


Can PIMS-TS lead to a facial nerve palsy?

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SUMMARY

Paediatric inflammatory multisystem syndrome—temporally associated with SARS-CoV-2 (PIMS-TS) is a recently described syndrome. We describe the case of a 17-year-old man presenting with a recent illness consistent with COVID-19 who presented with fever, chest pain and anterior uveitis. He was treated with aspirin, pulsed methylprednisolone and tocilizumab followed by oral steroids. On day 16 from initial presentation, he developed a facial nerve palsy. He was managed with ongoing steroids and the addition of valaciclovir. PIMS-TS is an under-recognised condition among adult physicians and may not be well known in adult neurology. It is important for adult physicians and neurologists to be aware of PIMS-TS and its possible sequelae.

BACKGROUND

COVID-19 rarely causes children to become unwell or require admission, however, there is a small minority of children who will present with a hyper-inflammatory syndrome following COVID-19 infection. Paediatric multisystem inflammatory syndrome—temporally associated with SARS-CoV-2 (PIMS-TS) should be considered in all children and young adults presenting with persistent fever, inflammation and evidence of single or multiorgan dysfunction.¹ PIMS-TS is known to cause cardiac and gastrointestinal involvement, but has not yet been associated with a facial nerve palsy (FNP). Neurologists and adult physicians should be aware of PIMS-TS and its management to enable a quick diagnosis and appropriate therapeutic intervention.

CASE PRESENTATION

A 17-year-old man, British born and of Nigerian heritage, presented to our emergency department with a 3-day history of fever, diarrhoea (4–5 times per day) and vomiting (over 10 times per day). He reported right-sided chest pain which was intermittent. Pain was exacerbated by lying flat, as well as on deep inspiration. On further questioning, he reported being unwell 1 month prior with fever, myalgia and lethargy. A family member in his household tested positive for COVID-19 at that time. Although the patient himself was not tested at the time, he was found to have antibodies to SARS-CoV-2 at presentation. The assumption was made that this original illness was likely to have been COVID-19 as no other likely cause was identified and he was a household contact of a confirmed COVID-19 case. His medical history was significant for childhood asthma only.

On admission, he appeared diaphoretic and had conjunctival injection. He was tachycardic and

febrile with a temperature of 40°C. His respiratory rate was high (range 25–44/min), though he did not require oxygen. His chest examination was unremarkable except for the tachypnoea and he had no joint swelling. His abdomen was soft and non-tender with no organomegaly.

On day 5 of admission and 2 days after completion of high-dose steroids, he developed bilateral painful red eyes. He was reviewed by ophthalmology and diagnosed with anterior uveitis.

He then developed further fevers with rising inflammatory markers, requiring further treatment. He improved clinically and was discharged on the day 11 from initial presentation. Of note, he developed raised blood pressure (systolic up to 150 mm Hg) requiring oral antihypertensive treatment.

Five days post discharge he was reviewed in clinic as planned. He reported that the previous day he developed a new right-sided facial droop, subjective reduced sensation over the right side of his face and a mild headache. He was taken to a hyperacute stroke unit where he had been diagnosed with a new right lower motor neuron VII palsy. The following day, he attended outpatient infection follow-up. On examination his heart rate was 79, blood pressure 131/78 mm Hg and on examination had a right-sided lower motor neuron FNP. He had subjective reduced sensation over the right side of his face. Otherwise he was neurologically intact. He had no vesicles or rash including in the auditory canal. He reported occasional palpitations since discharge.

INVESTIGATIONS

Blood test results at intervals throughout the clinical course are shown in [table 1](#). He had a normal chest x-ray (CXR) on admission. He had an elevated d-dimer at 1.57 mg/L (0.00–0.55 mg/L), therefore a V/Q scan was performed which did not demonstrate any pulmonary emboli. He had a negative SARS-CoV-2 respiratory viral panel, and no other respiratory viruses were identified. Blood and urine cultures identified no bacterial pathogen. Serum ACE was 24 (8–65 U/L), complement C3 was 1.51 g/L (0.90–1.80 g/L) and complement C4 was raised at 0.420 g/L (0.10–0.40 g/L). Rheumatoid factor was raised at 41 IU/mL (0–13 IU/mL). There was no blood or protein evidence on urine dip.

Due to a rising troponin and N-terminal (NT)-pro hormone BNP (NT-proBNP) during admission, an echocardiogram was performed on day 4, revealing mild to moderate impaired systolic function (visual ejection fraction estimated at 35%–40%). No valvular pathology was identified. Repeat echocardiograms throughout admission showed a gradual improvement in ejection fraction. At discharge it had improved to normal for age. A CT of the coronary arteries was normal.



