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NEUROMUSCULAR DISEASE MIMICKING MYASTHENIA GRAVIS IN A NIGERIAN FEMALE ADOLESCENT: COULD THIS BE NEMALINE ROD DISEASE?

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ABSTRACT

***Background*: Nemaline rod disease is a congenital myopathy, presentation of which may mimic myasthenia gravis.**

***Methods*: We report a suspected case of nemaline rod disease in a female adolescent who presented with features similar to myasthenia gravis but failed to respond effectively to its conventional management. She had features of respiratory failure and cardiomyopathy**

***Result:* Patient had a turbulent clinical course and finally succumbed to illness on the fifth day of admission.**

***Conclusion:* This report is meant to sensitize child neurologists and general paediatricians on the need to have a broad spectrum of considerations in the management of suspected myasthenia gravis, especially when response to anticholinesterase is poor.**

Keywords: Nemaline disease, Myasthenia gravis, Anticholinesterase

INTRODUCTION

Nemaline Rod Disease, otherwise known as Nemaline Myopathy (NM) is a congenital myopathy characterized by hypotonia, muscle weakness and often skeletal deformities with the presence of nemaline rods in the muscle biopsy[1-3]. Facial and respiratory muscles can be involved in NM and several patients with the condition have been known to experience respiratory failure[2-4]. Cardiac involvement, particularly dilated cardiomyopathy, may occur[3,4] and cardiac and respiratory involvement have been documented as indices of worse prognosis[1,2].

Myasthenia Gravis (MG) is a group of autoimmune neuromuscular diseases characterized by abnormal neurotransmission at the motor endplate resulting from destruction of acetylcholine receptors by anti acetylcholine receptor antibodies[3,4]. It is characterized by varying degree of muscle weakness, most patients (85%) presenting with ocular symptoms ranging from ptosis, diplopia or blurred vision while others could present with leg, arm, face, neck and trunk weakness, bulbar symptoms and generalized fatigue[4]. Autoimmune MG in children is most commonly divided into neonatal transient and juvenile types, onset of which is usually after 10 years of age[4]. Without treatment, MG can become progressive and life threatening, especially when the bulbar and respiratory muscles are affected[1, 2]. The heart is not involved in myasthenia gravis and electrocardiographic findings remain normal while roentgenogram of the chest often reveals an enlarged thymus[1]. Most patients usually respond well to anticholinesterases with or without a variety of immunosuppressive medications[2].

We present the case of an 11 year old Nigerian girl with suspected nemaline rod disease.

CASE REPORT

AAM was an eleven year old female adolescent who was referred from a tertiary paediatric centre to the Paediatric Neurology Clinic, University College Hospital, Ibadan on account of drooping of the eyelids of 2 years duration, easy fatigability and breathlessness of 6 months duration and 1 week history of swollen feet.

She was apparently well until 2 years prior to presentation when she developed drooping of both eyelids which usually worsened as the day progressed. There was associated limbs weakness, difficulty with swallowing of solid diet and occasionally of liquids with concormitant reduced calorie intake and weight loss over about 18 months. She was initially commenced on oral Pyridostigmine and Prednisolone without any significant improvement and later tried on oral Neostigmine which improved ocular symptoms but was later discontinued when patient developed severe diarrhoea. She was admitted twice in the 4 months preceding her presentation at our facility on account of severe respiratory distress, during

one of which she was placed on mechanical ventilation. A week prior to presentation, her condition deteriorated with severe effort intolerance, difficulty with breathing, orthopnoea, Paroxysmal Nocturnal Dyspnoea (PND) and swelling of both feet all of which were not associated with cough or change in urinary output and frequency. There was no history of bluish discoloration of the lips or extremities.

Pregnancy, delivery and neonatal periods were uneventful and developmental milestones were within normal limits. She was born into a monogamous family setting and there was no similar history in any other member of the family.

Findings on examination revealed a chronically ill girl, mildly pale with bilateral periorbital and peripheral oedema up to the mid-thigh, anicteric, not cyanosed and without significant peripheral lymphadenopathy. She was dyspnoeic with flaring of the alae nasi and shallow respiratory excursions. Respiratory rate was 36 cycles per minute with fine crepitations at the right lung base. Pulses were small volume and regular with a rate of 124 beats per minute. Blood pressure was 100/60mmHg, Jugular venous pressure was raised. The apex beat was displaced to the fifth left intercostal space lateral to the mid-clavicullar line. Auscultation revealed a gallop rhythm with a loud pulmonic component of the second heart sounds. The abdomen was distended with ascites demonstrable by shifting dullness and a non-tender hepatomegaly measuring 2cm below the right costal margin. She was conscious, alert and well-oriented with intelligent conversation. There was no ptosis or opthalmoplegia on arrival. Cranial nerves were intact with normal muscle tone and grade 5 muscle power in all limbs. Gait was normal. An assessment of background Myasthenia Gravis in remission with Cor Pulmonale to rule out Cardiomyopathy and Chronic renal failure was made. She was commenced on intravenous frusemide 40mg (1mg/kg/dose) 8 hourly for 24 hours and oral spironolactone, hydrochlorothiazide and lisinopril. Electrolyte, Urea and Creatinine were within normal limits. Chest x-ray showed cardiomegaly (Cardiothoracic ratio = 66%) and fluffy cotton wool opacities in both middle and lower lung zones. No enlargement of thymic shadow was noticed. Electrocardiographic features were in keeping with right ventricular hypertrophy while Echocardiography by the paediatric cardiologist showed biventricular dysfunction worse on the right, all in keeping with cardiomyopathy. Patient was reported to be seronegative for acetycholine receptor antibody at the referral centre.

