To the Editor

Rigidity and HyperCKemia as Presenting Signs of Hashimoto's Encephalopathy

Hashimoto's encephalopathy (HE) is a rare and poorly understood syndrome affecting the central nervous system. Because of association with Hashimoto's thyroiditis and high serum antithyroid antibody titers, it is a disease of presumably autoimmune origin.[1] The exact nature of the immune response in HE is still unclear. The clinical picture may include cognitive impairment, psychiatric manifestations, impairment of consciousness, seizures, myoclonus, tremor, and stroke-like episodes.[2] It is generally accepted that the syndrome is recognized when the following conditions are met: encephalopathy manifesting as cognitive dysfunction, impairment of consciousness, seizure, or neuropsychiatric disorder; elevated serum levels of antithyroid antibodies; good response to glucocorticoid treatment; exclusion of infectious, vascular, metabolic, toxic, or neoplastic etiologies.[3] In the case presented, a patient presented initially with acute progressive rigidity and hyperCKemia but was ultimately diagnosed with HE.

Case Report

A 71-year-old male was referred to a neurologist for rapidly progressive stiffness in both legs, more pronounced in left, lasting for six days. He was complaining of difficulty walking, a symptom which he had never experienced before. During the whole time, he experienced no pain whatsoever. Besides a history of arterial hypertension, his medical history was otherwise unremarkable. He denied taking any medication other than antihypertensive agents. He did not notice an increase in body temperature. He denied loss of consciousness, abnormal physical trauma, or recent intramuscular injections. On examination he was afebrile, fully conscious and oriented. Blood pressure was initially 210/120 mmHg. Foot dorsiflexion strength was bilaterally slightly decreased (4/5), muscle tone was increased in all extremities but more severely in legs, and muscle resistance was velocity-independent. Initial laboratory testing showed: white blood cells (WBC) 10.19 x10^9/L, creatinine 110 μmol/L, bilirubine 21.6 μmol/L, aspartate aminotransferase (AST) 120 U/L, alanine aminotransferase (ALT) 49 U/L. Serum creatine kinase (CK) was markedly high (3016 U/L), and its isoenzyme CK-MB was slightly elevated (66 U/L). Other routine laboratory studies, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), electrolytes, and blood sugar were unremarkable. The patient was hospitalized for further observation.

Over the next 24 hours the patient became drowsy and dysphonic with further deterioration to somnolence and akinetic mutism. Patient was afebrile and normotensive. The neurologic examination showed generalized rigidity and normoreflexia with bilateral Babinski's sign. Repeated laboratory studies revealed: CK 2770 U/L, blood urea nitrogen (BUN) 14.7 mmol/L, creatinine 276 μmol/L, AST 103 U/L, ALT 52 U/L, serum phosphate 1.60 mmol/L, serum copper 10.1 μmol/L. Thyroid profile revealed normal levels of free triiodothyronine (FT3), free thyroxine (FT4) was at the lower end of the normal range (0.72 ng/dL), and thyroid stimulating hormone (TSH) was elevated (12.65 U/L). Antithyroglobulin antibodies (TgAb) and antithyroid peroxidase antibodies (TPOAb) were elevated (38.5 and 597.1 U/L, respectively). Values of ESR, WBC and CRP were normal. Cerebrospinal fluid (CSF) analysis revealed elevated protein (0.99 g/L) without pleocytosis. Electroencephalography (EEG) showed background activity with theta waves. Brain computed tomography (CT) revealed bilateral diffuse hypodensities in the subcortical white matter.

Fulfilling generally accepted criteria for the diagnosis of HE, patient was treated with intravenous (IV) methylprednisolon 1g per day for the next four days. Patient was also treated with diuretics considering progressive renal impairment development. Fluid balance was carefully monitored. The patient initially responded well to treatment, regaining full consciousness and improving diuresis. Levels of serum creatinine (190 μmol/L) and CK (715 U/L) gradually declined. On control examination muscle tone was normal but bilateral Babinski's sign persisted. Patient had intermittent fever up to 38.5°C during corticosteroid treatment. Nevertheless, ESR, WBC and CRP levels were unremarkable. Patient's condition suddenly became worse on the first day after withholding corticosteroid therapy. Fulminant septic shock developed, and the patient eventually died due to multiple organ dysfunction syndrome.

Discussion

Since its first recognition in 1966,[1] HE remains a controversial disorder. It has been described as an encephalopathy of acute or subacute onset, accompanied by various symptoms including seizures, myoclonus, ataxia, tremor, behavioral disorder, psychosis, stroke like episodes.[2,4] The highly variable clinical spectrum of the disease may mislead clinical decisions and cause diagnostic delay thus affecting outcome.

