Original Research Article

Monsoon Fasciculation - Paralysis Syndrome: Possibly a new Myasthenic Syndrome

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Abstract

Background: Cases of quadriplegia, oculobulbar palsy and fasciculations are reported to two tertiary teaching hospitals of Hyderabad during monsoon season.

Objective: To describe the clinical and electrophysiological features of cases of acute quadriplegia with oculobulbar palsy, fasciculations and myokymia reported during monsoon season.

Materials and methods: All the patients with presentation of overnight onset rapidly progressive quadriplegia admitted in both teaching hospitals of Hyderabad, over the period of 11 years. All patients were subjected to routine biochemical tests and Electrodiagnostic tests. Patients were treated symptomatically along with invasive ventilator support when required.

Results: A total of 97 such patients were identified. The clinical features observed were bilateral ptosis, external ophthalmoplegia, bulbar, facial, masticatory, axial and proximal muscle weakness. There were extensive fasciculations and myokymia. Respiratory insufficiency occurred at nadir of weakness. The electrodiagnostic tests showed normal motor, sensory conduction studies without any decrement on repetitive nerve stimulation tests. Concentric needle EMG showed fasciculation, fibrillation potentials and repetitive discharges with normal interference pattern. All patients made total functional recovery in a week time. Mortality was due to respiratory paralysis and its related complications.

Conclusion: These unusual cases with typical clinical and electrophysiological features are not reported in the literature and might constitute "Monsoon Fasciculation - Paralysis Syndrome" possibly a new myasthenic syndrome of unknown etiology.

Key words

Quadriplegia, Fasciculation, Myasthenic syndrome, Myokymia, Ophthalmoplegia, Neurotoxin, Neuromuscular junction.

Introduction

During the monsoon months of June to September, two government tertiary teaching hospitals viz., Gandhi Hospital (GH) and Osmania General Hospital (OGH) of Hyderabad get cases of acute onset flaccid quadriplegia with extensive fasciculations and myokymia. The onset is almost always overnight except one wherein it was after an afternoon nap. There is proximal and axial muscle weakness. There is bifacial weakness, external opthalmoplegia, masticatory weakness and bulbar palsy of varying degrees. Respiratory paralysis often occurs during the nadir of weakness usually within nine hours after onset. Nearly half of the patients needed ventilator support. Mortality was due to respiratory paralysis. There was total recovery in a week time. All patients had normal sensorium and preserved sensory modalities. None of the patients gave history of any bite.

Materials and methods

The study was conducted in two phases in the calendar years 1990 to 1995 at OGH and 2010 to 2013 at GH. All patients with the typical clinical features described as above and admitted in emergency department were recorded and analyzed. Care was taken to record the ethnicity, area of residence, place where they were sleeping and ingestion of any toxic material. History of any bite, bite marks, scratches, smell of organophosphates (OP), embedded ticks and local tissue reaction was evaluated. A detailed neurological examination was carried out. Routine investigations – blood sugar, urea, creatinine, liver function tests, hemoglobin, blood counts, calcium, creatine phosphokinase, electrolytes, urine analysis, ECG and X-ray chest was done in all patients. Gastric aspiration for organophosphates was done when OP poisoning was suspected. Supportive and symptomatic treatment was given. Patients with respiratory insufficiency were put on invasive ventilator support.

Nerve conduction studies: motor - bilateral median, ulnar, peroneal and tibial nerves with F wave latencies, sensory – bilateral median, ulnar and sural nerves were studied in all patients. Repetitive nerve stimulation (RNS) test was done on facial (orbicularis oculi), median (abductor pollicis brevis), ulnar nerves (abductor digiti quinti) with Low Stimulation Rate (LSR) of 3Hz in all and High Stimulation Rate (HSR) of 50Hz in median nerve in some patients. Concentric needle EMG was done in orbicularis oculi, deltoid, abductor pollicis brevis, quadriceps within 4 hours of admission in patients who were not on ventilator. Electrophysiological tests were repeated before discharging the patients. Medelec Neurostar MS92B and Nicolet 8-channel Viking electromyograph machines were used under optimal laboratory conditions.

Patients who had received anti snake venom, atropine and neostigmine were excluded from the study. The patients had follow up for 2 to 4 months. Unaffected family members when available were interviewed for any of the symptoms, which the patient was suffering with. Informed consent was taken from the patients or their attendants when the patient was unable to give a valid consent. This study has approval from Dr. NTR University of Health Sciences Vijayawada. Standard protocols for research of the Institutes were followed. The data was computed for statistical analysis.

