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Locked-in Syndrome as a Presentation of Snakebite

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Snake bite is a common condition in tropical countries. Neurotoxic features of snake bite vary from early morning neuroparalytic syndrome to various cranial nerve palsies. Locked in syndrome (LIS) is a rare presentation. We present four children that had LIS; three patients had total and one had incomplete LIS. All patients made successful recovery with polyvalent anti-snake venom and supportive management. This case series highlights the importance of early diagnosis of LIS in snake bite.

Key words: *Children, Locked in syndrome, Snakebite*.

Snake envenomation is a major cause of mortality and morbidity all over the world but more so in developing countries because of lack of advanced life support equipment [1]. Various presentations of snake bite may include neuromuscular paralysis, bleeding disorder, renal failure and so on. Neurological manifestations are caused by elapidae group (Cobras, kraits). The common krait is nocturnally active snake with painless bite; so many patients with neurological manifestations present to emergency without history of snake bite [2]. In 60%-70% of cases, snakebite occurs when the patients were asleep and site of bite is undetectable in 17% cases [3]. Thus, high degree of suspicion is required in such cases to reach at a diagnosis.

Locked in syndrome (LIS) is a neurological syndrome in which despite being conscious patient is unable to communicate [4]. It is rarely reported in snake bite [5,7]. We report 4 children with LIS following snake bite.

CASE-REPORTS

Case 1: A 2-year-old child presented with bleeding from ear, followed by altered sensorium and respiratory failure within two hours of initial complaints. At admission, child had respiratory arrest with severe bradycardia, absent peripheral and central pulses, and Glasgow coma scale (GCS) score of 3; pupils were fixed and dilated and doll's eye movements were absent. After initial resuscitation, he was noted to have some movement of right toe. Seven hours later, snake bite was suspected and polyvalent anti-snake venom (ASV) was administered. Thirty hours later, after receiving 25 vials, child had spontaneous respiration, movements of lower limbs and eye opening but pupils were still fixed and dilated. Pupillary reactions became normal on day three, doll's eye movement appeared a day later, and the child was discharged in premorbid condition on day ten.

Case 2: A-ten-year-old boy presented with history of anxiety, pain abdomen and vomiting appearing acutely early morning, while sleeping on the floor of his cottage.

His sister had died an hour back with similar complaints. Parents did not report any venomous bite. At admission, he had bradycardia, gasping respiration and GCS of 3. Pupils were fixed and dilated and doll's eye movement were absent. He was put on respiratory support. There was no improvement over next 48 hours. Detailed examination revealed fang marks on one foot so ASV was given. On day six, parents noted fluttering of eyelids and next day he had spontaneous respiration and limb movements. After one week, doll's eye movements appeared but internal ophthalmoplegia persisted. CT head was normal and fundus examination did not show features of optic neuritis. At discharge, five weeks later, internal ophthalmoplegia was persisting.

Case 3: A One-and- half-year old child with history of snake bite presented to the emergency department with breathing difficulty. At admission, she had gasping respiration, bradycardia, GCS of 3, fixed dilated pupils and absent Doll's eye movement. There was no response to ASV. After 36 hours, she started having spontaneous respiration and occasional movement of limbs. She used to cry on looking at parents. On day four, pupillary size and reaction became normal. She was discharged on day 10 in premorbid condition.

Case 4: A Seven-year-old boy presented with history of sudden onset of pain abdomen and vomiting, while in the playground. At admission, he had gasping respiration. Two hours later, he was atonic, areflexic; pupils were fixed and dilated with absent doll's eye movements. After ruling out other causes (normal cerebrospinal fluid examination, CT head, and liver function tests); possibility of snake bite was entertained and ASV was given. After 10 vials of ASV, ptosis resolved and child started responding using eye movements; 25 vials later, spontaneous limb movements appeared but internal ophthalmoplegia persisted. Three weeks later, at discharge, internal ophthalmoplegia was persisting.

DISCUSSION

Neurotoxic manifestations of snake bite vary in severity but pediatric case reports of LIS due to snake bite are rare [7].

In LIS, patient is conscious yet unable to communicate. It can be of three types: classic, in which patient has quadriplegia and anarthria with preservation of consciousness and vertical eye movements. Incomplete LIS is similar to classic except remnants of voluntary movement other than vertical eye movement are present. In total LIS, there is total immobility and inability to communicate, with preserved consciousness [4]. Usual causes of LIS are stroke, trauma or encephalitis of ventral pontine area but it can also be caused by extensive bilateral destruction of corticobulbar and corticospinal tracts in the cerebral peduncles [8]. LIS can also be caused by peripheral causes such as severe Guillan-Barre's syndrome, neuromuscular junction blockade (myasthenia gravis, toxins, snake bite), etc.

