Case Report

Limbic encephalitis association with tuberculosis: A case report


Introduction

Paraneoplastic neurological syndrome (PNS) is a neurological entity that may occur in cancer patients. PNS is not caused by the tumor nor can be explained by metastasis, opportunistic infections or side-effects of cancer therapy. The majority of the symptoms are considered to be mediated by autoimmune mechanisms (1). This entity is more common among women. Neoplastic diseases that are most closely associated with PNS include small-cell lung cancer, thymomas, and plasma cell dyscrasias. Besides the basic signs such as short-term memory loss, epileptic seizures and behavioral changes, confusion, irritability, depression, psychosis, sleep disorders and hallucinations may be seen in limbic encephalitis (2). Limbic encephalitis characterized by the presence of antibodies against intracellular antigens such as Hu, Ma2, CV2 and amphiphysin is always accompanied by a cancer, whereas cancer is not detected in a substantial portion of the cases with limbic encephalitis associated with antibodies against cell surface antigens such as N-methyl-D-aspartate (NMDA) receptor and voltage-gated potassium channel (VGKC) antibodies. Moreover, response to treatment is poor in cases with limbic encephalitis characterized by the presence of antibodies against intracellular antigens, while it is better in cases with limbic encephalitis associated with antibodies against cell surface antigens (3).

In the present paper, a patient who was admitted to our out-patient clinic with headache, memory impairment, crying, and gait disturbance, and was diagnosed with limbic encephalitis based on medical examinations and rapidly progressing clinical course after being hospitalized, was presented.

Case Report

A 53-year-old female patient was admitted to our clinic on February 2011 with complaints of headache, memory impairment, crying, and gait disturbance. Her medical history revealed that the complaints started 1-year ago and that she was examined for the same complaints in different centers with no results. Patient’s relatives expressed that her headache was variable, her memory impairment gradually worsened, and she was not able to perform the activities of daily living on her own. It was also stated that she had crying attacks from time to time during the day, and she was unable to walk on her own for the last few months.

Her personal medical history revealed thyroid surgery 25 years ago and hospitalization with the pre-diagnosis of tuberculosis 20 years ago; she had been...
followed-up for 10-15 days and discharged without treatment. Her family history was unremarkable.

On her neurologic examination, she was conscious and partially cooperative, and her orientation to time and place was impaired. The cranial nerves were intact, there was no motor deficit, but there were bilateral dysmetria and dysdiadochokinesia. The Romberg’s sign was positive. Her gait was ataxic. The deep tendon reflexes were normoactive. TCRs were the bilateral flexor, and she had no extrapyramidal signs. The Mini Mental State Examination score was 15/30, the Montreal Cognitive Assessment score was 12/30, and the clock drawing test score was 1/4. Systemic examination was within normal limits.

Cerebrospinal fluid (CSF) analysis was normal. Her erythrocyte sedimentation rate was 91 mm/h. Complete blood count, routine biochemistry; laboratory indicators of a vasculitic or viral disease, and tumor markers were unremarkable. Her electroencephalographic (EEG) findings were within normal limits. Although, she was considered to have limbic encephalitis at the first place based on the findings on cranial magnetic resonance imaging (MRI) examination performed approximately one year ago (Figure 1), we could not exclude the possible presence of a low-grade tumor, even at a low probability. The brain stem and cerebellum were normal. Cranial MRI was repeated. The increased signal intensities observed in the temporal lobe and in the right hippocampal region on the previous MRI were not observed on the repeat MRI (Figure 2a). However, bilateral increased signal intensities and two tuberculomas were reported in the cortical areas of the cerebellum (Figure 2b and c).

The patient was screened for possible neoplastic diseases. Pelvic computed tomography (CT) revealed multiple lymphadenopathies (LAPs) adjacent to the iliac vascular structures and in the sacral region. The size of the largest lymph node was 5.5 cm × 2.5 cm (Figure 2d). Thoracic CT revealed a nodular formation measuring 1 cm in diameter with lobulated contours, which was located in the laterobasal segment of the lower lobe of the right lung. Multiple lymph nodes were observed in the portocaval, aortocaval and paraaortic areas, the largest being 12 mm in diameter in the portocaval area. Findings of transvaginal ultrasonography and thyroid ultrasonography were unremarkable. Whole-body bone scan showed a focal hypermetabolism in the left frontal and left parieto-occipital regions of the brain. Multiple conglomerated hypermetabolic lymph nodes extending from the submandibular area to the supraclavicular and left upper paratracheal areas were detected in the left cervical neck. In addition, there were multiple LAPs with intense fluoro-2-deoxyglucose (FDG) uptake in the abdomen, in the lung periphery, and in the paratracheal, paraaortic, pelvic and retroperitoneal regions. In addition, hypodense and hypermetabolic solid lesions, measuring approximately 7-8 cm, were observed in the pelvis and abdomen. Some of these lesions had a hypometabolic center. Focal pathological FDG uptake in the left suprarenal gland was interpreted as a probable metastasis.