Results

A total of 97 patients (64 at OGH and 33 at GH) were identified during the study periods. The mean age was 26 years (7 to 60). The male female ratio was 2.3:1. All patients were from rural background hailing from the neighboring districts of Hyderabad and belonged to low

socio-economic status. Most of the patients were farmers by occupation and their dwellings were near to open fields. Eighty five percent of patients were sleeping on the floor. The occurrence was only during Southwest monsoon between June and September. None of the patients gave any history of ingestion of stale/tinned food, drugs or insecticide. None of the patients had smell of organophosphate poison from mouth, skin or clothes. There were no excessive bronchial or oral secretions. All patients were asymptomatic before retiring to bed and could not get up next day morning except one lady who became symptomatic after a midday nap.

The presenting symptoms were inability to open eyes, dysphagia and limb weakness. All patients had varying degrees of bilateral ptosis, external ophthalmoplegia, bulbar, facial, masticatory (jaw-hanging), axial and proximal muscle weakness. At admission complete ptosis was seen in 35%, partial in 65%. Ocular movements were absent in 63% and weak in the rest however pupils were normal in size and reaction. Masticatory weakness was seen in one third of the patients. Bifacial weakness was seen in 90% of patients. Bulbar palsy was seen in 100% patients and 80% required nasogastric feeding during acute illness. Neck and trunk muscle weakness was present in all. Proximal muscle weakness of less than grade 2/5 on MRC scale was seen in 70% of patients whereas distal muscles were relatively preserved. The nadir of weakness was around 9 hours (4 to 14 hours). Ventilatory support was required by 43% of patients. The time of intubation after admission was 30 minutes to 6 hours. Ventilation was started from 30 minutes to 9 hours and the duration of ventilation ranged from 6 hours to 4 days. There were fasciculations in 100% and myokymia (like writhing bag of worms) in 38% of patients more prominent in thigh and calf muscles getting cleared in 48 hours. Deep tendon reflexes were hypoactive whenever there was profound weakness. All patients had normal sensorium and preserved sensory modalities. Nearly one third of patients had mild dull abdominal pain at the time of onset. ECG and blood pressure monitoring did not reveal any autonomic dysfunction. Routine biochemical tests viz., blood sugar, urea, creatinine, liver function tests, hemoglobin, blood counts, calcium, creatine phosphokinase, electrolytes, urine analysis, ECG and X-ray chest were normal in all patients. Gastric aspirate for OP poison was negative in tested patients.

Routine EDX studies showed normal motor and sensory conduction studies including the F wave latencies. RNS tests did not show any decrement on LSR. Concentric needle EMG showed fibrillation potentials **Figure - 1** (Channel-1) ranging from grade 2 to 5 in all muscles tested and fasciculation potentials **Figure - 2** in deltoids and quadriceps in 60% of patients. There were complex repetitive discharges of 50μV to 600μV in amplitude and frequency of 20 to 50Hz at rest. Rest EMG showed plenty of spontaneous activity **Figure - 3** (Channel-2). Recruitment and interference pattern was normal. The Motor Unit Potentials (MUP) analysis was normal in duration and amplitude for the respective muscles. Repeat EMG after total functional recovery did not reveal any abnormalities.

None of the patients gave history of any bite except one lady who was awakened by some crawling sensation in her fabric, which she whisked and went back to sleep. There were no bite marks, local tissue reaction in any of the patients. No offending animal specimen was produced by any of the patients / attendants. None of the family members who shared meal had similar symptoms. However more than one member were affected simultaneously in two instant cases. In one family husband and wife were affected, wherein the wife had profound weakness than her husband. In another family mother and her 4 year old child were affected wherein the child died due to respiratory failure on the day of hospitalization. In both instances none of the other family members who shared meal were affected. All patients who survived respiratory paralysis and related complications had total functional recovery in seven days time

(4-12 days). At OGH 10/64 (15%) patients died due to respiratory paralysis and related complications and 1/33(3%) at GH. The mortality was minimized by good care in Respiratory Intensive Care Units. There was no neurological deficit in the follow up period.

Figure – 1: EMG of frontalis muscle: channel-1 showing fibrillation potentials; channel-2 showing normal recruitment.

