Case Report

JMR 2019; 5(2): 50-53

March- April

ISSN: 2395-7565

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www.medicinarticle.com

Received: 24-03-2019

Published: 26-05-2019

Salivating, Aspirating and Convulsing- An Unusual Case of Post-Infective Polyradiculopathy and Encephalopathy

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Abstract

A young girl presented one week after a sporadic diarrheal illness with copious salivation and progressive motor weakness. Initially this was more prominent in her bulbar muscles and resulted in an aspiration pneumonia. During the course of her illness she had multifocal seizures; flaccid then spastic quadriplegia; intense dysautonomia; dysconjugate gaze; truncal and limb ataxia; respiratory failure requiring mechanical ventilation; and CSF abnormality. Available tests and assessment for alternate pathology, did not yield results. Despite a stormy course, she made a complete recovery and was discharged after 42 days of hospitalization. Intravenous Immunoglobulin and ventilator therapy influenced the outcome.

Keywords: Guillain Barré Syndrome (GBS); Dysautonomia; Bulbar palsy; Multifocal Seizures; Flaccid quadriplegia; Spastic quadriplegia; Ataxia; Dysconjugate gaze; Respiratory failure; IVIg.

Abbreviations: GBS- Guillain Barré Syndrome; IVIg- Intra-venous immunoglobulin; NCDC National Centre for Communicable Diseases; ADEM- Acute Demyelinating Encephalomyelitis; Anti-GQ1b Ab- Anti ganglioside Q1B antibody.

INTRODUCTION

Public health care system in the National Capital of Delhi, attracts several cases of acute and sub-acute immune mediated polyneuropathies, mainly from urban slums and neighbouring districts. This is because expensive treatment options like intravenous immunoglobulins and ventilator therapy are available free of cost. Availability of other facilities like nerve conduction studies, EEG, MRI and neuro-immunological tests like anti-ganglioside antibodies, viral studies, etc; are restricted to specialized higher centres; and are not always accessible. Ours is a secondary- level care hospital which caters mainly to the inner-city population of North Delhi and migrants.

We treated 36 adult in-patients of Guillain Barre Syndrome between January to December 2017 and witnessed a wide range and severity of clinical manifestations. One case stands out amongst all, for some of the most unusual developments during her clinical course. Luckily, she recovered and went home after 42 days in hospital. During follow up, improvement was maintained.

CASE REPORT

A 20-year-old girl developed a diarrheal disorder during a family wedding, where vegetarian food was served. The patient was brought to our Centre on 20 March 2017. Within a week of diarrhoea, she had developed difficulty in swallowing both solids and liquids; ineffective coughing spells triggered by swallowing attempts; mild soreness in the throat and dribbling of copious amounts of saliva from the mouth. She also complained of uncomfortable palpitations. There was no rash, joint pains or significant fever.

At presentation there was no history of headache, photophobia, syncope, seizure, diplopia, weakness, unsteadiness, sensory complaints or bowel and bladder involvement. There was no history of fever, animal or insect bites, exposure to toxins or poisons, pain abdomen, dysuria or dark coloured urine.

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She was unmarried and not sexually active. She had non- disabling facial asymmetry since infancy. There was no past history of heart or any other disease.

Examination showed a frail young girl, afebrile with resting regular pulse rate varying between 110 to 140/ min, average BP 90/ 60 mm Hg, respiratory rate of 24/ min, sPO2 90 % on room air and a normal JVP. There were no exanthems or enanthems, pharyngitis or pharyngeal membrane, dehydration, goitre, lymphadenopathy, bite marks, cyanosis, pallor, icterus, oedema, or unusual pigmentation. Dentition was healthy.

Neurological examination showed normal higher mental functions, a striking lower motor neuron pattern left facial nerve paralysis (present since infancy) with mild hypoplasia of the left side of the face. There was dribbling of copious saliva from the left side of her mouth. Palatal and pharyngeal reflexes were blunted (especially the gag- component). Cough was ineffective and volume of voice low. Eye movements and pupils were normal. No long tract or cerebellar signs were noted. Motor power in the limbs was normal, tendon jerks were elicited normally and plantar reflexes were flexor. Some jitteriness and coarse tremulousness were observed during purposive movements, which in hindsight, might have been the initial manifestation of ataxia.

Cardiovascular examination including resting ECG, X ray chest and echocardiography were normal. This was undertaken in view of palpitations and documented disproportionate tachycardia. Respiratory system assessment including X Ray chest, suggested aspiration pneumonia of right lower lobe. Abdominal examination was normal.