She was recommenced on low dose pyridostigmine (30mg qds) on the second day of admission, having been off the medication and oral prednisolone for about 3 weeks prior to presentation. This was however discontinued on the third day when she developed tremors and muscle fasiculations after about 24 hours of commencement. About 42 hours into admission, she developed worsening respiratory distress necessitating Intensive Care Unit admission with mechanical ventilation. She was subsequently reviewed after which MG was then considered unlikely on the basis of (1) Lack of response to anticholinergic agents; (2) repeated episodes of cholinergic crisis even with low dose anticholinesterase; (3) lack of response to corticosteroids; (4) features of congestive cardiac failure with acute pulmonary oedema and (5) recurrent episodes of severe respiratory distress requiring mechanical ventilation. A possibility of Congenital myopathy ? type to keep in view Nemaline Rod Disease with respiratory muscle weakness was subsequently entertained.

She was weaned off anticholinesterase and Electromyography, Muscle biopsy and serum creatinine kinase were requested but could not all be done before demise. Clinical conditions remain turbulent until she succumbed to the illness on the fifth day of admission.

DISCUSSION

It is well documented in the literature that ocular symptoms (ptosis, diplopia or blurred vision) are the earliest, commonest and the most constant signs in patients with MG[1,2]. It is therefore not surprising that MG was the foremost diagnosis considered in the management of this patient. The presence of limb weakness and associated difficulty in swallowing further strengthened this consideration. Although MG could sometimes present with respiratory difficulty especially when not promptly diagnosed and treated, most of the patients respond well to anticholinesterase and immunosuppressive therapy[1,2]. The poor response of this patient to anticholinesterase and immuno-suppressive therapy with prednisolone, which is considered by many as the most effective oral immunosuppressive agent in MG [2], the presence of recurrent respiratory difficulty requiring mechanical ventilation and cardiac involvement in this patient add weight to the possibility of NM, a condition which has been reported to be associated with facial and limb weaknesses, cardiac involvement and respiratory failure[3-5] all of which were present in this patient.

Our inability to obtain muscle biopsy for definitive diagnosis in this patient before her demise makes

diagnostic challenges in a developing economy like ours very obvious. Six different forms of NM have been described with variable prognoses[6] while several authors have reported variable clinical manifestations of the conditions from infants with the infantile type through adolescent to the adults forms[3,7,8] but sufficient data depicting the condition in Nigerian and African children are lacking. However, the onset of symptoms in this patient in late childhood suggest she had the juvenile variant of NM. In addition, the fact that patient was a female with symptoms beginning with drooping of the eyelids before involvement of other muscle groups make the diagnosis of muscular dystrophy unlikely.

Tensilon test could not be done in this patient because of its inavailability. Although neostigmine was available and could have been utilized as an alternative, patient had earlier showed adverse effect when she was tried on neostigmine in the past (She had profuse diarrhoea when she was tried on neostigmine as earlier stated). Hence, attempting neostigmine test in the setting of such adverse reaction could have been fatal and might have accelerated patient's demise. Even when low dose pyridostigmine was commenced as an alternative, patient still manifested adverse effect on the second day which eventually led to the withdrawal of anticholinesterase from her therapy. We acknowledge that ice pack test should have been performed in this patient since it is very cheap and reports has shown that cold improves neuromuscular transmission[9]. This could have further assisted in clarifying the diagnosis. However, situations in which ice pack test was positive in patients with ptosis and underlying diagnosis still remain unclear have been reported, thus leading to a cautionary note on relying on it solely for diagnosis of myasthenia gravis[9]. Plasmapheresis and intravenous immunoglobulin were not readily available for utilization during the course of management.

Although evidences abound that NM is a genetic disease commonly involving the mutation of the nebulin gene[10], there have been documented reports of its demonstration in Human Immunodeficiency Virus (HIV) myopathies[4,11], thus suggesting a possible autoimmune component in its aetiopathogenesis. There is no cure for NM as at present[12]. Some patients with the disorder are able to lead an active life, especially when there is no cardiac and respiratory involvement[3].

Patients with cardiac involvement have been reported to benefit from Angiotensin Converting Enzyme inhibitors, â blockers or angiotensin receptor blocker[4] while some authors have documented the beneficial effects of L-tyrosine, a non-essential amino acid which is a precursor or catecholamines which possibly explain its beneficial effects[6]. Ivabradine, a cardiotonic agent, has been used in some patients with NM who developed heart failure unresponsive to â blockers[11].

CONCLUSION

Although this report is limited by lack of definitive diagnosis with muscle biopsy, the diagnostic puzzle between MG and NM at the presentation of this patient is very obvious and the eventual consideration of NM during a later review in the course of management on the ground of previous history of facial weakness, dysphagia, respiratory and cardiac involvement and poor response to anticholinesterase and immunosuppressive therapy with oral prednisolone agrees with documented clinical course of NM[3-5], while the presence of respiratory failure and cardiovascular compilations likely worsened the prognosis in this patient. We wish to therefore sensitize clinicians in resource poor setting and developing economies to these rare conditions which could sometimes present as diagnostic and management challenges.

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