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UNILATERAL LATERAL RECTUS PALSY, PAPILLOEDEMA,IN AN ADOLESCENT GIRL WITH MULTISYSTEMIC INFLAMMATORY SYNDROME ASSOCIATED WITH SARS-COV-2 INFECTION.

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ABSTRACT

Background: Unilateral acquired isolated lateral rectus paralysis is a very rare entity seen in children. It usually occurs due to trauma, tumour and congenital causes. but postinfectious immune-associated cranial mono-neuropathy is frequently postulated as plausible cause. We report an Indian girl who presented with isolated left lateral rectus palsy following a coronavirus disease 2019infection. **Clinical Description**: A 11 -year-old girl child presented with fever, cough , swelling and pain over left cervical region and bilateral conjuctival congestion. There was no evidence of any other neurological involvement. There was no history suggestive of any of the common causes usually attributed to lateral rectus palsy. Examination revealed febrile, tachycardia with gallop, left tender cervical adenitis, bilateral conjuctival hemorrhage and later on developed left lateral rectus palsy and papillodema on fundus examination. . **Management:** Routine investigations suggestive of dengue NS1 antigen positive, covid RT PCR – negative. Secondary HLH investigations were positive. The severe acute respiratory syndrome–corona virus 2 (SARS-CoV-2) immunoglobulin G antibody test was positive. The final diagnosis was postinfectious immune-mediated isolated left lateral rectus palsy. The child responded dramatically to intravenous immunoglobulin and a short pulse of methylprednisolone for 5 days , hypertonic saline infusion and acetazolamide were given and did not display any sequelae on follow-up. Conclusion: In the setting of the current pandemic, we recommend including SARS-CoV-2 serology in the routine workup of children presenting with isolated lateral rectus palsy.

KEYWORDS: COVID-19, SARS-CoV-2, sixth cranial nerve palsy, pediatric, anti-SARS-CoV-2 antibodies.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, emerging first in the Chinese city of Wuhan in December 2019, may lead to coronavirus disease 2019 (COVID-19).[1] Generally mild or moderate respiratory disease is attributed to affected pediatric patients. The most common symptoms in children include fever, cough, shortness of breath, diarrhea, myalgia, headache and sore throat; severe pneumonia requiring oxygen support or critical illness as observed in the adult population is rare.[1]

SARS-CoV-2 may also lead to neurological symptoms. Neurological symptoms have predominantly been reported in adults with up to 36% of patients.[2] In the pediatric population, neurological symptoms may occur either as complication of acute infection with SARS-CoV-2 or in the context of associated multisystemic inflammatory syndrome in children (MIS-C) and include seizures, peripheral neuropathy, demyelination disorders, encephalopathy, Guillain-Barré syndrome and stroke. Some of these conditions may lead to altered mental status, weakness, fatigue and even long-term sequelae. In contrast to adult patients, anosmia and dysgeusia are rare.[1, 3, 4]

Besides known involvement of the olfactory bulb, COVID-19 may also present with other cranial nerve dysfunctions including the optic, abducens, oculomotor and facial nerve as well as lower cranial nerves.[5-7] There are only few reports of cranial nerve involvement for children.[3,6,8–11] We present a 12-year-oldgirl with unilateral abducens nerve palsy as a likely post-infectious complication of COVID-19. Hereby, we want to show that cranial nerve involvement may occur as post-infectious complication of pediatric SARS-CoV-2-infection in addition to the previously described context of acute SARS-CoV-2-infection and MIS-C.[3,6,8,9,12] In addition, this case lays special emphasis on pediatric sixth cranial nerve palsy in the context of SARS-CoV-2.

Clinical Description

11 year old girl presented with fever for 3 days, dry cough for 1 day, pain in left side of neck for 1 day. h/o

covid positive in girl's relative 6 weeks back and recovered uneventfully. On examination: Child febrile, conscious, tender cervical lymphnodes palpable on left upper cervical region, bilateral conjunctival congestion noted. Respiratory examination revealed tachypnoea, 55 breaths per minute. Bilateral crepitations present, spo2-84% in room air. cardiac examination- first and second heart sounds heard. tachycardia, heart rate- 160/min. and gallop rhythm noticed. Abdomen examination – normal. Central nervous examination- normal.

Investigations revealed anemia (hb-8.5g%), thrombocytopenia (platelet count- 1,33000/cumm). Leucopenia (3500cells/cubmm). CRP- positive (30mg/l). Dengue serology – NS1 antigen positive, scrub typhus PCR- negative, Covid RTPCR- Negative, urine complete- normal. APTT- elevated. Liver function tests-both AST and ALT – elevated. 125U/L &65U/L respectively and renal function tests- normal. Chest x-ray- bilateral homogenous opacities in right middle lobe and left lower lobe. ECG- sinus tachycardia. Echo - mild left ventricular dysfunction EF- 45 %, Globally hypokinetic left ventricle. Mild tricuspid regurgitation and pulmonary artery hypertension. Features suggestive of myocarditis. Nasal swab for swine flu- negative.

She was started on iv fluids, oxygen, inj meropenem, inj vancomycin, inj azithromycin and tablet oseltamivir and other supportive care. HRCT chest – minimal bilateral pleural effusion , moderate sized consolidation Later on heated humidified high frequency nasal cannula connected. Fresh frozen plasma transfusion given. CKMB elevated (162IU/l). Troponin T quantitative assay- positive (64.4 ng/l). Inj Lasix added in view of myocarditis. She had persistent fever spikes, secondary HLH or multisystemic inflammatory syndrome were kept as differential diagnosis.

