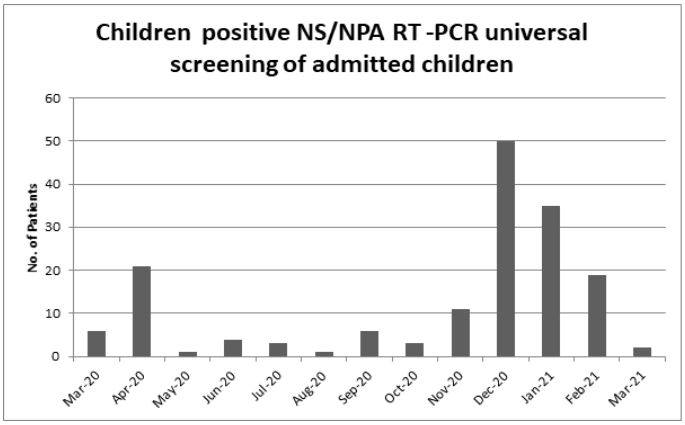

Figure 3: Spike in children testing positive for SARS-CoV-2 on NPA/NS RT- PCR in December 2020 and January 2021 done as a part of universal screening for all admitted children.

Demographics and clinical presentation

During the study period, twelve patients were diagnosed with PIMS-TS of which six children presented in the second week of February 2021 to this hospital The median age was 7.5 years (IQR- 2 -11 years) versus 9.8 years in the children who presented with PIMS -TS to this hospital in the first wave of the pandemic. There were equal number of males and females in this study. In the first wave of the pandemic children of Afro-Caribbean origin represented a significant proportion of children with PIMS-TS in this centre. In 2021, three children with PIMS-TS were Asian, four children were White and four were Afro-Caribbean. The percentage of White children was higher in this cohort, however Black and Asian children are still over represented. 13/14 children were identified and admitted on the first presentation to ED.

A four year old girl presented to ED with a history of fever of three days and sore throat. She had tonsillitis, was treated with antibiotics and discharged. Her discharge observations were normal. She presented to ED four days later with pain abdomen, rash, conjunctival injection and fluid refractory shock. She was diagnosed with PIMS-TS, treated and transferred to PICU. She had a good outcome. The presence of a focus, normal discharge observations and the child looking relatively well appear to be the confounding factors in the first presentation. Her serology was positive for COVID-19 antibodies. The patient highlights the challenges with prompt identification of children presenting to ED with PIMS -TS as symptoms can be heterogeneous.

All children presented with fever more than three days. With in this cluster, five children presented with partial Kawasaki features, ten children were treated for shock, nine needed inotropic support and four presented with gastrointestinal symptoms and rash. The number of children treated for shock and needing transfer to PICU from this hospital was higher in the second wave of the pandemic.

One child presented with features suggestive of meningitis and was later diagnosed to have sigmoid sinus thrombosis.Two children presented with a clinical picture of appendicitis, one child was transferred to surgical centre, appendicectomy was considered but was eventually managed conservatively.Serology for SARS-CoV-2 antibodies was positive in eleven children. NPA/NS RT-PCR for SARS-CoV-2 was positive in two children. Mean CRP was 174mg/L(Range 60-246mg/L)Four children showed irritability and behavioural changes, EEG done in PICU showed changes suggestive of mild to moderate encephalopathy. A diagnosis of PIMS encephalopathy was made.

The younger age of the children and the clinical characteristics in this case series highlighted a significant overlap between Kawasaki disease and PIMS-TS. Making a clear distinction between the two conditions can be challenging. Ten children in this case series required admission to PICU predominantly for shock. Four children were transferred to tertiary centres under surgical, neurology and infectious diseases teams. All children improved with treatment that included immunoglobulins and glucocorticoids. All children had good outcomes.

Conclusion

We describe an unusual clustering of children presenting with PIMS-TS to an emergency department in the second wave of the COVID-19 pandemic. These children presented four weeks after the peak in the number of cases of laboratory confirmed SARS-CoV-2 infection in adults and children in the hospital and the community in this region. This illustrates the geographical and temporal relationship of PIMS-TS with SARS-CoV-2. Whether the increased SARS-CoV-2 NPA/NS RT- PCR positivity was because of increased infectivity of the new SARS-CoV-2 lineage B.1.1.7 variant needs to be considered. This case series shares similarities with several international case series of children with PIMS-TS, except for the younger median age of children in this series. It is however important to emphasise that the proportion of children presenting with a febrile illness to ED without serious pathology remains far higher than the proportion of children presenting with PIMS-TS. Overall children remain minimally affected by SARS-CoV-2.

A strategy of education and continuous updates with case-based discussions and literature review on PIMS-TS was put in place in ED in this centre to inform frontline doctors and nurses. This resulted in timely identification of the 13/14 children who presented with PIMS-TS/Kawasaki disease. Children with PIMS -TS can present with varied and heterogenous symptoms highlighting the diagnostic challenges when they present to ED. Clinical acumen is key and is the mainstay of management for the emergency clinician in making the diagnosis and instigating supportive measures with early involvement of specialist teams.

Table 1: Characteristics of children who presented to the Emergency Department with PIMS-TS and Kawasaki disease/ Kawasaki disease on PIMS-TS spectrum.

Characteristics of children	Age PIMS-TS cases n=12	Kawasaki disease/Kawasaki disease on PIMS-TS spectrum n=2	Shock present n=10	SARS -CoV-2 antibody Positive n=11	SARS- CoV-2 NPA/NS RT-PCR positive n=2
Age in years, Median (IQR)	7.5 (2-11)	2.3 (1.7 -3)			
Sex					
Male	6	1	4	5	1
Female	6	1	6	6	1
Ethnicity					
Black	4	1	3	4	1
White	4	1	4	4	1
Asian	3		2	2	
Other	1		1	1	
Clinical features at presentation					
Fever	12	2	10	11	2
Conjunctival injection	5	2	6	4	
Rash	10	1	7	6	
Pain abdomen	9	1	8	7	
Vomiting	6	2	5	4	
Diarrhoea	2	-	1	1	
Mucous membrane changes	2	2	1	2	
Sore throat	3	-	2	3	
Lymphadenopathy	3	-	2	2	

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