Post-Mumps Extrapyramidal Syndrome in a Young Child

Sir,

Mumps is an acute contagious RNA viral infection of children and adolescents, manifesting initially as fever with parotid swelling. However, post mumps complications can occur in 47% cases[1] which include orchitis/oophoritis, aseptic meningitis, encephalitis, deafness, and pancreatitis. Neurological involvement is an important post-infectious complication manifesting commonly as aseptic meningitis, encephalitis, and sensorineural deafness and less often as Guillain Barre syndrome, cerebellar ataxia, transverse myelitis, hydrocephalus, and facial palsy.[2] Post-mumps extrapyramidal syndrome is very rare, but it is one of the vital entity in the spectrum of

neurological complications of mumps. The exact pathogenesis of such neurological manifestation is yet to be determined.

A 9-year-old male child presented with symptoms of fever along with bilateral parotid swelling one month ago. It was followed one week later by the change in behavior, apathy, hypo-responsiveness, decreased phonation, decreased sleep, emotional lability in the form of frequent excessive cries, inability to get up from bed, sitting, or walking. The patient had two episodes of generalized tonic-clonic seizures along with extrapyramidal features like limb rigidity, tremulousness of limbs, and abnormal limb posturing. During his illness, both of his sisters suffered from mumps but unlike him recovered within 2 weeks spontaneously without any residual defects; however, all of them were being previously adequately vaccinated. There is no history of similar illness or any other significant abnormality in the past.

On examination, his pulse rate was 90/min, blood pressure 100/70 mm Hg, respiratory rate 16/min, and was in the afebrile state. There were no rash, pallor, icterus, edema, significant lymphadenopathy, joint swelling/tenderness, liver, and spleen were not palpable. The cardiovascular system, respiratory system, and ocular examination did not reveal any abnormal findings. The external genitalia was normal in the assessment. The KF ring was not seen on slit-lamp examination. His neurological study revealed a confusional state on mental status evaluation. Limb rigidity was present bilaterally in all limbs, more on the left side. The dystonic postures were observed with tremors (dystonic tremors), more on the left side. The deep tendon jerks were exaggerated on both sides with a normal plantar response. The cranial nerves, sensory, cerebellar, autonomic, meningeal, and spine examination was essentially non-significant.

His hematological investigation showed leucocytosis (total leucocyte count 15200/cumm) with neutrophilia (89%) with lymphopenia (8%), hemoglobin 12.9 g/dL, platelet count 3.79 lakhs/cu mm.Biochemical examination showed random blood sugar 84.3 mg/dL, creatinine 0.49 mg/dL, urea 21.91 mg/dL, bilirubin 0.88 mg/dl, aspartate transaminase 36.19 IU/L, alanine transaminase 40.91 IU/L, sodium 132.6 mmol/l, potassium 4.1 mmol/l, calcium 4.8 mg/dL, creatinephospho-kinase 167.1 IU/L (55–170), ammonia 64.5 µmol/l (10–47), erythrocyte sedimentation rate 17 at the end of first hour, C reactive protein 1.06 mg/L (0–5), and a normal urine routine examination. His arterial blood gas analysis showed elevated lactate levels only. He was evaluated for Wilson's Disease, and his serum ceruloplasmin level was 33.98 mg/dl (20–60) and serum copper level 89.36 ug/dL (80–180). His thyroid function panel was tested to show thyroid-stimulating hormone level of 0.17 IU/ml (0.35–4.94), total T3 0.62 ng/dl (0.58 − 1.59), total T4 8.53 ug/dl (4.87-11.72), anti-thyroid peroxidase antibody titer 32.25 IU/mL (<20) and anti-thyroglobulin antibody titer 11.53 IU/mL (<4.11). His serological workup was positive for mumps with serum mumps IgM antibody >4 Index (positive > 1.1) on day 6 of onset of clinical symptom. His serology was negative for anti basal ganglia antibody 0.12 OD (<0.2 OD by ELISA), anti-streptolysin O titer 15.91 IU/ml (<240). The testing for autoimmune encephalitis panel, dengue, typhoid, scrub typhus, HIV, hepatitis B and C virus, malarial parasite, and chikungunya showed negative results. The serology for Japanese encephalitis virus was negative. Cerebrospinal fluid (CSF) examination which initially showed pleocytosis (35 cells/cu mm, 80 neutrophil and 20 lymphocyte, protein 42 mg/dL, sugar 68/serum 119 mg/dl) became normal by 10 days. CSF for mumps showed IgM antibody of 8.72 U/mL (negative <8), and mumps IgG antibody >150 U/mL (negative <8) on day 18, but real-time PCR for mumps was not detected in CSF at that time. CSF was negative for herpes simplex virus 1 and 2, KOH mount, acid-fast bacilli stain, gram stain, and oligoclonal band.