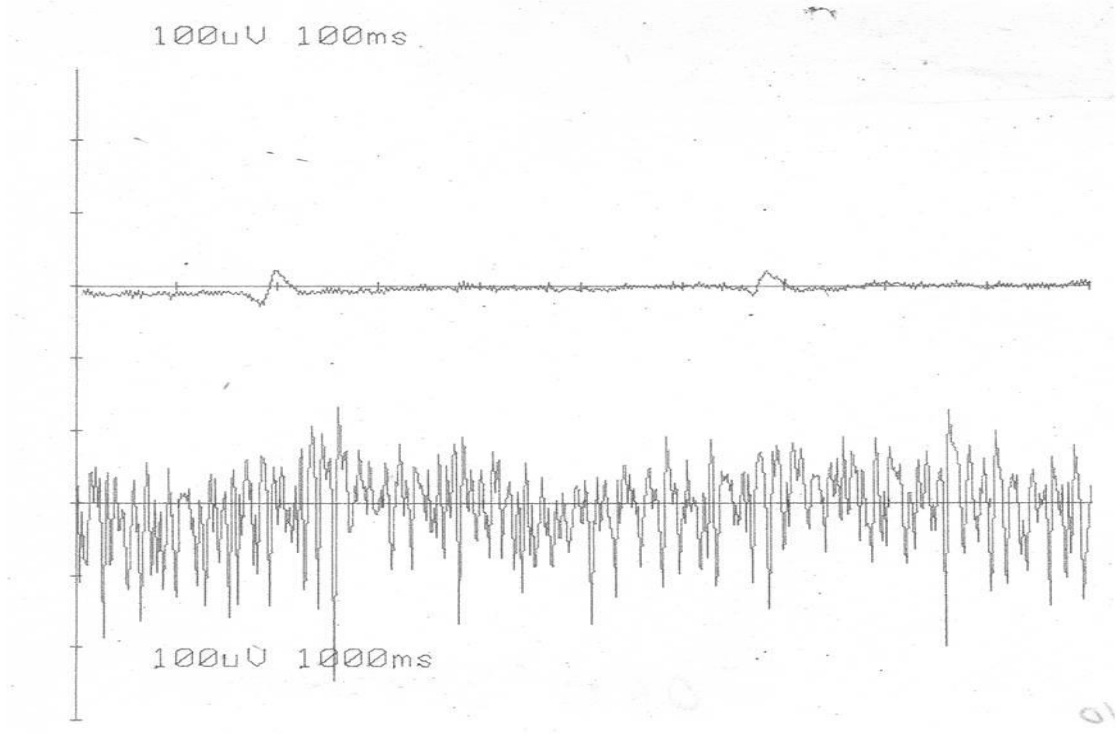


Figure – 2: EMG of vastus medialis muscle: channel-1 and 2 showing fasciculation potentials.

