A case of thyroid follicular carcinoma with paraneoplastic polyneuropathy, Lambert-Eaton myasthenic syndrome and paraneoplastic cerebellar degeneration

Tiroid foliküler kanserine bağlı paraneoplastik polinöropati, Lambert-Eaton myastenik sendrom ve paraneoplastik serebellar dejenerasyon olgusu

Akpinar C K¹  Dogru H²  Balci K²
¹Vezirkopru State Hospital, Clinic of Neurology, Samsun, Turkey
²Ondokuz Mayis University, Faculty of Medicine, Department of Neurology, Samsun, Turkey

Summary

Patients with paraneoplastic neurological syndromes (PNS) have a variety of neurological symptoms that are considered to be triggered by autoimmune mechanisms. The current valid opinion for the pathogenesis is that an autoimmune response caused by similar antigenic properties in the underlying tumor and the nervous system is responsible for the emergence of PNS. We present a case a patient with follicular thyroid cancer who had a combination of symptoms due to paraneoplastic cerebellar degeneration, Lambert-Eaton myasthenic syndrome and paraneoplastic polyneuropathy.

Key Words: Multiple paraneoplastic syndromes, thyroid follicular carcinoma.

Introduction

Patients with paraneoplastic neurological syndromes (PNS) have a variety of neurological symptoms that do not occur due to diffuse and/or local effects of the underlying tumor, and that cannot be explained by metastasis, opportunistic infections or the side effects of treatment of cancer but are considered to be triggered with autoimmune mechanisms (1,2). The current valid opinion for the pathogenesis is that an autoimmune response caused by similar antigenic properties in the underlying tumor and the nervous system is responsible for the emergence of PNSs (2). Neurological complaints usually start as subacute and advance gradually over weeks and months (1). Although the incidence is not known exactly, PNS are seen in less than 5% of cancer patients (2). In diagnosing PNS these are very important because they develop usually when the cancer is still too small and treatable in majority of cases. Symptoms of PNS occur before diagnosis of cancer in 60% of patients (3). Sensorimotor polyneuropathy is the most frequently seen PNS (3,4). Small cell lung cancer (SCLC) is the most common malignancy that causes paraneoplastic polyneuropathy (5). PNS in patients with follicular thyroid cancers are rarely reported. We present a case of a patient with follicular thyroid cancer who had a combination of symptoms due to paraneoplastic cerebellar degeneration, Lambert Eaton myasthenic syndrome and paraneoplastic polyneuropathy.

Case Report

A 47 year old male patient was admitted for proximal limb weakness, especially in the lower extremities, which began 5 months earlier and progressed over the...
following month. He was unable to manage his own care within the last month. He lost about 10 kg in the previous ten months. He had nothing remarkable in his history other than smoking. On neurological examination, he was alert and cranial nerve examinations were all normal. Motor examination showed that the proximal segments of upper and lower extremities had a strength of 4+/5 (MRC score). Deep tendon reflexes were absent globally. In the lower extremities, the vibration sense was decreased and joint positions were normal. Although the muscle strengths were sufficient to walk, the patient had great difficulty in performing his daily activities, and he could only walk with two sided support. He had truncal ataxia along with bilateral dysmetria and dysdiadochokinesia.

Single-fiber EMG examination was compatible with conduction abnormalities in the nerve muscle junction, and a repetitive nerve stimulation test obtained from the nasal muscles showed incremental response at high frequencies (>10 Hz). Nerve conduction studies were compatible with symmetrical sensorimotor polyneuropathy that were predominantly axonal in character. Laboratory investigations and the history of the patient did not reveal any risk factor for polyneuropathy. The patient was diagnosed with paraneoplastic Lambert Eaton myasthenic syndrome and paraneoplastic polyneuropathy. Although the patient's muscle power was not too weak to prevent walking, a severe walking difficulty was present with the neurological examination findings of cerebellar degeneration. Anti-Hu (+++) and voltage-gated calcium channel (VGCC) antibodies were positive. The brain MRI, thorax and abdomen CTs were found to be normal. A scrotal ultrasound was normal. No significant pathology was detected in cranial MR imaging. Thyroid USG revealed two homogeneous hyperechoic nodules sized 9x6 mm and 23x9 mm in the upper pole of the thyroid right lobe. In the lower right lobe, a nodule with intrathoracic extension and sized 35x26mm was detected. The nodule had significantly marked boundaries and was heterogeneous, hyperechoic and contained occasional coarse calcifications. A similar nodule with less marked boundaries was detected in the lower left pole (approximately 19x14 mm in size). There was no pathology in laboratory parameters. A pathological report revealed follicular carcinoma of the thyroid.

