Neurological Case Reports

Case Report
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A Case of Long-Lasting Paraneoplastic Polyneuropathy without the Clinical Evidence of a Primary Tumor

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Introduction

Paraneoplastic neurologic syndromes are a heterogeneous group of disorders associated with cancer and caused by mechanisms other than metastases, metabolic and nutritional deficits, infections, coagulopathy or side effects of cancer treatment. These syndromes may affect any part of the central and peripheral nervous system, neuromuscular junction and muscles, damaging either one area or multiple areas.

Although the pathogenesis of paraneoplastic neurologic syndromes is incompletely understood, immunologic factors are believed to be important, because antibody and T-cell responses against nervous system antigens have been described for many of these disorders. The immunologic response is directed against shared antigens that are ectopically expressed by the tumor, but otherwise exclusively expressed by the nervous system [1,2]. For unknown reasons, the immune system identifies these antigens as foreign and organize an immune attack against them.

Paraneoplastic neurologic syndromes are rare syndromes that occur in 1% of patients with neoplasm, but in a half of these patients they represent the first sign or symptom of an unknown tumor.

Sometimes the injury to the nervous system is reversible with therapy directed toward the cancer and the immune system. However, these diseases can also rapidly result in severe damage to the nervous system that cannot be reversed [3].

We recognize some typical or atypical pattern of neurological disorder related to tumor.

One of typical pattern is paraneoplastic subacute sensory neuronopathy presenting with pain, dysesthesias, loss of vibratory and joint position sense, and sensory ataxia; other sensory modalities are or soon become impaired as well. Electrophysiologic studies (EMG) help distinguish the syndrome from a sensory polyneuropathy. Cerebrospinal Fluid (CSF) examination often reveals pleocytosis and elevated protein.

Most patients have Small Cell Lung Cancer (SCLC), anti-Hu antibodies, and, less commonly, anti-CRMP5 (CV2) or Amphiphysin antibodies. Early diagnosis and treatment of the underlying tumor may result in neurologic stabilization or improvement.

Case Presentation

We describe a case of a 72-year-old man who underwent a neurological evaluation in October 2017 presenting paresthesias in 4 arms growing quickly since July 2017.

An EMG showed an axonal and sensory polyneuropathy in 4 arms, mainly in upper limbs and in lower left leg.

So, he was admitted in our Neurological Unit to screen the causes of neuropathy.

His medical history consisted in hypercholesterolemia, previous endoscopic exeresis of polyps from intestine, cardiac pacemaker arranged after syncopes.

Neurological examination showed tendon reflexes widely reduced, normal muscular strength, mild hypopalesthesia distally in legs and normal other modalities of sensitivity, mild ataxia, positive Romberg test. INCAT Sensory Sum Score (ISS) was 12/33, the Overall Disability Sum Score (ODSS) was 5/12.

We performed the following laboratory tests: Complete blood count, blood glucose, liver and

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renal function tests, serum vitamin B12, thyroid panel, specific tests for autoimmune disorders (such as Antinuclear Antibody ANA), serum protein electrophoresis, CPK was normal. Anti-Hu antibody was also normal. Paraneoplastic antibodies (PSA, GICA, alpha-fetoprotein, beta-HCG) were normal, but CEA was elevated (79.24 ng/mL).

Cerebrospinal fluid analysis showed normal cells and glucose, elevated proteins (99.1 mg/dL).

We proceeded looking for a neoplasm with US of abdomen and testicles, RX scan of the chest and total body CT scan. We found at CT scan a mediastinic adenopathy (a node in Barethy cavity about 22 mm × 18 mm).

The neurological symptoms and the EMG pattern (subacute sensory neuronopathy) suggested a probable paraneoplastic origin of the polyneuropathy.

The PET/CT scan images revealed the presence of an uptake of 18F-FDG as an adenopathy in mediastinum at Barethy cavity, about 18 mm size, SUV 5.3. The distribution of 18F-FDG in the other sections of the body was normal.

An Endobronchial Ultrasound with biopsy (EBUS) revealed the presence of neoplastic cells of poorly differentiated epithelial neoplasm.

We finished standardization with Esophagogastroduodenoscopy (EGDS) that was normal.

On November 2017, using a thoracoscopic approach, were removed right hilar nodes (station 10R), lower and upper paratracheal nodes (station 2R and 4R) and subcarinal area (station 7). The histologic diagnosis was massive metastasis from lung solid adenocarcinoma, 6 of 15 mediastinal nodes; the immunophenotypic analysis of neoplastic cells was positive for TTF1, negative for PAX8, p40, synaptophysin, CDX2.

At this time (December 2017), while the EMG parameters were stationary, neurological symptoms worsened, particularly sensory deficits in both hands (ISS 6/33, ODSS 5/12).

A Total Body CT scan performed on January 2018 didn't show neoplastic masses; laboratory tests and mutation of EGFR, ALK, ROS-1 and PDL-1 were negative.

In January 2018 the patients was treated with high dose intravenous immunoglobulins: 0.4 g per kilogram body weight per day for 5 consecutive days (total dose 110 g).

We did not see any side-effects and after a week he had a mild positive response in balance and walking.

After that, the patient underwent a program of radiation therapy of mediastinum (total Gy 50) and a therapy with oral prednisone 50 mg per day per one month, then 25 mg per day.

During 2018 patient underwent other 4 cycles of high dose of intravenous immunoglobulin with few transient good effects on balance, no benefit on limb paresthesia's.

We performed a clinical and neurophysiological revaluation in September 2019 that showed a global worsening of all the EMG parameters and of the sensitive symptoms and walk.

During 2019 there was no clinical or radiological evidences of cancer. Even CEA was normalized, but neurological symptoms worsened slowly.

After oncological evaluation in another department, patient was treated with gemcitabine (3 cycle from February to march 2019). There was no benefit on neuropathy and but several side effects to the drugs.

From July to October 2019 the patient underwent 11 sessions of plasma exchange. During this period neurological symptoms were stable.

Since then, the patient has not been treated and has maintained stability of neurophysiological parameters at EMG, sensory deficits and motor performances until his last check up in October 2022; however, he lives in a wheelchair and takes few steps with help.

Oncology follow up has been carried out regularly without signs of disease recurrence to date.

The peculiarity of this clinical case is that after 6 years of observation, the primary tumor could not be detected, though neurological symptoms have been slowly worsened.

An early clinical and neurophysiological framework must drive to the correct etiological diagnosis of neuropathy. In this case a combined antineoplastic and immunomodulatory treatment seems to be useful to contain the primary disease even if neurological and oncological symptoms often do not proceed coherently with each other.

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