Treatment for aspiration pneumonia was started, while cause of her bulbar muscle weakness and tachycardia was sought. Feeding in upright position through tube was initiated to prevent further aspiration, and appropriate injectable antibiotics (Clindamycin and Ceftriaxone) were started, along with other supportive measures. Oxygen saturation normalized with supplemental oxygen through face mask. Excessive salivation persisted. Haemoglobin, haematocrit and RBC indices were normal. She had polymorphonuclear leucocytosis of 16,200/ cu mm (88% neutrophils). Gram stain on throat swab showed gram positive cocci in chains and culture was negative for diphtheria or pathogenic streptococci. ASO titre was not raised. Initial blood, urine and sputum cultures showed no growth. All biochemical parameters including serum potassium and thyroid function tests were normal. The patient and her relatives could not be convinced to retain the feeding tube, or undergo CSF examination. After improvement of her aspiration pneumonia, 3 days later she left hospital against medical advice (24 Mar 2017). Excessive salivation, bulbar muscle weakness and disproportionate tachycardia persisted.

Within 48 hours, she was brought back to the emergency department (26 March 2017); deeply unconscious, cyanosed and limp, with hardly any respiratory efforts, a feeble, rapid though regular pulse; and an unrecordable BP. There has been a preceding generalized tonic clonic seizure at home. Immediate resuscitation and assessment were initiated. She was intubated, tracheal suction yielded copious amount of secretions. Tracheal toilet and ambo bagging were instituted followed by mechanical ventilation. Nasogastric tube was re- inserted. Inotropes were started along with crystalloids to ensure adequate urine output. In the emergency department she threw multiform seizures- atonic, tonic-clonic and myoclonic with complex component; and regained full consciousness once seizures were pharmacologically controlled. After regaining consciousness, she displayed grade 3 weakness, atonia and areflexia in all limbs, that lasted for few hours and from which she made partial recovery. Random blood glucose was 78 mg/dl, electrolytes, liver and renal function tests were normal. CBC showed neutrophilic leucocytosis. Once stabilized, imaging studies were done for the likelihood of a structural abnormality. CT scan of

brain & brain stem, carotid doppler studies and echocardiography were normal. Fundoscopy was also normal.

Over the next 2 days (27 & 28 Mar 2017) she developed symmetrical lower motor neuron weakness of all 4 limbs and respiratory muscles. Muscle power was grade 2 to 3 in different groups with areflexia. Level of consciousness was normal. In fact, she self- extubated on 2 occasions and needed restraint for continued ventilation since she could not maintain satisfactory oxygen saturation on her own. Distressing sialorrhea and bronchorrhea continued. Pulse and BP showed wide swings. Pupils and ocular movements were normal. Clinical and radiological evidence of progressive right sided pneumonia was present. Her clinical condition remained labile. She was managed in the high dependency unit where invasive ventilatory support was continued. Additionally, antibiotics were upgraded (Vancomycin and Meropenem) to cover nosocomial pathogens in light of new fever, sepsis and clinico-radiological evidence of progressive pneumonia. Anticonvulsants, tube feeding, aggressive monitoring and other supportive measures were also continued. It was a challenge to keep the airway dry. Anticholinergics were used by both inhaled and parenteral routes. Short acting beta blockers were needed for the cardiovascular instability.

First CSF examination was undertaken on 29 March 17 which showed albumino-cytological dissociation (appearance- clear, glucose 64 mg/dL, protein 80 mg/dL, no cells, no micro-organisms, CSF ADA- 7.2U/L, culture sterile). Samples were also sent to National Centre for Diseases Control (NCDC) for IgM Japanese Encephalitis, Rabies and Herpes Simplex which returned negative. Kit for IgM Rabies was not available.

Her neurological condition continued to evolve. By Day 5 of second admission (30 Mar 2017), she again had generalized tonic- clonic seizures, which were pharmacologically controlled. After the post- ictal period, new findings evolved and persisted over the next few days. Spastic quadriplegia, hyperreflexia, symmetrical ankle clonus, bilateral extensor plantars, dysconjugate gaze, mydriasis (possibly due to glycopyrrolate), ataxia, and altered sensorium were noted. She remained arousable and could follow simple commands. Sialorrhea and bronchorrhea continued unabated and posed a challenge in airway management. Glycopyrrolate was initiated to dry secretions. Additionally, wide swings in her blood pressure and pulse rate were managed with short acting beta-blockers and inotropes as required. Fever with unusual sweating occurred sporadically.

Too sick to be moved out of our facility for fresh neuroimaging; and keeping a primary progressive demyelinating disorder/ ADEM in mind, Injection methylprednisolone 1 gram daily was given on days 6, 7 and 8, with no improvement. Other supportive care including supplemental nutrition and physiotherapy were intensified. All investigations were regularly repeated including surveillance cultures. Repeat CSF on 31 Mar 17, showed a further rise in proteins (appearance- clear, glucose 58 mg/dL, protein 128 mg/dL, no cells, no micro-organisms, CSF ADA- 6.5 U/L, culture-sterile). CBC, X Ray Chest and tracheal aspirate culture showed worsening sepsis due to ventilator associated pneumonia which was treated as per culture and sensitivity results. There was no improvement in her neurological condition. MRI brain, craniovertebral junction and upper cervical cord done under ventilator support, were normal (Figure 1). The family could not afford to pay for additional investigations like EEG, nerve conduction studies, oligoclonal band in CSF and anti-GQ1b antibody.