After positron emission tomography (PET) scan of the patient, who was being followed-up with the pre-
diagnosis of limbic encephalitis, was obtained, general surgery consultation was requested. The patient underwent excisional biopsy of the right inguinal lymph nodes. Pathological examination of the biopsy material revealed a caseating granulomatous lymphadenitis (tuberculosis). The clinical course progressed during the hospital stay, there was significant impairment in the cerebellar tests; infantile speech and nausea/vomiting began. High erythrocyte sedimentation rate persisted. The patient was diagnosed with limbic encephalitis and was given 30 g intravenous immune globulin (IVIg) daily for 5 days. Consultation was requested from the infectious diseases and chest diseases departments with the pre-diagnosis of tuberculosis. The patient had a negative culture for acid-resistant bacilli. The result of polymerase chain reaction testing of CSF specimen for tuberculosis was negative. The result of testing for non-tuberculosis mycobacteria was negative. The patient was discharged on anti-tuberculosis treatment with 5 drugs and was asked to return for follow-up. It was considered that tuberculosis accompanied a probable, paraneoplastic limbic encephalitis picture in this case.

Discussion

Although the pathophysiology of paraneoplastic syndromes are not fully understood, the notion that IgG autoantibodies (antineuronal antibodies), which are produced as a result of an immune reaction triggered by the cancer cells, cross-react with central or peripheral nervous system structures, which are perceived as antigens, gains importance. The most common PNSs include limbic encephalitis, subacute cerebellar degeneration, Lambert-Eaton myasthenic syndrome, sensorial neuropathy, opsoclonus-myoclonus ataxia syndrome, dermatomyositis, and motor neuropathy (3). Besides the basic signs such as short-term memory loss, epileptic seizures and behavioral changes, confusion, irritability, depression, psychosis, sleep disorders and hallucinations may be seen in patients with limbic encephalitis (4). This patient case as well had normal CSF findings. EEG may show unilateral or bilateral slowing or epileptiform discharges in the temporal lobes. EEG examinations repeated at intervals revealed normal findings in the present case. In a study performed on 50 patients, 30 patients had serum antineuronal antibodies (18 anti-Hu, 10 anti-Ta, 2 anti-Ma), and 20 patients were antibody negative (2). It is known that the antibody negativity does not exclude the diagnosis. It has been reported in the literature that one third of the cases are antibody negative, whereas 5-10% have antibodies not detected yet (3). This patient case as well was examined for antineuronal antibodies, and the result was reported as negative. The most common finding on cranial MRI is the signal changes in the medial temporal lobes without contrast enhancement (5). Cranial MRI of this patient showed increased signal intensity on T2-weighted and fluid-attenuated inversion recovery sequences in the bilateral temporal lobes, hippocampal and parahippocampal gyrus, subcortical region and white matter, being more prominent on the left side. The repeat MRI showed regression of the high signal intensity changes observed in the right temporal lobe and in the right hippocampal region on the previous MRI, but contrarily, showed bilateral increased signal intensity in the cortical areas of the cerebellar hemispheres. Hyponatremia, rapid eye movement sleep disorders, neuromyotonia, and autonomic signs frequently occur in patients who are positive for VGKC antibodies (1,6). Hypoventilation, catatonia, autonomic signs, orofacial dyskinesia, dystonia, and choreoathetosis may be seen in addition to the limbic signs in patients with NMDAR-antibody associated encephalitis. Tumor (generally ovarian teratoma) is detected in only 60% of such cases (7). In the present case, sodium concentration was found between 125 and 133 mmol/L on repeated measurements and but we were unable to detect a primary tumor. Studies have reported that FDG-PET studies may show hypermetabolism in the temporal lobes even in cases with normal MRI findings (8). In addition to the pathological findings on MRI of this case, FDG-PET scan showed a focal hypermetabolism in the left frontal and left parieto-occipital regions of the brain. Small-cell lung cancer has been reported to be the most common malignancy that accompanies this syndrome, with a rate of 50% (9). Other concomitant malignancies include testis (20%) and breast (8%)
Additional therapy was given for the lymph nodes found while searching for the primary tumor and for the caseating granulomatous lymphadenitis (tuberculosis) specified in the pathology report and their co-occurrence is being investigated.

The best outcome in paraneoplastic limbic encephalitis is obtained by the treatment of the primary tumor; nonetheless, studies have reported that immunomodulatory therapies can be used as well (8,3). In this case, rapidly progressing clinical picture was slowed down with IVIg therapy. A repeat cranial MRI, which was performed when the patient was re-hospitalized for control purposes, showed no abnormal findings except for the findings consistent with tuberculosis in the supratentorial areas and sequelae of encephalitis in the temporal lobe without contrast enhancement. On thoracic CT, multiple cystic necrotic LAPs were noted in the retroperitoneum. It was decided to continue with current tuberculosis treatment. Her control EEG was within normal limits.

During our research concerning the association of limbic encephalitis with tuberculosis, we found out that Ghosh et al. (10) treated a 46-year-old female patient presented with headache, behavioral abnormalities, fever, weight loss, seizures and meningeal symptoms with a pre-diagnosis of limbic encephalitis and tuberculosis. Thereafter, the authors diagnosed lung adenocarcinoma and excluded the diagnosis of tuberculosis by laboratory tests. Although, PET findings of the present case were in favor of malignancy, biopsy findings were positive for tuberculosis.

In conclusion, limbic encephalitis is a rare clinical entity, in which memory impairment and psychiatric symptoms are seen together. The underlying malignancy could not always be shown, and it has been reported in the literature that approximately one third of the cases are antibody negative. The present case showing the association of limbic encephalitis with active tuberculosis was considered noteworthy to report.

References