Discussion

Paraneoplastic syndromes (PNS) are autoimmune clinical conditions that occur without cancer mass or metastases effect (6). The findings usually occur before the identification of the primary tumor. It was first diagnosed by Denny-Brown in 1948 when degeneration in the dorsal root ganglion and neuronal loss were discovered in the autopsy of 2 patients with rapid progressive sensory neuropathy and ataxia (7). Pathologically, there might be involvement in the anterior horn motor neurons, sensory neurons in the dorsal root ganglia, in axons, or nerve terminals, in the neuromuscular junction, or in muscle or autonomic nervous systems (8,9). Initially, it is usually subacute. The clinical condition often advances in a progressive manner and there is mild or fluctuating evidence. After that, it becomes stable or rarely shows rapid progression (1). Defined autoantibodies in patients with PNS develop against the antigens in membranes of central and peripheral nervous system neurons, or inside the cell (cytoplasm and/or nucleus) (1-2). Supportive laboratory findings are; pleocitose, increased protein and IgG, myelin basic protein/oligoclonal band positive in BOS investigation, as well as specific antibodies (antiHu, antiYo, antiRi) found in serum and CSF (2). In our case, the anti-Hu antibodies against calcium channels VGCC antibodies were found to be growing. In an electrophysiological examination, sensorimotor polyneuropathy was evident with axonal involvement is apparent. Improvement can rarely be seen with immunotherapy and tumor resection (6-8). Clinical and electrophysiological findings in our patient were consistent with sensorimotor polyneuropathy with sensory involvement in the foreground. Paraneoplastic cerebellar degeneration presents with pancerebellar syndrome with a rapid onset and which begins as acute or subacute due to Purkinje cell death. It is most frequently seen with gynecologic cancers, breast tumors, SCLC, and Hodgkin’s lymphoma (10). The antibodies associated with cerebellar degeneration are anti-Yo antibodies, En, Hu, Ma2 and Ri (10,11). The syndrome associated with Yo antibodies in paraneoplastic cerebellar degeneration is the most common and most well-defined type. People with this antibody are mostly women who have breast, ovarian and other gynecological cancers, but male patients are also reported to be admitted in with various tumors (12). Cerebellar degeneration can be seen in some SCLC cases with Hu and VGCC antibodies. MRI and CSF studies are usually normal initially in paraneoplastic cerebellar degeneration, however, inflammatory findings in CSF examination and severe cerebellar atrophy in MR imaging may occur soon after. Cerebellar degeneration is the most resistant paraneoplastic syndromes to treatment, but fast and effective treatment can prevent progression of symptoms. It occurs as a result of an autoimmune response against the P / Q-type VGCC channels in the presynaptic membrane of the neuromuscular junction. This antibody is found in 95% of cases and there is a correlation between antibody level and severity of clinical signs of the disease. Patients usually suffer from proximal muscle weakness, reduced or lost deep tendon reflexes and...
autonomic dysfunction (dry mouth, orthostatic hypotension, and blurred vision due to abnormal pupil functions). Approximately 50-60% of cases with LEMS are diagnosed with cancer, and almost all the cancer cases with LEMS have SCLC, while a minority of other types of cancer, primarily lymphoma, is also detected (13).

LEMS occurs in 3% of cases of SCLC. In 43% of the SCLC cases with LEMS, there are antibodies called antiglial nuclear antibody (AGNA) which react with nuclei of cerebellar Bergmann glial cells. Agna linked to SOX1 antigens in SCLC cells cannot be detected in patients with paraneoplastic LEMS. It is highly likely to detect Agna in patients with limbic encephalitis associated with anti-VGCC detection (13).

Our case of paraneoplastic sensorimotor polyneuropathy, is presented as a rare cause of paraneoplasia with cerebellar degeneration and the nerve muscle junction involvement in the etiology of thyroid follicular carcinoma.

References