Case Report

Neuroacanthocytosis with comorbid depression – a case report

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ABSTRACT

Neuroacanthocytosis (NA) referred to as Neuroacanthocytosis syndromes, are a group of genetically transmitted diseases diagnosed based on peripheral blood acanthocytes and central nervous system as well as neuromuscular symptoms. More often several of psychiatric manifestations and cognitive symptoms are also present significantly in form of obsessive–compulsive disorder, depression and schizophrenia-like psychosis. Here, we discuss a case of a patient presenting in a psychiatry clinic with some strange complaints like biting her own lips and tongue, eating clothes and plastics and difficulty in swallowing, which turned out to be due to Neuroacanthocytosis and on detailed mental status examination, she also had depressive features which had started nearly 3 years after the onset of the illness. Peripheral blood smears revealed 70% acanthocytes. A diagnosis of Neuroacanthocytosis and Major Depressive Disorder was made and treatment was initiated.

Key words: neuroacanthocytosis, depression, acanthocytes, major depressive disorder

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INTRODUCTION

Neuroacanthocytosis (NA) referred to as Neuroacanthocytosis syndromes, are a group of genetically transmitted diseases diagnosed based on peripheral blood acanthocytes and central nervous system as well as neuromuscular symptoms [1-2]. Neuroacanthocytosis (NA) refers to a heterogeneous group of syndromes in which nervous system abnormalities coincide with red blood cell acanthocytosis, i.e. deformed erythrocytes with spike like protrusions [3]. It is an exceedingly rare autosomal recessive disorder. Psychiatric co-morbidities in the form of depression, anxiety, personality change, cognitive impairments and obsessive compulsive symptoms have been described with Neuroacanthocytosis [4]. All NA disorders have an unrelenting progressive course and all of them are eventually fatal. Death results, usually due to the self injurious behavior or as a consequence of severe dyskinetic movements of the pharynx [5]. Neither curative nor disease-modifying treatments are available so far and currently the management of the NA disorders is only symptomatic [2]. We present a case of a 32 years old female with no family history of choreoathetosis presenting with dystonias, choreoathetosis, depressive symptoms and plenty of acanthocytes seen in the peripheral smear. This case highlights the rarity of the disorder, the need for vigilance and the possible psychiatric co-morbidity and its successful treatment.

CASE REPORT

A 32 yr old single lady was brought to the outpatient department with history of altered behavior in the form of biting herself, eating clothes and plastics and spitting inappropriately since past 6 years. These symptoms were insidious in onset, gradually progressing and were worsening day by day. These symptoms disappeared completely during sleep. When awake, she had an uncontrollable desire to bite her own lips and tongue. The patient had to keep a cloth or some plastic article in her mouth for the whole day, which she kept on chewing, to prevent biting her lips and tongue. She had also chewed and injured all her fingers in the process. The relatives perceived this to be weird behavior and thought she was trying to eat the cloth or plastic. She also had difficulty in deglutition and so would spit out the saliva which would accumulate. On examination, she was found to have multiple lacerations on her lips, which, by then, were reduced to mere thin lines and had multiple half healed wounds. She was continuously chewing her clothes. She also had motor tics and choreo-athetotic movements involving both the upper limbs. On Mental Status Examination, she was conscious, oriented and attentive. She conveyed her mood to be pervasively sad and reported preoccupation with her physical symptoms and decreased interest in all her routine activities. She had frequent passive death wishes and reported loss of appetite and disturbed sleep, with problems in the onset and maintenance. There were no psychotic features like delusions or hallucinations as well as no Obsessive Compulsive symptoms. She had attended multiple physicians and psychiatrists in these six years of her illness.

She had been treated with Clonazepam (0.5-2 mg/day) and Haloperidol (0.5-5 mg/day) most recently, but had not shown any improvement with these medications. There was no past history of seizures, abnormal behavior or other movement disorder. There was no history of similar illness in her family. However, her elder real brother suffered from epilepsy which was being treated successfully. She was born of a non-consanguineous marriage and had one elder brother (one who suffered from epilepsy) and one healthy younger brother. From her father's second marriage with his own wife's sister, she had two sisters and two brothers, who were not suffering from any disease. With the dictum in mind to chase Wilson's disease in every movement disorder case, the patient was advised to undergo routine blood investigations, along with 24 hour urine copper, Serum Ceruloplasmin, MRI Brain and later advised Apolipoprotein A and B levels too. Although these investigations were advised, they could not be done, as the patient was very poor and could not afford the costs. She however got her Complete Blood Counts and Peripheral Smear done along with a Liver Enzyme assay from the Government Hospital. Her Hemoglobin was 10.3 gm%, WBCs Total : 10,300/cumm and differential counts were Polymorphs: 80%, Lymphocytes : 18%, Eosinophils :2%, Monocytes : 0% and Platelets : 5,04,000/cumm. However, peripheral smear showed RBCs with more than 70% acanthocytes. Her liver enzymes were SGOT 82 u/l, SGPT 49 u/l.

The prognosis of the disease was explained to the parents and the patient and genetic counseling was done. The patient was treated on outpatient basis and was started on Capsule Fluoxetine 20 mg and clonazepam 0.5 mg at night for her depressive symptoms. Tablet Tetrabenazine (Ticstop) 25 mg per day was started for her dytonias, tics and choreoathetotic movements, which was gradually increased to 150 mg per day over next 20 days (samples were provided with the help of pharmaceutical company). There was only a partial improvement in all her symptoms in a week's time. Tablet Clonazepam was increased to 1mg at night. On next couple of follow-ups a week apart, patient did not have any further improvement in her dystonic and movement symptoms. Capsule Fluoxetine was optimized to 60 mg per day. Tablet Lithium in the dose of 900mg in three divided doses was added based on a few case reports of its effectiveness and easy availability. The patient showed improvement in her depressive features and denied having any death wishes. Also, her sleep and appetite were better. Her motor symptoms, however, showed only slight improvement. There was relief in tics and movements but difficulty in deglutition persisted.

