Case Report

Deep Brain Stimulation for the Treatment of Tremor and Ataxia Associated with Abetalipoproteinemia

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Abstract

Background: Abetalipoproteinemia is a rare disorder of fat absorption, characterized by vitamin deficiency, acanthocytosis, and neurologic symptoms including ataxia and tremor.

Case Report: A 41-year-old male with abetalipoproteinemia is presented. He underwent staged bilateral thalamic deep brain stimulation (DBS) for the treatment of his tremors. After DBS, the patient achieved significant improvements in his tremors, ataxia, and quality of life.

Discussion: Thalamic DBS proved to be both safe and efficacious in the management of ataxia and tremors in a patient with abetalipoproteinemia. This is the first report of DBS in abetalipoproteinemia in the literature.

Keywords: Deep brain stimulation, tremor, ataxia, abetalipoproteinemia


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Introduction

Abetalipoproteinemia or Bassen-Kornzweig syndrome was first reported by Bassen and Kornzweig in 1950, when they observed the malformation of erythrocytes in a case of retinitis pigmentosa. The association of this syndrome with hypocholesterolemia was made in 1958 by Jampel and Falls. The term abetalipoproteinemia was coined by Salt et al. in 1960, when he noticed the absence of beta-lipoprotein in the serum of a patient with acanthocytosis and steatorrhea. The cause of abetalipoproteinemia is attributed to a mutation in the microsomal triglyceride transfer protein, whose large subunit is found on chromosome 4q22-24. This subunit forms a heterodimer with protein disulfide isomerase, and the complex facilitates the transfer of lipids onto apolipoprotein B. The net result of this is the absence of apolipoprotein B-containing lipoproteins, such as chylomicrons, very-low-density lipoproteins, and low-density lipoprotein. The absorption of fat and fat-soluble vitamins is deficient, resulting in vitamin E deficiency, which leads to many of the neurologic sequelae including retinal degeneration, hyporeflexia, reduced proprioceptive and vibratory sense, and ataxia. Tremor, although not a classic feature of the disease, has also been reported in the literature, but as a rest tremor. We report on a case of a 41-year-old male with abetalipoproteinemia and a family history of tremors, who underwent staged bilateral thalamic deep brain stimulation (DBS) for tremors and ataxia, with significant improvement.

Case report

The patient is a 41-year-old right-handed male who developed a voice tremor around the age of 15, followed soon thereafter by axial tremors that impaired his walking, and then bilateral upper extremity tremors. He had a family history of tremors, including a maternal aunt and cousin with "hunchback" and tremors of an unspecified type, and a mother with "thumb tremors". None of the affected family members was examined, and the nature of the tremors could thus not be
Spiral drawings before (A) and after (B) initial programming, demonstrating improvement in tremor with stimulation.
extremities. His gait, which had transiently worsened post-operatively, stabilized, and improved somewhat compared with baseline, as was also evidenced by comparing his ON vs. OFF-stimulation examination (see Video 1). The pre- and post-stimulation video was analyzed by a movement disorder specialist not involved with the case and blinded to stimulator status in regards to the clinical efficacy of stimulation. These assessments were made using the essential tremor rating assessment scale (TETRAS), rating head, right upper extremity, left upper extremity, standing and spiral (scored 1–4, with 1 being least severe), and the brief ataxia rating scale (BARS), scoring gait (scored 0–8, with 0 being normal), and left and right finger-to-nose (scored 0–4, with 0 being normal). These results are summarized in Table 1.

He was weaned off sodium oxybate and reduced his propranolol dose by one-third. His stimulator settings were as follows: Left: 3+0-1-2-, 3.6 V, 90 μs, 145 Hz; Right: 3+0-1-2-, 3.6 V, 90 μs, 135 Hz.

**Discussion**

Thalamic DBS is a well-established modality for the treatment of refractory tremor and is currently approved for treatment of essential tremor and Parkinson’s disease. Targeting the VIM thalamus for many different tremor types has been extensively reviewed in the literature. We are not aware, however, of any previously reported cases of DBS in the treatment of tremor associated with abetalipoproteinemia.

In this report, we present the case of a patient with a history of abetalipoproteinemia whose presenting symptom was axial and appendicular action tremor. The patient responded well to stimulation, with marked improvement of the appendicular component of the tremors, and moderate but appreciable improvement of the axial symptoms following bilateral VIM stimulation. Interestingly, rather high settings using multiple contacts were required. These settings could reflect the need to compensate for paresthesias found using monopolar stimulation. It is also possible, however, that more medial stimulation (as suggested by the presence of facial paresthesias) was a factor contributing to improvement of the midline tremors. We further hypothesize that the extensively involved somatotopy (axial and appendicular) required a wider field of stimulation. Given the unblinded nature of the report, the possibility of a placebo component cannot be excluded, but the dramatic improvement beyond 6 months and immediate return of symptom severity off stimulation noted on numerous assessments argues against this being a prominent confound. Evaluation of a pre- and post-stimulation video performed by a movement disorder specialist not involved in the case and blinded to stimulator status also supports the clinical efficacy of the intervention (Table 1).

Bilateral DBS of the VIM thalamus can be effective in the treatment of tremors associated with abetalipoproteinemia and should be considered in cases refractory to medications. This is the only report of DBS being used in abetalipoproteinemia. Further experience is necessary, but these results encourage consideration of DBS even when there is a component of concomitant ataxia.

**References**


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Abbreviations: BARS, brief ataxia rating scale; DBS, deep brain stimulation; TETRAS, The Essential Tremor Rating Assessment Scale.


