Adalimumab-Associated Depressive Symptoms in a Patient With Vasculitis, Autoinflammation, Immunodeficiency, and Hematologic Defects Syndrome

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Vasculitis, autoinflammation, immunodeficiency, and hematologic defects syndrome (VAIHS) is an autosomal recessive disorder. The phenotype is highly variable, with clinical features ranging from intermittent fever and rash to hepatosplenomegaly and systemic vasculopathy.[1] Adalimumab, a biological agent used in risk reduction for vasculitis and stroke in adenosine deaminase 2 (ADA2) deficiency,[2] is reported to be linked with suicide and depression.[3] Here, we present the case of a 16-year-old boy with VAIHS and taking adalimumab who presented with features of depression.

Case Report

A 16-year-old boy with a history of low birth weight and normal developmental milestones was referred to us by a rheumatologist. The patient initially presented with upper abdominal pain, which was managed symptomatically. Subsequently, he experienced an episode of fever, tingling sensation in bilateral lower limbs, weakness progressing from distal to proximal muscles, and a seizure. The physical examination revealed marfanoid body habitus, poor nourishment, and elevated blood pressure. The neurological examination showed weakness predominantly in the right upper and lower limbs with preserved tone and deep tendon reflexes. Investigations including nerve conduction study and brain magnetic resonance imaging (MRI) revealed features consistent with acute motor sensory axonal neuropathy. The patient was treated with intravenous immunoglobulin.

One year later, the patient experienced a recurrence of symptoms, including ptosis of the right eye, worsening weakness, recurrent fever, weight loss, and loss of appetite. Further investigations revealed multiple T2/fluid-attenuated inversion recovery hyperintensities in deep white matter on brain MRI, asymmetric sensory and motor axonopathy on nerve conduction study, microcytic hypochromic anemia on peripheral smear, and necrotizing vasculitic neuropathy on nerve biopsy. Clinical exome sequencing identified ADA2 mutation suggestive of VAIHS.

The patient was given adalimumab 40 mg every 2 weeks by the rheumatology department. After 1 month, the patient began expressing pessimistic thoughts regarding his condition and uncertainty about his future. He reported intermittent awakening from sleep at night and expressed sadness, prompting referral to psychiatric services. On evaluation by the consultant psychiatrist, he was found to have depressed mood and depressive cognitions. Treatment was initiated with escitalopram at a dosage of 5 mg, which was subsequently increased and maintained at 10 mg. Follow-up mental state examinations indicated symptomatic improvement in the patient.

Discussion

VAIHS is characterized by vasculitis, dysregulation of immune function, and hematologic abnormalities.[2] This disorder is caused by homozygous or compound heterozygous mutation in the cat eye syndrome critical region protein 1 gene (ADA2) on chromosome 22q11. ADA2 is primarily expressed in immune cells and is produced by activated monocytes, macrophages, and dendritic cells, indicating its involvement in inflammatory responses.[4]

Increasing evidence suggests that major depressive disorder (MDD) is linked to inflammation, with inflammatory molecules implicated in symptoms such as anhedonia and fatigue.[5] Interestingly, individuals with MDD have been found to exhibit low ADA levels, suggesting a potential association between ADA2 dysfunction and depressive symptoms.[6]

Vasculitis-related disorders can manifest with a wide range of psychiatric symptoms, from psychotic features to mood disturbances, underscoring the intricate relationship between autoimmune and mental health disorders.[7] The management of vasculitis often involves the administration of antitumor necrosis factor agents such as infliximab, etanercept, adalimumab, and other biological agents.[8]

Adalimumab has been associated with the emergence of symptoms of MDD and increased suicide risk.[3] In the present case, the patient developed depressive symptoms, including low mood, pessimistic views of the future, and sleep disturbances,

shortly after initiating adalimumab therapy, suggesting a potential causal relationship between the medication and the onset of depressive symptoms. Further research is warranted to elucidate the co-occurrence of psychiatric disorders in VAIHS and the adverse effects of treatment-related medications on inflammatory conditions.

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