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Case report

Paraneoplastic brainstem encephalomyelitis and atypical form of chronic inflammatory demyelinating polyneuropathy in patient with testicular germinal tumor—Is this an overlap syndrome? A case report

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ABSTRACT

Paraneoplastic neurologic syndromes are diagnosed when neurologic symptoms are associated with neoplasm and other causative factors are excluded. They may precede or be simultaneous to various types of neoplasms, mainly malignant. In men up to 45–50 years old the most common cancer causing the paraneoplastic syndrome is testicle tumor, manifesting usually as limbic/brain stem encephalitis and myelitis. Usually effective treatment of underlying neoplasm brings resolution of neurologic symptoms. But corticosteroids and intravenuous immunoglobulins are also used. In the presented case a 37-year-old man was primarily diagnosed and treated for progressive tetraparesis with signs of both upper and lower motor neuron dysfunction, associated with bulbar symptoms. Having various diagnostic procedures performed an atypical form of chronic inflammatory demyelinating polyradiculoneuronopathy was primarily suspected, but eventually a discovery of endodermal sinus tumor in the testicle enabled to state the diagnosis of possible paraneoplastic syndrome. In spite of chemotherapy the patient died shortly after the diagnosis because of infectious complications. Histopathology displayed intense inflammatory changes in the brain stem as well as in cranial nerves and cervical spinal cord. The same immunological process evoked by various pathogenetic factors (infection vs. neoplasm) may cause similar clinical picture and hinder the diagnosis. Most importantly it may delay the proper way of treatment.

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1. Introduction

Yolk sac tumor (YST) is a rare malignant germ cell tumor found in the testis or ovary, and occasionally in extragonadal location. Only single case reports have described the presence of this tumor in the head, lung, stomach, liver, mediastinum, peritoneum, kidney, prostate, vagina, vulva, and presacral regions [1–4]. Like other cancers, YST may be associated with paraneoplastic syndromes. The syndrome most commonly related to YST and other germ-cell cancers of the testis is paraneoplastic encephalitis. The association of the limbic/brainstem encephalitis concurrent with the anti-Ma2 onconeural antibodies was widely described, as well as the presence of testicular tumors as its causative factor in more than 80% of patients, usually men younger than 45–50 years old [5,6].

Paraneoplastic neurologic syndromes are diagnosed when neurologic symptoms are associated with neoplasm and other causative factors are excluded [5]. It is believed that they result from an immune response to an antigen shared between the cancer and the nervous system. They are rare, less than 1% of all patients with various cancers suffer from such disorders. However, depending on the kind of a cancer this may be as high as 30% in small cell lung carcinoma [7,8]. The eight paraneoplastic syndromes most likely to be associated with cancer, the so called ''classic'' syndromes, include encephalomyelitis, limbic encephalitis, subacute cerebellar degeneration, opsoclonus-myoclonus, subacute sensory neuronopathy, chronic gastrointestinal pseudo-obstruction, Lambert–Eaton's syndrome and dermatomyositis [5].

There are other neurologic syndromes such as acquired neuromyotonia, motor neuron disease, stiff-men syndrome, Guillain–Barré syndrome, and chronic inflammatory demyelinating polyradiculopathy (CIDP) that may be the so-called ''non-classic'' paraneoplastic syndromes. They constitute a peculiar diagnostic challenge.

We would like to present a case report of a patient with a non-classic paraneoplastic syndrome or an overlap syndrome associated with testicular germ-cell tumor.

2. Case report

Thirty-seven year-old man, physical worker and current smoker, complained of progressive four-limb weakness (at first lower then upper limbs) followed by swallowing and speech problems, which he attributed to the upper respiratory tract infection that preceded symptoms by one month and was treated with antibiotics.

First neurologic examination (in another hospital) revealed triparesis – proximal in the right upper limb and distal in lower limbs – with decreased muscle tone, but brisk reflexes, muscle atrophy corresponding with the sites of paresis and bilateral Babinski sign. Deep sensation in the lower limbs was disturbed and bilateral Laseque's sign was noted. Involvement of cranial nerves resulted in right-sided facial and tongue muscles paresis, dysarthria and dysphagia.

Lumbar puncture revealed albuminocytologic dissociation in the cerebrospinal fluid (discreet cell count elevation of 14 μl, with preponderance of lymphocytes and monocytes and almost threefold elevation of protein concentration of 129 mg/dl). Electrophysiology showed acute axonal-demyelinating poliradiculoneuropathy of the motor fibers with acute denervation and reinervation in muscles. Performed twice MRI scans of the brain with contrast enhancement were negative, and central nervous system diseases such as boreliosis, herpes simplex and HIV infections were excluded. Based on clinical picture and results of additional tests the diagnosis of post-inflammatory encephaloradiculoneuropathy was stated and pharmacological treatment was introduced. Initially, high-dose intravenous corticosteroids (1.0 g per day for five days of methylprednisolone) were administered, and slight improvement in the muscle strength was observed.

On admission to our clinic (four months later) further aggravation of clinical symptoms was observed especially considering bulbar symptoms (left abducens nerve palsy). Treatment with intravenous immunoglobulin was started as the second-line treatment (maximum dose of 2.0 g/kg body weight), which again resulted in the improvement in muscle strength and swallowing problems. Afterwards, long-term oral therapy with prednisolone was initiated with the starting dose of 1.3 mg/kg body weight and the patient was discharged home. Meanwhile the neoplastic markers (AFP, total PSA, CEA, CA-15-3, CA 19-9) were investigated as well as CT scans of the chest and abdomen, and physical examination and USG of the testis, but none showed abnormalities.

Three months after the first one, the EMG investigation showed pure axonal motor polyneuropathy.

Nearly one year later the patient was again admitted to our clinic with deterioration of symptoms. This time external ophtalmoparesis was notable (only vertical eye movements were spared) and other cranial nerves damage of the bulbar origin. Due to respiratory failure he needed non-invasive mechanical ventilation by means of facial mask (Bi-level Positive Airway Pressure). Once again the MRI scans of the brain showed no abnormalities that could explain the symptoms.

The patient informed on the left testicle swelling and pain that he had consulted by urologist and had treated with antibiotics for the last two months. Performed USG showed the presence of a pathological mass in the left testicle suggestive of a cancer. It was associated with the highly elevated alpha-fetoprotein level in the blood (around 52 times upper limit). The mass was surgically removed and the histopathology investigation revealed yolk sack tumor with foci of embryonic carcinoma. The patient underwent chemotherapy with cisplatin and ethoposide. Unfortunately, shortly after the first course he developed severe leukopenia with agranulocytosis, which was complicated by pneumonia and sepsis. The patient eventually died.

The necropsy was performed. Post-mortem examination revealed pneumonia but not metastases of the testis tumor. Microscopic examination of the brain and spinal cord showed inflammatory process involving both the central and peripheral nervous systems particularly severe in the brain stem, cervical spinal cord and cranial nerves. The most evident morphological manifestation of the inflammation was vasculitis involving small-sized arteries (Fig. 1A) and capillary vessels. Inflammatory mononuclear cells infiltrating vessel