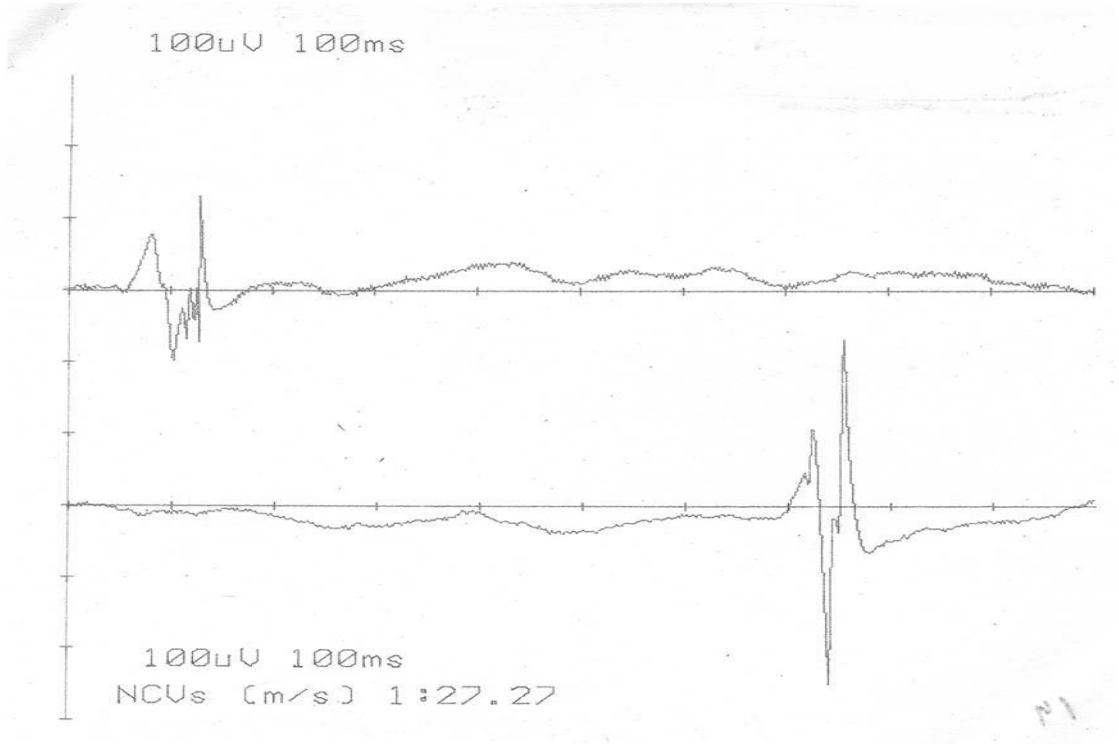
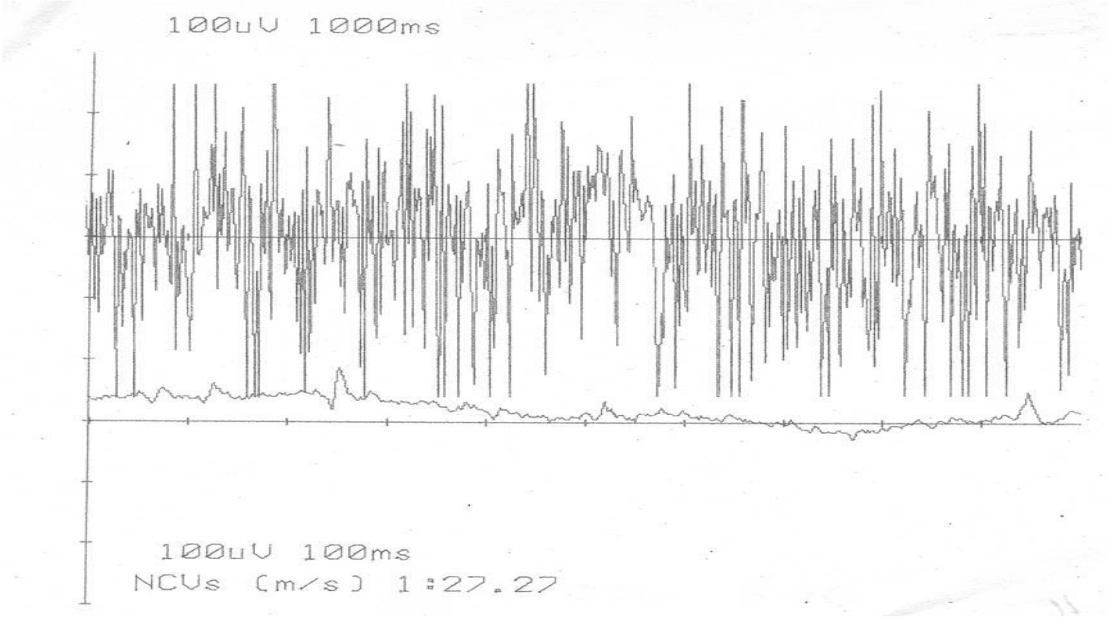


Figure – 3: EMG of orbicularis oculi muscle: channel-1 showing normal recruitment; channel-2 resting EMG showing spontaneous activity.



Discussion

All patients were asymptomatic before going to bed. Ninety percent were sleeping on the floor. None of the city dwellers were affected by this disease indicates that environment plays an important role in the causation of this disease. Open fields and farms have a strong relationship. The characteristic neurological involvement with total recovery in 4 to 12 days time indicates that there must be some reversible factor like a toxin affecting the neuromuscular junction (NMJ) directly. A large number of naturally occurring neurotoxins are known to act at NMJ and induce muscle paralysis of a pattern similar to myasthenia gravis [1]. Immunological mechanism is unlikely owing to rapid total recovery in short duration of time.

