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CASE SERIES

Case Series - Respiratory Paralysis Responding to Vitamin D Therapy

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SUMMARY

Acute ascending flaccid paralysis with areflexia were considered as Guillain-Barre Syndrome by medicine and neurology department as tradition. We present two patients 46 years old female and 57 years old male with acute ascending flaccid paralysis admitted in intensive care unit. They developed respiratory paralysis requiring mechanical ventilation. The male patient developed cardiopulmonary arrest during shifting to intensive care unit. Both the patients responded to vitamin d therapy dramatically. Respiratory paralysis on mechanical ventilation responding to vitamin d therapy dramatically were unique events. Vitamin d deficiency is a worldwide problem but its presentation as acute ascending paralysis with areflexia requiring mechanical ventilation is not cited in medical literature.

Keywords; Acute ascending flaccid paralysis with areflexia, Respiratory paralysis, Vitamin D deficiency, Vitamin D therapy,

INTRODUCTION

It is hard to find a case report of acute ascending paralysis leading to respiratory paralysis requiring mechanical ventilation due to vitamin d deficiency. During the last century, predominant cause of acute flaccid paralysis was poliomyelitis. Effective vaccination has dramatically reduced poliomyelitis worldwide. Several studies have concluded Guillain-Barre Syndrome, the most common cause of this illness. Other causes include neuroparalytic snake envenomation, Hypokalemic paralysis, acute intermittent porphyria, viral meningoencephalitis, early acute transverse myelitis, Miller Fisher syndrome, and myasthenic crisis. But acute ascending paralysis with areflexia in adults is considered as G.B.Syndrome[1].

We managed two adult patients of acute ascending paralysis and areflexia with provisional diagnosis of G.B. Syndrome by medicine and neurology departments. Both the patients required mechanical ventilation. One patient while shifting to intensive care unit developed cardiopulmonary arrest before intubation. Strangely enough, pattern of illness was similar to G.B. Syndrome except paresthesia but both patients responded dramatically to vitamin D therapy.

G.B. syndrome is primarily a clinical diagnosis presenting as acute ascending flaccid paralysis, areflexia , paresthesia, motor weakness may involve respiratory muscles and cranial nerves. It is a sensorimotor neuropathy[1]. Vitamin d deficiency is widespread disorder. Rickets and osteomalacia are most common presentations of vitamin d deficiency. Muscle weakness due to vitamin d deficiency is not emphasized in literature[2] but respiratory paralysis responding to vitamin d deficiency is not mentioned in literature until now.

CASE REPORT 1

A 46 years old married lady had three children, belonged to low socioeconomic condition. She was a resident of a town of South Punjab. She presented in emergency of tertiary care hospital with bilateral weakness of both legs led to involve both upper limbs over 8 hours. The patient did not complain of pain or paresthesia. She was shifted to intensive care unit due to progressive respiratory difficulty. There was a history of constipation, vomiting, cough and palpitations three weeks before this event but no history of sore throat and fever. No history of smoking and alcohol intake. No history of similar condition in family. No history of diabetes, hypertension, I.H.D, C.O.P.D or asthma.

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On examination, patient was conscious, oriented in time and space. Heart rate was 105/minute and blood pressure 130/90. There was a complete loss of sensation in both upper and lower limbs. Patient was unable to create any contraction in upper or lower limb. Reflexes were absent in both upper and lower limbs. There was no evidence of cranial nerve involvement.

When the respiratory rate increased to 34 per minute and oxygen saturation dropped to 88% on supplemental oxygen, patient was intubated and put on mechanical ventilation. Lumber puncture was done and cerebrospinal fluid was sent for examination. Laboratory investigations were unremarkable except serum calcium was 07mg/dl (Serum albumin 4.4 gram/dl). Twenty ml of calcium gluconate were administered over 40 minutes, followed by a continuous infusion of 40ml of calcium gluconate per day. Next day, prolonged QT interval was noticed by author despite infusion of calcium gluconate. Corrected QT interval was 0.55 seconds.

