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Case Report

A rare case of paraneoplastic neurological syndrome with ovarian teratoma

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ABSTRACT

Paraneoplastic neurological syndrome (PNS) is a neuropathological disorder of central nervous system, in this the patient presents with a tumor anywhere in the body with diverse neuropsychiatric symptoms. The clinical manifestation of the tumor may be preceded by PNS. We are reporting a case of a 23-year-old married nulliparous female who came to the gynaecology outpatient department (OPD) with the history of mass per abdomen for the past four months and also undergoing treatment for acute psychosis, memory loss and cognitive impairment for the past five months. Her symptoms were not relieved on treatment. After clinical, laboratory and radiological evaluation possibility of paraneoplastic neurological syndrome associated with ovarian teratoma was made. Patient was taken up for staging laparotomy with U/L salpingoophrectomy. After surgical treatment her psychiatric symptoms rapidly improved and her psychiatric medications doses was reduced. PNS should be suspected in female patients presenting with an acute history of neuropsychiatric symptoms. Tumor resection should be performed at the earliest to improve patient outcomes.

Keywords: Paraneoplastic neurological syndromes, Immature teratoma, Gliomatosis peritonei, Case report

INTRODUCTION

Paraneoplastic neurological syndrome (PNS) is defined as the pathological involvement of the nervous system in the course of malignancy. In case of ovarian malignancy, the patient may present with neuropsychiatric symptoms prior to the symptoms of ovarian neoplasm. Autoimmune mechanism is suggested as the ovarian tissue and the nervous tissue share some common antigens (eg- CDR2, NMDAR). Antibody mediated immune response is responsible for the neurological symptoms. The detection of onconeural antibodies (eg- Anti-yo) strongly indicates the presence of ovarian tumor in patients with neurological deficit. Due to wide array of symptoms multidisciplinary approach is required for PNS including surgery and immunomodulation.[1]

CASE REPORT

We are reporting a case of a 23-year-old married nulliparous female who came to the gynaecology OPD with a history of a mass per abdomen for past four months and with gradual onset of gait disturbance, dysphonia, memory loss and cognitive impairment for the past five month. She was not able to perform her daily activities without someone's help. She had no prior history of psychiatric or neurological condition. There was no family history of psychological and psychiatric complaints. No history of alcohol, drugs consumption or smoking. History was given by her mother. She had taken psychiatry and neurology consultation and was prescribed medications but her symptoms were not relieved. She had started complaining of abdominal pain also for which she was brought to gynaecology OPD. On neurological

examination patient's gait was broad based and unsteady. She had dysmetrial, dysdiadocokinesia, dysarthria, and ataxia. Plantar responses were equivocal and she was unable to do tandem walking. She had normal tone, bulk and power in the limb muscles. Bilateral pupils were equally reacting to light. On abdominal examination, a mass of 28 weeks size was palpable, which was firm, non-tender, smooth with regular well-defined margins and side to side mobility was present. Inguinal and supraclavicular lymph nodes were not palpable. Rest of her general physical examination was within normal limits.

Ultrasonography (USG) abdomen and pelvis revealed a large solid-cystic well defined heterogeneously echogenic lesion of size 12×7.2 cm with multiple cystic areas along with internal vascularity, arising from left adnexa and suggestive of germ cell tumor. Right ovary was normal. Contrast enhanced computed tomography (CECT) abdomen and pelvis was suggestive of mature ovarian cystic teratoma with possibility of malignant transformation (Figure 1). Magnetic resonance imaging (MRI) brain showed non-specific ischemic changes.

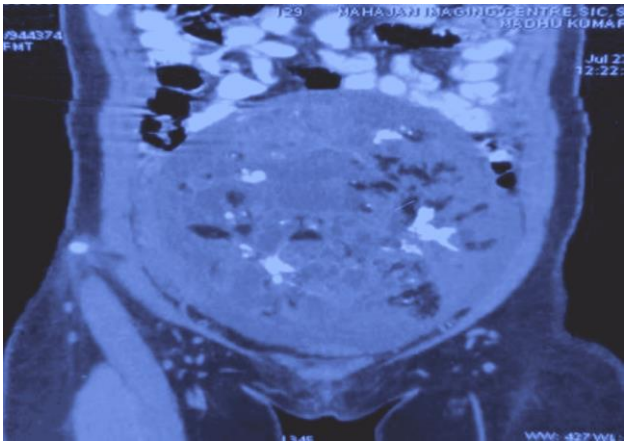

Figure 1: MRI of abdomen.