Absence of increased bronchial, oral secretions, miosis, typical smell and lack of ingestion differentiates this condition from organophosphate poisoning [2]. Moreover there are no repetitive compound muscle action potentials to a single stimulus or decrement on HSR. Food-borne botulism is unlikely as the habit of people from rural community to prepare fresh meal every time, no ingestion of canned food. Lack of diarrhea, nausea vomiting, dilated pupils and sparing of other family members who shared meal [3]. Tick paralysis is unlikely because of good hygiene and absence of ascending paralysis, ataxia, paresthesias and conduction blocks on EDX tests [4]. Moreover ticks are not prevalent locally. The possibility of scorpion bite is excluded because there is no history of bite and absence of local pain and autonomic storm. It is unlikely to be Black Widow Spider bite as this part of the world is not the habitat and moreover myasthenic features are addition to its typical clinical picture [5]. The species of spiders in this geographical area are non poisonous to humans. Hypokalemic periodic paralysis is excluded in view of dominant faciobulbar muscle involvement. One section of society is reported to have deficiency of Pseudocholinesterase enzyme, but none of the patients belonged to that ethnic group.

Bungarus species which is mostly arboreal in habitat, usually nocturnal and signs of local envenomation can be minimal with profound muscle paralysis is a close differential diagnosis. Offending snake is often found in the bed itself or a killed specimen brought for identification [6]. The nocturnal snakes have a chance of biting on head and trunk, which cannot go unnoticed by so many patients even during sleep. Awareness

of being bitten is seen in nearly two third of patients. Bite marks of varied appearance either single, double, scratches with minimal local reaction / paresthesias are seen in one third of cases [7, 8]. No such observation was made in the present cases. Abdominal pain of krait envenomation is severe colicky often associated with vomiting in almost all cases whereas in the present series the pain was mild dull ache in one third of cases [9]. Reduced CMAP amplitude and decrement on 3Hz stimulation is reported in Bungarus envenomation whereas no such abnormality found in the present series [10]. Characteristic EMG findings seen in the present cases are not reported in krait bite. Systemic manifestations though uncommon in krait bite are often reported [7]. The average annual snakebite reporting at OGH and GH is 543 and 26 respectively. Viper and cobra bites are common in these areas. Krait bite accounts for less than 10% of total snakebites reporting at these hospitals. Incidents of snakebite marginally increase during rainy and summer seasons but occur sporadically throughout the year, whereas these cases occurred only during monsoons in 11 years study period. The differences between Bungarus envenomation as per literature and present series of patients were as per **Table - 1**.

Table – 1: Differences between Bungarus envenomation and present study cases.

Features	**Bungarus envenomation**	**Present study**
Occurrence	All through the year	Only during monsoon
Awareness of bite	69%	Nil
Offending animal produced	30-47%	Nil
Bite marks	35-50%	Nil
Abdominal pain	Severe colicky in 91%	Mild dull ache in 33%
Local reaction	18-30%	Nil
Altered sensorium	71%	Nil
Pupillary abnormality	66%	Nil
Paralytic ileus	41%	Nil
Hypokalemia	71%	Nil
Antegrade amnesia	40%	Nil
Myokymia	Not documented	Documented in 38%
CMAP amplitude	Decreased	Normal
RNS at 3Hz	Decrement	Normal
EMG - spontaneous activity	Not documented	Present in 100%
EMG – fasciculation potentials	Not documented	Present in 100%
EMG – fibrillation potentials	Not documented	Present in 100%

CMAP = Compound Muscle Action Potential; RNS = Repetitive Nerve Stimulation; EMG = Electromyography

The author proposes this syndrome must be due to a neurotoxin following accidental bite of some venomous animal or insect, which would change its natural habitat at the onset of rains and enters the dwellings. It is small enough to go unnoticed and undetected in sleep. In 1992 Hyderabad received monsoon early and two cases were recorded in the month of May, which usually happens to be summer. An attempt is made to correlate trend of cases and the magnitude of rainfall in the second phase of the study **Figure - 4**, but in view of low incidence of the disease no statistical conclusions could be drawn. **Figure - 5** shows the scatter plot of cases and rainfall (R^2 value 0.33012).

In those two instant cases wherein two members in a family were simultaneously affected, the

wife might have been bitten first and received more dose of toxin and had profound manifestations than the husband. In the second case, the mother had profound weakness and had to be supported on ventilator for four days and child probably succumbed in view of small body mass.