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Table 1 Trend of blood results over time for a 17-year-old with PIMS-TS

| | Hb (g/L) | WBC ($\times 10^9$) | Neutrophil ($\times 10^9$) | Lymphocyte ($\times 10^9$) | C reactive protein (mg/L) | Ferritin ($\mu\text{g/L}$) | Troponin (ng/L) | Creatine kinase (IU/L) | NT-proBNP (nmol/L) | Lactate |
|---|----------|-----------------------|------------------------------|------------------------------|---------------------------|------------------------------|-----------------|------------------------|--------------------|---------|
| Admission blood value (day 0) | 117 | 10.8 | 9.4 | 0.5 | 203 | 253 | 8 | 108050 | 85 | 2.3 |
| Post pulsed methylprednisolone (pulsed day 1–3) (day 4) | 127 | 16.9 | 15.5 | 0.7 | 81 | 418 | 139 | 313 | 6964 | n/a |
| Post tocilizumab (day 7) | 127 | 10.2 | 7.9 | 1.4 | 75 | 402 | 75 | 587 | n/a | n/a |
| At time of clinic appointment (day 17) | 129 | 9.5 | 7.0 | 1.9 | 1 | 459 | 9 | 71 | n/a | n/a |

Hb, Haemoglobin; NT-proBNP, N-terminal (NT)-pro hormone BNP; WBC, White Blood Cells.

DIFFERENTIAL DIAGNOSIS

His initial differential diagnosis at presentation included sepsis, with a suspicion of PIMS-TS. The definition of PIMS-TS has been identified by the Royal College of Paediatrics and Child Health (RCPCH) as a child presenting with persistent fever, inflammation (increased C-reactive protein (CRP), neutrophilia, lymphopaenia) and evidence of single or multiorgan dysfunction such as shock, cardiac, gastrointestinal or neurological disorder. A microbial cause of illness should be excluded. Patients do not require a positive SARS-CoV-2 PCR for diagnosis.¹ There is a clinical phenotype which may present as Kawasaki-like disease.¹ This phenotype can be diagnosed with the following criteria: fever for at least 5 days with at least four of the five principal clinical features. These clinical features are: erythema and cracking of the lips, and/or erythema of oral and pharyngeal mucosa, bilateral bulbar conjunctival injection (without exudate), a rash which can be diffuse erythroderma, erythema multiforme-like or maculopapular, erythema and oedema of the hands and feet with desquamation in the subacute phase and cervical lymphadenopathy which is usually unilateral.² Our patient did not meet this criteria, and so was not thought to have this clinical phenotype.

Other rheumatological and autoimmune diagnoses were also considered at presentation in the context of the patients' raised rheumatoid factor and complement levels. The patient does not meet the criteria for diagnosis of juvenile arthritis, which must present prior to the age of 16 and have symptoms which persist for longer than 6 weeks.³ Importantly, the PIMS-TS daily multi-disciplinary team (MDT) included rheumatology opinion, enabling expert opinion on the differential diagnosis. The multi-disciplinary approach was vital for diagnosis and management, and is advised by the RCPCH.¹

With respect to the FNP, we considered whether the development of the FNP could be related to the administration of tocilizumab. Indeed, there have been spontaneous reports of facial paralysis in patients who have received tocilizumab, however, a recent analysis reported that incidence of FNPs among patients receiving disease modifying drugs in one international register was comparable to that of the general population.⁴

The subjective altered sensation in the same distribution as the FNP experienced by our patient is not an uncommon symptom in an FNP.⁵ An acute infarct is an important differential, but would present with upper motor neuron (UMN) signs. This was excluded based on clinical examination and subsequent imaging.

Sarcoidosis is another plausible diagnosis in a patient of Nigerian descent. Sarcoidosis is a chronic granulomatous disease that affects multiple systems, and can have cardiac involvement, cause anterior uveitis and in some cases neurosarcoidosis with facial palsy. Furthermore, FNP is the most common manifestation of neurosarcoidosis. The management of FNP, PIMS-TS and neurosarcoidosis is similar in the use of steroids and further follow-up of this patient may bring clarity to the diagnosis.

TREATMENT

On admission, he was initiated on intravenous fluids, broad spectrum antibiotics and commenced on dexamethasone. He was reviewed at a PIMS-TS MDT and was concluded to have a likely diagnosis of PIMS-TS. He was treated with pulsed methylprednisolone (950 mg once daily for 3 days), which commenced the same day (day 1). Aspirin 75 mg was also commenced.