There was a unique finding of increased lactate levels [arterial blood 3.8 mmol/L (0.5 − 1.5), venous blood 6.97 mmol/L (0.5 − 2.22 mmol/L), and CSF 34.93 mg/dL (10 − 22)] in our patient. His chest x-ray, abdominal ultrasound, 2D echocardiography were normal. However, his brain magnetic resonance imaging showed T1 hypo-intensities, T2 hyper-intensities, FLAIR hyperintensities, and DWI restriction in corpus striatum symmetrically without contrast enhancement [Figure 1]. His whole-genome sequencing was done to look for any underlying mitochondrial disease that could have been precipitated by the mumps infection, which reported a heterozygous "variant of uncertain significance" variant in SGCE (epsilon-sarcoglycan) gene of chromosome 7:94232639.

He was diagnosed as post mumps extrapyramidal syndrome and was managed conservatively during his stay in the hospital and treated with pulse dose methylprednisolone, intravenous immunoglobulin, inj piperacillin-tazobactum, tab trihexyphenidyl, tab oxcarbazepine, cap duloxetine, tab pramipexole, tab clonazepam, cap coenzyme Q, and thiamine therapy.

During his stay in the hospital, the clinical spectrum of manifestations changed from the initially altered sensorium post-seizure to a state of abnormal cries, agitation, decreased sleep, increased food craving, generalized rigidity, followed later by dystonia, fixed limb posturing along with tremors [Video 1], and lastly followed by asymmetric choreiform movements [Video 2] and restlessness which decreased eventually. He was discharged after 15 days of hospitalization in a stable state.

On the second follow-up after 1 month, the patient was stable with some residual features in the form of akathesia, and minimal choreiform movements and repeat MRI of the brain showed almost complete resolution of the symmetric lesions of corpus striatum with remaining symmetric hyperintensities in anteromedial putamens [Figure 1e, 1f].

Mumps is an acute highly infectious disease, caused by a single-stranded RNA paramyxovirus affecting children