Pathophysiologically most of the clinical features could be postulated by reversible cholinesterase inhibition at neuromuscular junction (NMJ). The residence time of Acetyl choline (Ach) in the synaptic cleft increases allowing rebinding of neurotransmitter to multiple Acetyl choline receptors (AchR). Successive stimulation of neighboring AchR results in prolongation of decay of the endplate potential. Quanta released by individual nerve impulses are no longer isolated. This action alters the synchrony between the endplate depolarization and the development of action potentials and consequent asynchronous excitation leads to fibrillations. With sufficient inhibition of AchE, depolarization of the endplate predominates and blockade owing to persistent depolarization ensues leading to NMJ transmission failure. When excessive Ach persists in the synaptic cleft, it may also depolarize the axon terminal resulting in antidromic firing of motor neurons, which involves the entire motor unit thus giving rise to fasciculations **Figure - 6**. Thus repetitive bursting of motor units i.e., grouped fasciculations gives rise to myokymia. The dull abdominal pain can be explained by the similar effect of the proposed neurotoxin on gut.

Figure – 4: Trend of cases and rainfall during Southwest monsoon. Month wise cases are shown in red. Rainfall in millimeter is superimposed on cases in green in the second phase of the study (2010 to 2014).

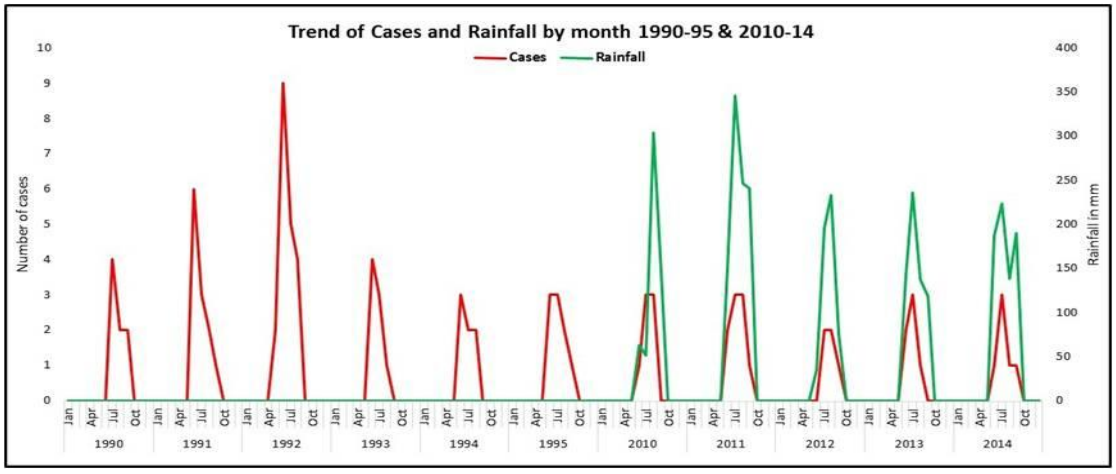


Figure – 5: Scatter plot showing of cases and rainfall showing R square value.