Treatment of his anterior uveitis on advice of ophthalmology was a reducing regimen of steroid eye drops, cyclopentolate eye drops and oral diclofenac.

When his inflammatory markers rose and he deteriorated following methylprednisolone, he then received a dose of tocilizumab. Following this, he was commenced on oral prednisolone at 40 mg on advice of ophthalmology due to worsening uveitis. Neutrophils rose after commencement of steroids rather than secondary infection.

His hypertension was treated with 5 mg amlodipine once daily.

His FNP was managed with eye drops and an eye patch. He was continued on the 40 mg prednisolone and 75 mg aspirin he had been taking since discharge and 1 g valaciclovir three times daily was added in case of Varicella-Zoster Virus (VZV) reactivation (he had evidence of prior infection with positive VZV antibodies).

OUTCOME AND FOLLOW-UP

Due to ongoing palpitations as an outpatient, a troponin, ECG and 24-hour tape were requested on day 16 post initial presentation. His troponin remained low at 9 and the ECG and 24-hour tape demonstrated no abnormalities.

An urgent gadolinium-enhanced MRI of this brain with facial nerve views demonstrated normal grey-white matter and no extra-axial collection or lesion. There was minimal increased enhancement of the tympanic portion of the right facial nerve, but otherwise the appearance of the facial nerve was normal. There was no parotid gland abnormality.

DISCUSSION

An FNP is a clinical condition which presents with a rapid onset of unilateral peripheral paralysis of the facial nerve (cranial nerve seven). It is the most common acute mono-neuropathy, with a reported incidence of 37.7/100 000 person years.⁶ The aetiology is often unclear, however, infection, autoimmunity and nerve compression have been suggested as driving forces in pathogenesis. Symptoms usually resolve within weeks or months, though some patients will be left with permanent neurological sequelae. The mainstay of treatment is conservative, with good eye care being vital to prevent corneal ulceration. For those who present within 72 hours of onset The National Institute for Health and Care Excellence (NICE) suggests that a course of prednisolone

can be considered.⁷ Our patient was unusual in that the syndrome evolved while he was already taking glucocorticoids.

The vast majority of children who acquire COVID-19 do not become seriously unwell. It is estimated that between 1 and 5 children in 100 000 with COVID-19 would require hospital admission. Of those children who do acquire COVID-19, PIMS-TS is estimated to occur in less than 0.5% of children.⁸ PIMS-TS consists of fever and inflammation. Both single organ and multiorgan dysfunction has been described, including cardiac and gastrointestinal manifestations.⁹ Clinical features overlap with other paediatric inflammatory conditions such as Kawasaki disease and macrophage activation syndrome. The Royal College of Paediatricians advise that the diagnosis should be considered in all children and young adults presenting with persistent fever, inflammation and evidence of single or multi-organ dysfunction.

There are case reports of Kawasaki disease being rarely complicated by an FNP,^{10 11} but to our knowledge there have been no case reports of such complications in patients with PIMS-TS. As the UK approaches 1 month after the peak of the second wave it is possible that further children and young adults

may develop PIMS-TS and present to primary and secondary care for review. Furthermore, teenagers and young adults may also, as in our case, be managed in hospital by the adult medical take. It is therefore vital that the diagnostic criteria, principles of management and therapeutics are known to acute, general medical physicians and adult neurologists.

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Contributors LH was the medical registrar on the ward while the patient was admitted. She wrote and edited the paper. PT saw the patient in clinic when he presented with FNP. She wrote and edited the paper. WS reviewed the document. His neurological advice was sought regarding the FNP. He made edits to the paper. AG was the consultant in charge of care. She edited the paper and advised on changes.

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Patient's perspective

I am not someone that usually gets nervous but this whole experience was very anxiety-inducing, from the environment to some of the conversations had about my situation. Especially because of the first few days of hospitalisation, the doctors and nurses I encountered did not fully understand why I was having such symptoms even though my COVID tests were negative. I understand there was and still is some uncertainty of my current and future situation which is expected because of how early doctors are in their research, but I am confident that my doctors will and are doing everything they can now to prevent anything from going out of control and having a significant effect on my future, of which I highly appreciate.

Learning points

- ▶ This is the first described case of facial nerve palsy in association with paediatric inflammatory multisystem syndrome—temporally associated with SARS-CoV-2 (PIMS-TS).
- ▶ PIMS-TS may become an increasingly common presentation following the second wave of COVID-19 and adult physicians need to be aware of the possibility of this diagnosis, particularly in younger adults.
- ▶ A multidisciplinary team approach in a tertiary centre helped to quickly establish a treatment plan for PIMS-TS early in admission.

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