However, the patient lost to follow up for the next 6 months. She however returned with worsening of her motor as well as depressive symptoms. The patient had received a couple of Botulinum Toxin Injections at some government institute in south India, for her dystonias, but as per the patient there was no benefit.

She was again restarted with Tetrabenazine, Lithium, Clonazepam, and Escitalopram. However, again after partial improvement the patient was lost to follow up for the next couple of months. Her husband later came and reported that she had developed severe feeding dystonias and hence was unable to swallow anything and was being fed by a "tube in the stomach".

DISCUSSION

NA disorders can be divided into two broad groups. These are the "core" NA syndromes and other NA conditions with alteration of lipoprotein metabolism. Chorea-acanthocytosis (ChAc), McLeod syndrome (MLS), Huntington's disease-like 2 (HDL2), and Pantothenate kinase associated neurodegeneration (PKAN), are the core NA syndromes, which manifest as movement disorders along with cognitive impairment and may be associated with psychiatric features due to the degeneration of the basal ganglia. Other NA conditions include abetalipoproteinemia (Bassen-Kornzweig syndrome), hypobetalipoproteinemia, Anderson disease and atypical Wolman disease, which are characterized by dorsal column degeneration due to vitamin E malabsorption and so present as peripheral neuropathy and sensory ataxia, without movement disorders. In addition, several other sporadic conditions are also associated with acanthocytosis [4].

NA is unusual for an autosomal recessive disorder. Any sibling has a 25% chance of developing NA. Children of cases inherit one mutant allele and are not affected. MLS, on the other hand, is X-linked, thus male cases will pass on the mutant X chromosome to their daughters, whose sons will have a 50% chance of developing MLS and daughters have a 50% chance of being carriers, who rarely develop any neurological signs. PKAN is also autosomal recessive, and siblings have a 25% chance of developing the disease. HDL2 is autosomal dominant, thus any child and siblings of a case has a 50% chance of developing the disease. As all the genes are now known, routine methods for prenatal testing can be applied for diagnosis [2].

NA disorders are all exceedingly rare, but also very likely to be under-diagnosed. Estimates suggest that there are probably around one thousand ChAc cases and a few hundred cases of MLS worldwide [2]. Typical MRI imaging finding is an "eye-of-the- tiger" appearance with associated peripheral blood smear study showing acanthocytes [6]. Psychiatric co-morbidity in the form of depression, anxiety, personality change, cognitive impairments and obsessive compulsive symptoms have been described with Neuroacanthocytosis [4]. All NA disorders have an unrelenting progressive course and all of them are eventually fatal. The mean life expectancy after diagnosis is about 10 years. Death results, usually due to the self injurious behavior or as a consequence of severe dyskinetic movements of the pharynx.[5] Neither curative nor disease-modifying treatments are available so far and currently the management of the NA disorders is only symptomatic [2]. Dopamine antagonists or depleters such as tiapride, clozapine or tetrabenazine may help to ameliorate the hyperkinetic movement disorders. Seizures usually respond to standard anticonvulsants like phenytoin and valproate. Lamotrigine and carbamazepine may worsen the involuntary movements [7]. A multidisciplinary approach using non-medical therapies along with medical therapies is often helpful. Speech therapy might be useful for dysphagia and associated weight loss might make it essential. Dystonia of the lower face and tongue can result in severe tongue and lip self-mutilation in NA and may be countered with a bite plate. Local botulinum toxin injections into the genioglossus muscle have been tried for dystonic tongue protrusion whilst eating in NA. This method, however, has to be applied with caution due to the risk of mechanical obstruction of the airway and inefficient swallowing by paretic muscles. Placement of a feeding tube, temporarily or even continuously, including percutaneous gastrostomy, may be necessary to avoid nutritional compromise and to reduce the risk of aspiration. Physical and occupational therapy may be needed for difficulties with gait, balance, and to improve other activities of daily living. Most importantly, patients and their families need extended and continuous multidisciplinary psychosocial support during the course of the illness.

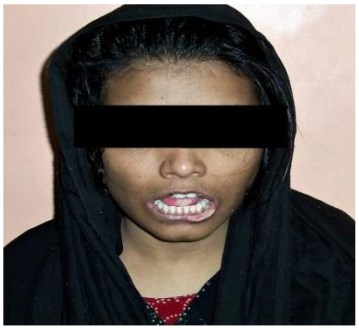

Figure 1 – oral ulcers of the patient

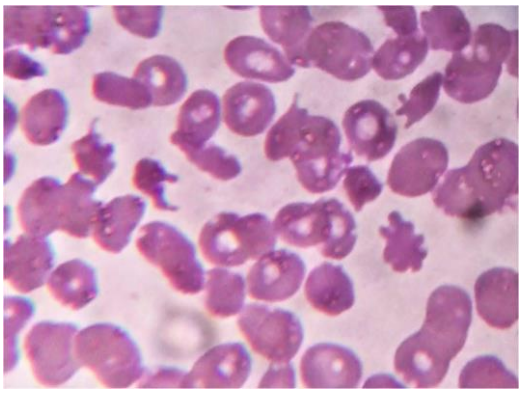

Figure 2 – Acanthocytes on the blood smear of the patient

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