Serum tumor markers revealed CA125 143 U/ml, alpha-fetoprotein (AFP) levels of 47.3 ng/ml and beta-human chorionic gonadotrophin (HCG) levels were 2 mu/ml, LDH 230 ng/ml. Other biochemical tests (kidney function test (KFT), liver function test (LFT), thyroid stimulating hormone (TSH), blood sugars and serum electrolytes) were within normal units.

After clinical, laboratory and radiological evaluation patient was discussed in institutional tumor board. Psychiatric and neurology consultation was taken. Possibility of paraneoplastic neurological syndrome associated with ovarian teratoma was made. Electroencephalogram (EEG), blood and cerebrospinal fluid (CSF) autoimmune encephalitis panel workup which includes antibodies to N-methyl-D-aspartate (NMDA) receptor (confirmatory for autoimmune encephalitis) could not be done due to the financial and COVID-19 lockdown issues as all the elective procedures including EEG lab were closed.

Patient was taken up for staging laparotomy in emergency operation theatre as elective surgeries were withheld. Intraoperatively there was minimal ascites. A 20×17 cm solid firm mass was arising from left ovary. The ovarian capsule was ruptured. Right ovary was normal in size with deposits noted over the surface. Both the fallopian tubes and uterus was grossly looking normal. Multiple miliary extra pelvic peritoneal implants were present. Rest of the intraperitoneal organs were looking normal on inspection and palpation. Retroperitoneal lymph nodes were not palpable. Left salpingoopherectomy was done. Multiple peritoneal biopsies were taken, deposits on surface of the right ovary were also taken for histopathology (HPE). Infracolic omentectomy was performed. Tumour along with all biopsy samples were sent for HPE. Surgical stage IIIb. Gross examination of specimen showed 20×17 cm lobulated soft to firm mass.

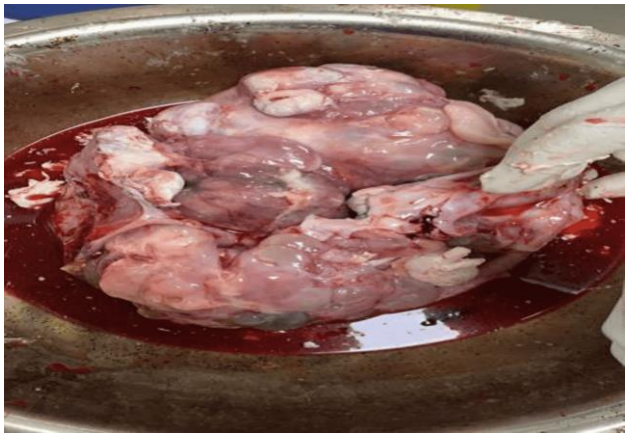

Figure 2: Cut section showing tumour mass.

Figure 2 showed solid (areas of bone and cartilage formation) with intermittent cystic areas (filled with serous and mucinous fluid). HPE report was immature teratoma (IT) grade 1 with gliomatosis peritonei (GP). Final diagnosis was, surgical stage Ic2 grade 1 immature teratoma ovary with GP. Case was discussed in tumour board and was planned for chemotherapy with BEP regime and close surveillance. Post operative period was uneventful. Stitches removal was done on day 7 after surgery. Relatives had been counselled about the need for chemotherapy and the importance of regular follow up. Patient was registered in the medical oncology department.

After surgical treatment there was fast improvement in her neurological sign and symptoms. Within 10 days of surgery, she was interacting with others and was doing routine activities on her own. Dose of the psychiatric medications was also reduced. Tumor markers values decreased after surgery (Table 1).

After surgical treatment patient and relatives planned to return to her native place and to take chemotherapy from there. Patient did not come for further follow up in gynae OPD as well as in medical oncology and could not be contacted telephonically also till date.