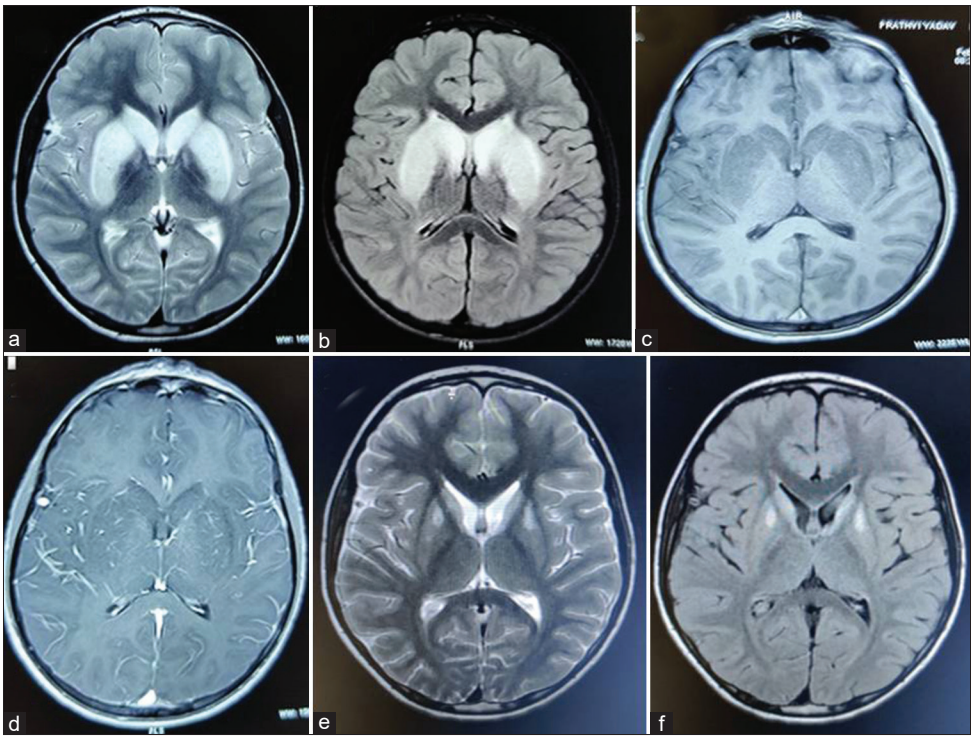

Figure 1: Magnetic Resonance Imaging of cranium demonstrated (a) T2 weighted image, (b) T2 Fluid attenuated inversion recovery, hyperintense signals at corpus stratum bilaterally, (c) T1 weighted image depicted hypointense signals at the same area without contrast enhancement (d). MRI brain (e) T2 weighted image and T2 FLAIR image (f) revealed predominant resolution of lesions

and adolescents typically during late winter to early spring period, being transmitted through respiratory droplets, direct contact, and fomites with an incubation period of usually 16 − 18 days (range 12 − 25 days) from exposure to onset of symptoms.[3] Just like any other viral prodrome, mumps also begin with fever, headache, myalgia, fatigue, and anorexia, which is followed by the involvement of the salivary gland within 48 h typical of mumps infection. Complications of mumps include orchitis/oophoritis, arthritis, myocarditis, pancreatitis, neurological manifestations, and may occur even in previously immunized people.[4] Aseptic meningitis is the most common neurological complication in mumps (1 − 10%)[5] clinically presenting with low-grade fever, headache, and nuchal rigidity, having a benign course and complete recovery. Mumps encephalitis typically presents with fever, altered sensorium, and convulsions, and it also courses with a full recovery. In our patient, there was a history of fever with parotid swelling, which was followed by altered sensorium, convulsions, dystonic tremors, fixed limb positioning, and rigidity and later choreoid movements, suggesting Mumps encephalitis along with features of extrapyramidal system involvement. Neurotropism is well-known in mumps infection, which manifests early in the form of encephalitis. However, the late-onset extrapyramidal features pointing toward parkinsonism may be a post-infectious inflammatory manifestation of mumps which might occur in the setting of host genetic susceptibility. These host susceptibility factors are yet to be determined.

The patient was diagnosed as post-mumps extrapyramidal syndrome based on the detection of mumps antibody in blood and cerebrospinal fluid, along with basal ganglial lesions in magnetic resonance imaging of the brain. However, he was extensively worked-up for diseases known to manifest or precipitate extrapyramidal syndrome in young.

The radiological imaging showed symmetric hyperintensities involving corpus striatum bilaterally during the encephalitis phase with subsequent near normalization of the scan at 2 months interval with residual hyperintensities in anteromedial putamens in T2 and FLAIR sequence of brain magnetic resonance imaging. This finding was different from the lentiform fork sign of metabolic acidosis. In two other case reports, there have been similar initial MRI pictures and one study has follow-up scans.[6,7]

However, there is the presence of elevated lactate in arterial, venous, and cerebrospinal fluid, for which whole-genome study was performed to determine the presence of any mitochondrial disorder which came out to be negative for the same but had a heterozygous "variant of uncertain significance" variant in SGCE gene of chromosome 7:94232639. Also, there has been no specific target antibody positivity in this patient to have such symmetric basal ganglial involvement among the ones that have been worked up except for the presence of mumps antibody.

We report a patient of post mumps extrapyramidal syndrome, which is a rare entity. We tried to explore some of the possible causes that might present or precipitate extrapyramidal

syndrome in young. However, our findings led us to scope for lactate study in post-mumps pyramidal syndrome, and for finding pathological correlation of mumps antibodies with target-specific loci on basal ganglia, and searching any other genetic or metabolic predilection for the occurrence of extrapyramidal syndrome as a post mumps sequelae.

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Conflicts of interest

There are no conflicts of interest.

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