The faculty of medicine diagnosed her suffering as Guillain-Barre Syndrome and plan was to administer intravenous immunoglobulnis. The husband of patient, a class 4 government servant requested Chief Minister Punjab to arrange immunoglobulins amounting rupee 4,75,000/-. The author advised inj. Vitamin D i.m. once a day for two days.

Next day, the author worried on looking vacant bed of patient. On inquiry, it was told that that the patient herself went to wash room on her feet without support. Patient was kept under observation for 5 days and discharged to home with normal muscle powers. Patient was advised to take oral vitamin d 200,000 units after every two months. Patient remained fine for ten years on follow up.

CASE REPORT 2

A 57 years old man had 5 children belonged to upper middle class. He presented to consultant of neurology with weakness of both lower limbs. He was unable to stand after sitting for defecation. He was raised with support and brought to bed. After a few minutes, while trying to walk, he fell down. The patient did not complain of pain or paresthesia. He had a history of backache and radiculopathy in right leg. He felt loss of sensation and power in right leg from time and again. He had received epidural steroid thrice by a renowned orthopedic professor at Lahore thrice with 3-4 months interval, the last administration was done 3 months before the event.

Considering the previous problem and management, consultant neuro physician advised him to consult after MRI. After 2-3 hours, patient felt weakness in both upper limbs as well. The patient was shifted to emergency of tertiary care hospital. There was no history of constipation, vomiting, diarrhea, sore throat cough or palpitations during preceding four weeks. Patient had

been smoking for the last 30 years. But no history of alcohol intake, no history of similar condition in family, no history of diabetes, hypertension, I.H.D, C.O.P.D or asthma. This patient belonged to the South Punjab in area adjoining of patient reported as case report 1.

On examination, patient was conscious, oriented in time and space. Heart rate was 118/minute and blood pressure 150/95. There was a complete loss of sensation in both upper and lower limbs. Patient was unable to create any contraction in upper or lower limb. Reflexes were absent in both upper and lower limbs. There was no evidence of cranial nerve involvement.

Patient developed difficulty in breathing and cyanosed. Patient was shifted to I.C.U. On reaching I.C.U., the patient developed cardiopulmonary arrest. Cardiopulmonary resuscitation was done. After return of spontaneous circulation, patient was intubated and put on mechanical intubation.

Blood sample were taken for Complete blood count, electrolytes, renal, liver function. Lumber puncture was done and cerebrospinal fluid was sent for examination. Laboratory results were unremarkable. The sample was also sent for 25-Hydroxy Vit D level. After taking sample, Inj. Vitamin D was administered i.m. once a day for 3 days. The report of 25-hydroxy vitamin D level received after 3 day reflected severe deficiency (04ng/ml=10 nmol/L). Adequate respiratory effort returned two days after completion of administration of vitamin d intramuscularly. Patient was able to walk as before the event on 5th day of start of injection vitamin D. Patient was advised to take oral vitamin d 200,000 units after every two months. On follow up until 10 years, the patient was fine. However, he forgot the recent conversation. He could not memorize the briefs of critical event.

DISCUSSION

It is hard to find case report of acute ascending paralysis leading to respiratory paralysis requiring mechanical ventilation due to vitamin d deficiency. Both the patients had clinical features similar to G.B. Syndrome, a sensorimotor motor neuropathy, classically a clinical diagnosis in adult patients presenting with acute ascending flaccid paralysis with areflexia[1].

Acute ascending paralysis with areflexia requiring mechanical ventilation is a very rare presentation of vitamin d deficiency, a much more common condition. Vitamin D deficiency being prevalent all over the world may be considered in differential diagnosis of muscle weakness.

In differential diagnosis, in G.B. Syndrome, recovery of muscle power would have been much slow and dramatic recovery with vitamin d therapy would not have occurred. There was no involvement of cranial nerves[1]. There was no history of snake bite. Even If we suspect, simultaneous weakness of both upper and lower limbs accompanied with bulbar and extraocular muscles would have been more likely[1]. There was no history suggestive of electrolyte especially potassium disturbance. Acute intermittent porphyria is least likely to present at ages above 45 years. There was no history of abdominal pain and psychiatric disturbances[3].