Rigidity is seldom recognized and reported symptom in patients with HE.[4,5] The most commonly observed symptom suggesting extrapyramidal involvement is tremor.[4] On the other hand, markedly elevated serum CK is a finding which is, to our knowledge, not yet described in patients with HE. The aforementioned case describes a patient who acutely developed rigidity combined with hyperCKemia (more than 10-fold the normal upper limit) as presenting signs of HE. Unusual coexistence of these findings raised suspicion of neuroleptic malignant syndrome. However, patient neither had fever nor had taken any antipsychotic or antidepressant medications. In this case, it is suspected that CK elevation is secondary to rhabdomyolysis arising from sustained muscular rigidity. However, subclinical hypothyroidism can also be associated with serum muscle enzyme elevations, although generally to a much lesser extent. It could be theorized that possible underlying autoimmune mechanisms of the disease could interfere with muscle function; a similar effect can be seen in other closely related autoimmune disorders such as stiff person syndrome and polymyositis.

Laboratory findings in patients with HE include elevated TPOAb with or without TgAb elevation. Among other laboratory findings, levels of ESR, TSH, AST, ALT and CSF protein are frequently found to be mildly elevated. Nonspecific EEG abnormalities are present in the vast majority of patients, usually comprising slow background activity.[4] Brain computed

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tomography (CT) and magnetic resonance imaging (MRI) may show no changes or reveal nonspecific abnormalities, usually cerebral atrophy, diffuse subcortical abnormality, and nonspecific subcortical focal white matter abnormality.[2]

Treatment of patients with HE is based on the use of corticosteroids. Most commonly, intravenous IV methylprednisolone (500–1000 g/day) is given for three to five days followed by oral prednisone taper.[4] When deciding optimal treatment strategy regarding corticosteroid regimen, proper balance between patient's condition and multiple factors contributing to serious side effects of corticosteroid use (e.g., age, nutritional status, comorbidity) should be taken into consideration. Antithyroid antibodies levels do not correlate well with the clinical picture of HE and do not reflect response to treatment.[4] Therefore, when evaluating patient's condition, physicians must rely solely on patient's symptoms and clinical course monitoring. In the presented case, it is likely possible that immunosuppression was induced by corticosteroid treatment. Unfavorable outcome in HE is not entirely unexpected but there is a lack of published data demonstrating which risk factors are more associated with it.

Conclusion

This case provides more insight in the diversity of clinical manifestations of HE. Acute rigidity and markedly elevated levels of CK could share common pathological process in HE. It is still unclear and yet to be determined whether the symptomatology of HE is consequence of abnormal autoimmune response. Further investigations are required to establish the optimal therapeutic approach for patients with HE.

Bojan Rugole
General Hospital Dr. Josip Benčević
Slavonski Brod, Croatia
Email: rugole.b@gmail.com

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To the Editor

Recovery from Deafness in the Contralateral Ear of Surgery in NF 2 Patient

Hearing loss due to vestibular schwannoma (VS) is one of the significant morbidities in patients with neurofibromatosis type 2 (NF 2). Advances in surgical techniques and intraoperative neurophysiological monitoring have enabled hearing preservation in surgeries for VS. Rarely, recovery from deafness can happen in some cases. Most of the reports for hearing improvements have occurred in the same area of the surgical procedure and were limited to cases with sudden hearing loss.[1] In this report, we present an unusual case of hearing improvement in the contralateral side of surgery in a NF 2 patient with bilateral vestibular schwannoma and deafness in both ears.

Case Report

A 23-year-old woman diagnosed with neurofibromatosis type NF 2 presented to our department at National Neuroscience Institute (NNI) in Saudi Arabia with a two month history of progressive bilateral hearing loss, gait unsteadiness, and blurred vision. On physical examination, there was right eye ptosis and partial ptosis of the left eye. She had grossly diminished hearing in both ears, with normal tympanic membranes. Brain and spine magnetic resonance imaging (MRI) showed findings consistent with NF 2. There were bilateral VSs, multiple intracranial and spinal meningiomas, and cauda equina schwannomas (Figure 1;A,B). The right large VS was causing a mass effect on the fourth ventricle with consequent third and bilateral ventricular dilatation.

Preoperative audiology assessment showed normal middle ear pressure and compliance. Ipsilateral and contralateral acoustic stapedial reflexes were absent bilaterally. Distortion product otoacoustic emissions (DPOAE) testing was normal in both ears. Pure tone audiometry (PTA) revealed moderate to severe sensorineural hearing loss in the left ear and profound sensorineural hearing loss in the right ear (Figure 2A). Speech recognition thresholds were consistent with the pure tone findings bilaterally. Although the patient can hear the tones, her speech recognition ability was significantly impaired in the left ear.

Patient underwent right suboccipital craniotomy and excision of the right VS with external ventricular drain (EVD) insertion. Her somatosensory evoked potentials, auditory brainstem responses and facial nerve function were monitored intraoperatively. Histopathology of the tumor revealed a benign schwannoma. After surgery, the patient was transferred to the intensive care unit. Postoperative brain MRI (Figure 1;C,D), showed normal postoperative findings and near total resection of right VS. The left VS and other intracranial lesions remained unchanged. Subjective improvement in hearing from the left ear (contralateral side) was noted immediately by the patient.

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