Table 1: Tumour markers before and after surgery.

Tumour markers	Before surgery	One month after surgery	Normal value
CA19.9	67.4	60.4	2.5
Alpha FP	47.3	6.6	2.56
HCG	2	0.1	2.5
LDH	230	123	
CA125	143	13.3	30

DISCUSSION

After analysis, the symptom complex of this patient described were fitting into the diagnostic criteria of definite PNS, this is defined as, the pathological involvement of the nervous system in the course of malignancy anywhere in the body. The most common features of PNS associated with ovarian tumors are subacute cerebellar degeneration and subacute sensory neuropathy. Paraneoplastic neurological syndromes associated with ovarian tumors may also appear as a peripheral polyneuropathy with diffuse paresthesia and anesthesia. There is no tumor infiltration, compression or metastasis of the nervous system. Since, ovarian tumors and nervous tissue share common antigens such as NMDAR and cerebellar degeneration protein-2 (cdr2) autoimmune etiology is the most probable mechanism of these neurologic disorders.[2]

NMDARs are ion channel. They play a significant role in learning, memory and synaptic plasticity. In anti-NMDA encephalitis the antibodies decrease the expression of NMDARs, thus causing the neurological and psychiatric symptoms.[3]

The striking clinical sign and symptoms of PNS seen in young females are abnormal behaviour, speech dysfunction, seizures, movement disorders, decreased level of consciousness, autonomic dysfunction or central hypoventilation. Presence of three of the above symptoms along with teratoma is adequate to make a provisional diagnosis of anti-NMDAR encephalitis but identification of anti-NMDAR antibodies is needed to make a definite diagnosis.[2]

Most patients develop psychiatric symptoms which are followed by neurological symptoms. CSF analysis will show presence of antibodies against NMDAR antigens and ovarian teratoma is present in 26.9% to 38% of patients.[4]

Other findings include EEG abnormality in the form of focal or diffuse slow wave, and pleocytosis in CSF. There can be variable presentations on MRI such as abnormality limited to hippocampus alone or present in other areas also. MRI brain can be normal in 50% cases.[5]

Although antigen specificity rather than the neurological symptoms is considered as more diagnostic factor of the tumor location, the most specific for diagnosis is the combination of both. In patients with anti-Yo, anti-Ri or anti- amphiphysin antibodies the possibility of ovarian cancer should be considered. In teratomas, anti-NMDAR antibodies are detected. The metanalysis of numerous studies conducted by Titulaer et al contains conclusions concerning management. The investigation of choice is transvaginal ultrasound.[6]

If it is normal, pelvic computed tomography or magnetic resonance imaging should be performed. In patients with antibodies suggesting ovarian cancer, an integrated FDG-PET/CT is indicated. It is important to perform it as soon as possible as combined PET/CT scan used in this context may significantly reduce the delay time to the surgery. If initial investigations do not detect any tumor, it is recommended to repeat them every 6 months for 4 years.[7] Subacute cerebellar degeneration has no single effective treatment. Given the immune-mediated pathogenesis, various, immunotherapy, such as plasma exchange, corticosteroids, and immunoglobulin injections, is often prescribed with only limited relief. Oncological treatments can provide various levels of relief or stabilization of the symptoms present case had dramatic improvement after surgery alone.

Histopathological examination revealed immature teratoma stage 1 grade 1 with gliomatosis peritonei (GP) which consisted mature glial tissue. Because the lesions in GP are extensive, complete excision is usually very difficult. The mature nature of the glial tissues implants generally implies a favorable outcome. These peritoneal implants may undergo fibrosis and eventually disappear or sometimes persist without any morphological changes. In rare circumstances, they can undergo malignant transformation therefore requires a careful monitoring of residual lesions using imaging modalities such as computed tomography; treatment of immature teratoma ovary with GP is according to the surgical stage and HPE of ovarian teratoma.[8]

CONCLUSION

PNS should be suspected in female patients presenting with an acute history of neuropsychiatric symptoms with ovarian tumour. As seen in the present case rapid detection and immediate treatment of the underlying tumor offers the best chance of stabilizing the patient and preventing further neurological deterioration.

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