Our case series is in favour of wise saying that rare manifestation of common diseases is much more common than common presentation of rare disease[4]. A recent study has reported that 24% population of USA, 37% of Canada and 40% of Europe are vitamin d deficient[5]. Riaz H et al reported grave situation in Pakistan reflecting normal vitamin d level only in 15.3% of population, 53% of Pakistani were vitamin d deficient and 31.2% had insufficient vitamin D[6].

In United States, G.B. Syndrome is the most common cause of acute flaccid paralysis with annual incidence of 1.2-3 per 100,000 population[7]. The prevalence of acute intermittent porphyria is 1:20,000[8].

Difficulty in walking upstairs due to Vit D deficiency was initially considered secondary to osteomalacia[9]. Floyed et al illustrated electromygraphic changes in patients suffering from osteomalacia[10.] Several researchers reported reversibility of muscle weakness associated with vitamin d deficiency[6]. After multivariate regression analysis, Glerup et al., found no correlation between markers of osteomalacia and muscle power. They concluded that only 25-Hydroxy Vitamin D level was significantly associated with maximum voluntary contraction, emphasized the importance of appropriate 25-Hydroxy Vitamin D level for maintenance of adequate muscle function[9]. Sato et al assessed histopathology of muscles and found that type 2 muscle fibers (initially recruited, fast twitch fibers) increased in content and mean diameter in Vit. D supplemented group while reduced in control group after 2 years[12].

Transcription of a range of proteins (including involved in calcium metabolism) is accelerated by binding of 1, 25-dihydroxy vitamin D to the Vitamin D Receptors. Calcium is a critical modulator of skeletal muscle function. Contractile and relaxation properties of muscles are influenced by handling of calcium[13]. 1,25 dihydroxy vitamin D improves muscle function by regulating total body calcium, calcium and phosphorus homeostasis, calcium related protein transcription and enhances IGFBP-3 transcription[14]. Khazai N et al found better results with administration of calcium and vitamin d than calcium alone**.** They explained their results by shifts of calcium rapidly by signal transduction pathway from the sarcoplasmic reticulum to the cytosol . The discovery of VDR a cognate nuclear receptor by Brubaugh and Haussler, in 1974 explained the genomic and non genomic effects in cells[15]. Vitamin d receptor in skeletal muscles explained direct association between myopathy and vitamin d deficiency[2].

Anu Prabhala reported two elderly and three young patients (one with type 1 diabetes, second with carcinoid syndrome and third malnourished) immobile patients confined to wheel chair. High index of suspicion led to identify low 25 hydroxy vitamin d and elevated parathyroid hormone level. Administration of vitamin d for 4-6 weeks restored their mobility[16].

Wise PM observed shorter weaning time from mechanical ventilation by increasing direct sunlight exposure[17]. Miri M demonstrated reduced duration of mechanical ventilation, hospitalization and mortality rate in critically ill patients by administration of high doses of vitamin d[18].

Limitations: These are only two case reports and both the patients belong to same area. Muscle biopsy to exclude primary myopathy were not performed. CT scan, M.R.I., Nerve conduction studies were not available in those days in the institution. 25-hydroxy vitamin d level in first patient was not checked. We suggest multicentre clinical trials by monitoring of 25 hydroxy vitamin d of critically ill patients requiring mechanical ventilation and their response to vitamin d supplementation.

CONCLUSION

In summary, we described two patients with typical presentation and provisional diagnosis of G.B. Syndrome. Both patients required mechanical ventilation and one developed cardiopulmonary arrest. Both the patients recovered dramatically with vitamin d therapy. Vitamin d deficiency is a common disorder. We suggest monitoring of 25 hydroxy vitamin d level in critically ill patients. Multicenter large sample clinical trials may be performed to evaluate the significance of problem. The clinicians must beware of unusual presentation of more common diseases[19] as reported in this case series.

Contribution of authors: HDD: Original concept,primary treating physician, Manuscript. **SS:** Member of treating team&Revised manuscript, **AZ:** Add intellectual content to manuscript, **RK:** Final approval of version of manuscript

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