Literature on central nervous system and autonomic involvement in Guillain Barre Syndrome was reviewed that showed similarities with her clinical presentation. Intravenous Immunoglobulin therapy was started on day 10 of second admission (0.4 g/kg bodyweight for 5 days). Within 2 days she started showing improvement and by the fifth dose, the spasticity, ataxia and dysconjugate gaze had disappeared.

Bulbar muscle weakness, autonomic dysfunction and pneumonia required ventilatory and pharmacological support for a few more days. Motor power of limbs and respiratory muscles returned gradually. She was weaned off the ventilator, oral feeding was introduced in a graded manner and an active physiotherapy regimen initiated. Autonomic dysfunction also settled down with passing time.

Six weeks after her initial presentation, she was discharged from hospital, walking and feeding independently. Improvement was maintained during follow-up visits for a year. Anticonvulsants were tapered and stopped after a year. Residual childhood Bell's palsy persisted (Figure 2).

Figure 1: MRI Scan after 2 weeks of onset showing no abnormality

Figure 2: Photo after recovery with residual Bells palsy that was present since infancy

DISCUSSION

At initial presentation, with excessive salivation, pharyngeal weakness, mild movement disorder (chorea) and palpitations; the possibilities considered were diphtheria, envenomation, botulinum-like toxins/drugs, organo-phosphorous poisoning, polyradiculopathy, acute rheumatic fever and possibly porphyria.

Later when she rapidly developed central nervous involvement with multiform seizures, flaccid followed by spastic quadriplegia, truncal

and limb ataxia, dysconjugate gaze, type 1 respiratory failure and florid dysautonomia; many other possibilities came to mind like viral encephalitis including rabies, ADEM, primary progressive MS, etc. It was review of published literature and the worsening albumino-cytological dissociation on serial CSF examination that led to our decision in administering full doses of IVIg. This, supported by ventilator therapy gave her a chance at recovery.

In the 1950s, Bickerstaff and Fisher independently described cases with a unique presentation of ophthalmoplegia and ataxia [1-3]. The neurological features were typically preceded by an antecedent infection and the majority of patients made a spontaneous recovery. In the cases with Bickerstaff brainstem encephalitis, there was associated altered consciousness and hyperreflexia, in support of a central pathology whereas in Fisher syndrome, patients were areflexic in keeping with a peripheral aetiology. However, both authors recognised certain similarities to Guillain-Barré syndrome as the presence of polyradiculopathy and cerebrospinal fluid albumino-cytological dissociation. By 2008, Bickerstaff's brainstem encephalitis and Fisher syndrome were recognized to form a continuous spectrum based on clinical analysis of several reported series. The largest study one could find, was of 581 cases [4]. A case showing features of Miller Fisher syndrome, Bickerstaff brainstem encephalitis and Guillain-Barré syndrome overlap; with persistent non-demyelinating conduction blocks was reported in 2018 [5]. As recently as 2019, a thorough literature review was published along with 2 paediatric cases in an elegant article [6]. A lot of similarities with our reported case, are recorded in these instances [5-7].

The discovery of immunoglobulin G anti-GQ1b antibodies in patients with Fisher syndrome and Bickerstaff brainstem encephalitis was crucial in providing the necessary evidence to conclude that both conditions were probably part of the same spectrum of disease, due to their common clinical and immunological profiles. Following this, other neurological presentations that share anti-GQ1b antibodies emerged in the literature. These include acute ophthalmoparesis and acute ataxic neuropathy, at the less extensive spectrum of the disease while pharyngo-cervico-brachial weakness and Fisher syndrome overlap with Guillain-Barré syndrome representing the more extensive end of the spectrum. The conditions are now referred to as the 'anti-GQ1b antibody syndrome' [8-11]. Anti-ganglioside antibodies, including anti-GM1 IgM, anti-GD1b IgG, and anti-GT1a IgG are all implicated. Some authors have discussed the possibility of shared pathogenic central and peripheral nervous system epitopes. Various triggering agents like campylobacter, mycoplasma, influenza and its vaccine, HIV and EBV have been studied in great detail [6]. Our case could not undergo these investigations due to financial constraints. Almost all standard text books and publications recommend IVIg or plasmapheresis for treatment of this condition; although timing of such an expensive treatment, is not the only predictor of outcomes [12-14].

MRI abnormalities are reported in some cases with purely peripheral nervous system involvement while there are no imaging abnormalities in others with dominant central nervous system affliction [6,7] and vice versa. On the whole, GBS is regarded as a predominantly symmetric motor neuropathy with few sensory features; and the CNS is rarely involved. Our case with predominant central nervous system features had normal MR imaging towards the end of the second week of illness. Visual evoked potentials and nerve conduction studies also show diverse pictures as reported by some investigators [5,15]. Multiple attempts at classification of this syndrome have been made [16,17]. They only serve to highlight the complexities this group of condition pose.

Conflict of interest

The authors of this article declare that there is no conflict of interest.

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