D-dimer by immunoturbidimetry elevated (4831 ng/ml). plasma fibrinogen – 3.7g/l (1.8-3.5 g/l). serum triglycerides- 215 mg/dl(2-150 mg/dl), serum ferritin – more than 2000ng/ml. Bone marrow aspiration- adequate cellularity showing trilineage hematopoiesis with brisk histiocytic activity. Histiocytes with engulfed platelets noticed. SARS-CoV-2 IgG antibodies- positive. 15.57 AU/ml.As a part of sepsis workup, csf analysis done revealed 25 cells with 55% neutrophils. Csf protein and sugar were normal.CSF viral and bacterial panel PCR-negative. Bone marrow culture revealed staphylococcus hominis. Blood bio fire sepsis panel- negative. CSF and sputum gene Xpert for mycobacterium tuberculosis-negative

She developed bilateral subconjunctival haemorrhage and restricted abduction movement in left eye.Both eyes Pupils were pharmacologically dilated and fundus visualized, optic disc margins were blurred, hyperaemic and obliteration of cup- features suggestive of papilledema. MRI brain revealed subtle ill defined edema seen in bilateral retro orbital fat.

She was started on intravenous immunoglobulin along with inj methyl prednisolone, hypertonic saline infusion and tablet acetazolamide. Papilledema resolved after 96 hours. Child's fever spikes reduced, discharged home on oral steroids and aspirin. Child reviewed after one month, left eye abduction movements improved. Oral steroids tapered and stopped over 2 weeks. Aspirin given for 3 months and child has been doing well on follow up.

DISCUSSION

Various pathologies may result in acute palsy of the abducens/sixth cranial nerve in children, such as trauma, inflammatory diseases (Guillain-Barré syndrome, multiple sclerosis), infections including meningitis, malignancy, sinus vein thrombosis or pseudotumorcerebri. Abducens nerve palsy clinically presents with diplopia, inward deviation of the eye and difficulty with lateral ocular movement. Accompanying symptoms such as headache, vomiting, unstable gait and fever may be present depending on the palsy's etiology.[13]

Our patient had no history of trauma. Neurological examination was unremarkable besides unilateral abducens nerve palsy and did not reveal any other deficits or meningism, especially no ataxia or areflexia as seen in Miller-Fisher-syndrome. There were no hints for multiple sclerosis on neither CSF nor MRI; MRI did not show cerebrovascular disease/ thrombosis or an intracranial tumor. No viral or bacterial antigens could be detected using the Multiplex-PCR Filmarray CSF panel.

In the context of MIS-C, SARS-CoV-2 may lead to increased intracranial pressure in pediatric patients as described in two cases, both presenting with headache, diplopia and unilateral abducens nerve palsy resolving within days following lumbar puncture.[14] We hypothesize that our patient's abducens nerve palsy was a temporary, self-resolving para- or post-infectious complication of COVID-19. Pediatric cranial nerve palsy following viral or bacterial infection or even in the context of immunizations is a well-known phenomenon, especially for Bell's palsy.[9, 16, 17] In children, cranial nerve involvement has been described related to acute COVID-19 or MIS-C[3, 8, 9] including one case with third cranial nerve palsy following MIS-C after an asymptomatic period.[12]

There is one pediatric case report about a child presenting with third nerve palsy in a presumed context of SARS-CoV-2-infection due to detection of SARS-CoV-2-IgM in patient's serum. However, no IgG antibodies were detected and infection was not confirmed by follow-up serology, so this case may not represent a COVID 19 associated pathology.[6] For adults, few cases have already been described showing a delayed manifestation of cranial nerve dysfunction after SARS-CoV-2 infection.[23]

While some children have been described to only show ophthalmoparesis as symptom of SARS-CoV-2-infection[6], adults tend to show additional (preceding) symptoms such as anosmia, respiratory or general complaints.[18,19] For the majority of both adult and pediatric cases, rapid recovery within 4 to 6 weeks has been reported.[6, 15, 18]

Several mechanisms have been proposed to explain central nervous system (CNS) involvement in COVID-19 and MIS-C, such as direct infection of the nervous system, vasculitis of corresponding blood vessels or inflammatory response secondary to local and/or systemic infection including molecular mimicry.[3, 20, 21] Earlier reports describing results from *post mortem* analyses on deceased SARS-CoV infected patients with neurologic symptoms revealing SARS-CoV in cerebrospinal fluid and autoptic brain tissue seem to suggest that neurologic symptoms could be attributed to viral involvement of the CNS.[22] Childhood COVID-19 or MIS-C is characterized by a strong immune-mediated inflammatory response.[3] Acute and delayed SARS-CoV-2-related CNS abnormalities have been demonstrated to occur in children with imaging patterns being primarily of postinfectious immune-mediated origin.[4] Similarly, immune-mediated or autoimmune mechanisms seem to be more likely than direct virus-induced damage in our patient since only SARS-CoV-2 IgG but no viral antigens were detected in CSF.

Few centres whom suspected post-infectious cranial nerve palsies has demonstrated that immunomodulators such as glucocorticoids or immunoglobulins might be a pharmacological treatment option.[23, 24]

We conclude that pediatric COVID-19 may lead to isolated temporary para- or post-infectious neurological complications. Although children tend to show less severe respiratory symptoms, they may experience prolonged complaints as in our case. As data about cranial nerve involvement in pediatric COVID-19 is rare and reports are primarily based on adult cases, we would like to raise awareness for this condition in children and advocate for increased vigilance of clinicians worldwide.

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