LIS in snake bite occurs due to neuromuscular paralysis of voluntary muscles which in turn is caused by neuromuscular transmission blockade (krait venom acts pre-synaptically while cobra venom acts post-synaptically) [2]. Irreversible binding of toxin to presynaptic portion makes clinical recovery slow in krait envenomation as recovery occurs only with the formation of new neuromuscular junctions [9], as was seem it our cases, especially case 2. Such long duration of LIS in snake bite is not reported previously. Duration of LIS varied from 30 hours to six days. In about 50% cases of LIS, it has been seen that family members are the first one to note that patient is able to communicate [10], as was seen in case 2.

Snake bite documentation was done only in one case by the caregivers, in the rest of the cases, clinical scenario was typical of painless krait bite [3]. Since differential diagnoses of unresponsive patient are exhaustive, high degree of suspicion is required in such cases, especially during rainy season. Fixed dilated pupils and absent doll's eye movement can easily be interpreted as brain death, if possibility of LIS is not considered. Physicians need to be aware of likelihood of snakebite presenting as LIS, especially in the appropriate clinical setting.

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Thrombotic Microangiopathic Syndrome: A Novel Complication of Diabetic Ketoacidosis

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Thrombotic microangiopathic syndrome secondary to diabetic ketoacidosis is an under reported entity in children. We describe 2 girls who developed thrombotic thrombocytopenic purpura (TTP) and thrombocytopenia associated multi organ failure (TAMOF) in new onset diabetes. Both patients presented with classical findings of DKA and were intubated due to low GCS, admitted in PICU and managed according to DKA guidelines. Later on, both patients developed thrombocytopenia, acute kidney injury, and low hemoglobin along with evidence of microangiopathy on peripheral smear. One patient developed paraparesis while other patient had high LDH levels. The clinical diagnosis of TTP and TAMOF was made respectively. Both patients were treated with plasmapharesis and renal replacement therapy. Both gradually improved and were discharged.

Keywords: Diabetes mellitus, Microangiopathy, Thrombosis, Ketacidosis.

Potential complications of diabetic ketoacidosis include dehydration, cerebral venous thrombosis, mucormycosis, pancreatitis, sepsis and electrolyte imbalance like hypokalemia and hypophosphatemia [1]. Acute kidney injury is fatal complication of diabetic ketoacidosis and development of renal failure in DKA is associated with high mortality in pediatric age group [1,2]. Thrombotic complications like thrombotic thrombocytopenic purpura (TTP) secondary to DKA are under-reported. Recently, a new thrombotic microangiopathic syndrome, called thrombocytopenia associated multi organ failure (TAMOF), has been described in literature. TTP is now considered to be a part of this syndrome. This syndrome is defined by presence of various clinical and laboratory markers including multi-organ dysfunction, new onset thrombocytopenia and elevated lactate dehydrogenase (LDH) levels [3]. Untreated TAMOF/TTP is associated with high mortality. Early diagnosis is the most important step for prompt intervention like plasmapharesis, which can be lifesaving. Therefore, pediatricians must be aware of microangiopathic complication of DKA. We report the development of this fatal syndrome in two girls presenting with diabetic ketoacidosis.

CASE-REPORTS

Case 1: A 14-year old girl presented with one day history of fever, vomiting, respiratory difficulty and altered state of consciousness. This was preceded by a 2-3 weeks history of polyuria, polydipsia, increased appetite and undocumented weight loss. On examination, she had tachycardia, hypotension, and altered sensorium with Glasgow Coma Scale of 4/15. She had evidence of severe dehydration, gasping respiratory efforts with oxygen saturation of 85-90% on room air. Initial investigations revealed hyperglycemia (random blood sugar=947 mg/dL), severe metabolic acidosis (pH of 7.00, bicarbonate 5.0), glycosuria and ketonuria. Blood counts were normal. She was intubated and started on insulin infusion along with fluid resuscitation. She was mechanically ventilated. The ketoacidosis resolved within 48 hours and she was switched to subcutaneous insulin. She was extubated on 3rd day of admission. Subsequently, she developed evidence of renal insufficiency (serum creatinine 4.4 mg/dL). Ultrasound kidneys, ureters, bladder (KUB) was reported normal. Continuous renal replacement therapy (CRRT) was started. Subsequently, she developed paraparesis along with low hemoglobin, low platelet count with evidence of microangiopathy on peripheral smear. A, clinical diagnosis of thrombotic thrombocytopenic purpura (TTP) was made. Plasmapharesis and hemodialysis were started. 5 cycles of plasmapharesis were done. She gradually improved, microangiopathy resolved and her platelet count returned