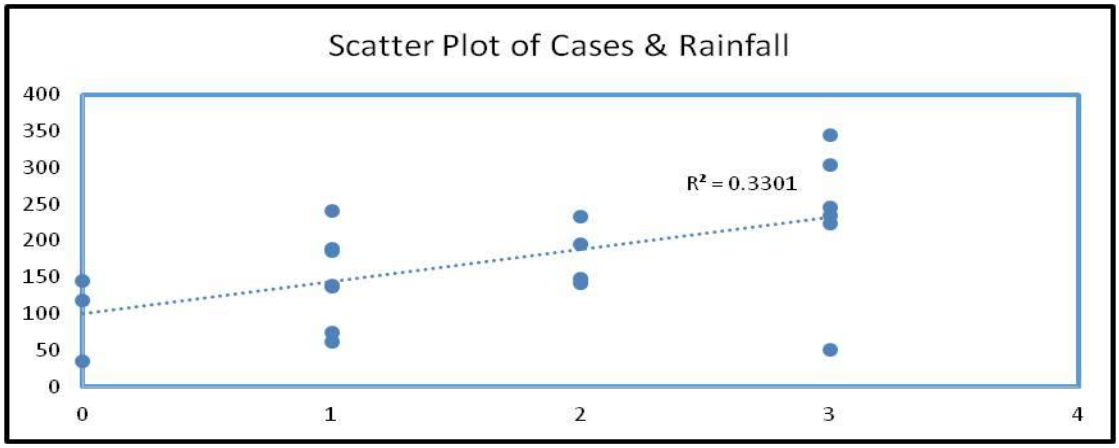
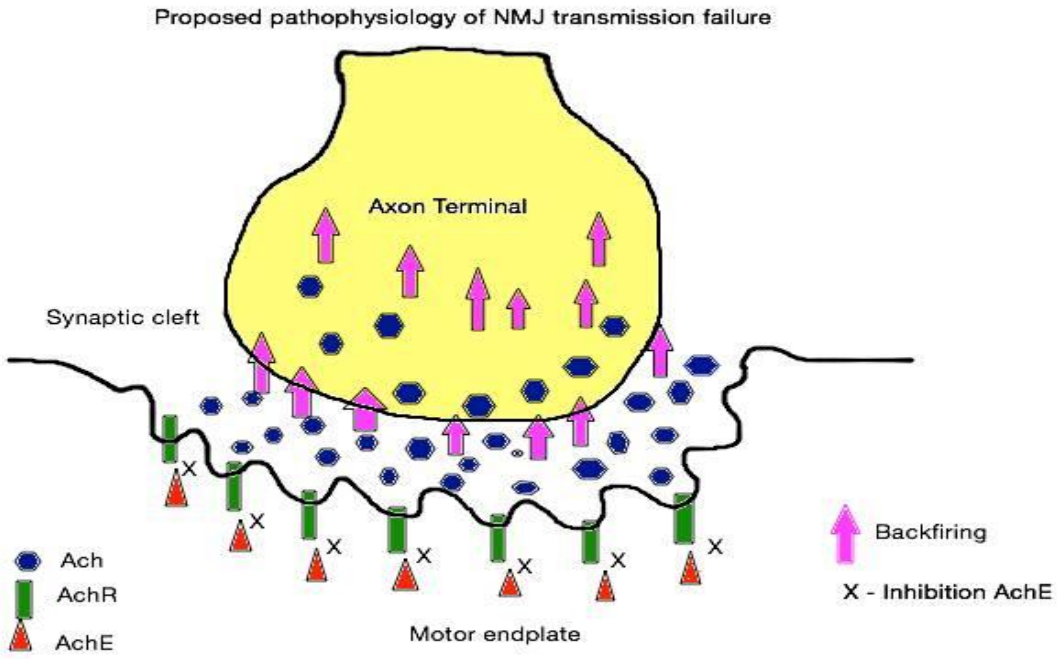


Figure – 6: Schematic diagram showing pathophysiology of NMJ transmission failure.



The patients and their senior attendants were not aware of such disease occurring in their villages. They assume that some insect or centipede might have bitten but not sure what it was. Some patients described one insect, popularly known in the local Telugu language as "kummari purugu" which resembles Gryllotalpidae member. There is paucity of literature on this subject and none of these organisms are known to possess toxin which could produce characteristic clinical features and of having potential to kill a human. Such cases may be occurring in other geographical areas also. Unless a detailed epidemiological study is undertaken, the causative agent would continue to be elusive.

Conclusion

It is of considerable interest to note that the characteristic clinical and electrophysiological features of these patients are not reported to the knowledge of the author and hence merit considering "Monsoon Fasciculation-Paralysis Syndrome" as a new myasthenic syndrome due to unknown animal envenomation possessing some neurotoxin capable of producing such a clinical disease. The plethora of clinical and EDX findings of this case study pose the following issues.

- Whether presence of fasciculation, myokymia, fibrillation and repetitive discharges on EMG are manifestations of an unknown poison content of a known animal bite.
- Whether it is due to an unknown animal with an unknown neurotoxin altogether, which escapes detection.
- A possible mechanism is proposed in these cases, however there could be complexity of sites of action on NMJ and if not NMJ what other sites the poison would act to explain these clinical findings remains to be explored.

Strength of the study

The clinical and electrophysiological features of the patients are defined in detail and the duration study period is eleven years from two different tertiary teaching centers.

Limitations

Detailed epidemiological study should have been carried out to identify the animal involved to know the venom in the causation of this disease.

Toxicological study of serum of patients for possible venoms and other toxins should have been done. No neuropathological study of NMJ was done.

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