CASE REPORT

Paraneoplastic Cerebellar Degeneration—A Rare Presentation of Ovarian Malignancy

Richa Sharma^{1,2} · Gita Radhakrishnan¹ · A. G. Radhika¹ · Anshuja Singla¹

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About the Author

Dr. Richa Sharma completed her MBBS from St. John's Medical College, Bangalore, and MS (Obs & Gynae) from KMC, Mangalore. She is currently working as an Assistant Professor in the Department of Obstetrics & Gynaecology at UCMS & GTB Hospital, Delhi. Her field of interest is high-risk pregnancy and infertility. This paper has won the best case report Prize at NARCHI Conference, 2014.

Introduction

Paraneoplastic cerebellar degeneration (PCD), a type of paraneoplastic syndrome (PNS), is a heterogeneous group of neurologic disorders caused by non-metastatic immune response to a primary malignancy, commonly lung, breast,

and ovarian cancers, and lymphomas. There are less than 100 cases reported worldwide, and only one Indian case has been reported till date [1]. It typically occurs in middle-aged to older patients. PNS may precede the diagnosis of cancer in 50–80 % of cases [2], with estimates ranging from 1 in 10,000 to 1 in 100. We present a case report of a 61-year-old female with PCD associated with ovarian carcinoma.

Dr. Richa Sharma is an Assistant Professor; Dr. Gita Radhakrishnan is a Director Professor and Head; Dr. AG Radhika is a Senior Specialist; Dr. Anshuja Singla is an Assistant Professor in the Department of Obstetrics & Gynecology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi.

✉ Richa Sharma
gautamdrricha1@gmail.com

¹ Department of Obstetrics & Gynecology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi 110095, India

² 206, Kangchenjunga, Kaushambhi, Ghaziabad, Uttar Pradesh, India

Case Report

A 61-year-old postmenopausal lady presented to the gynae OPD of our hospital with the complaints of abdominal distension, sudden inability to stand or walk, vertigo, slurring of speech, and decreased sensations in both the legs for 8 months. There was no history of trauma, headache, vomiting, fever, or loss of consciousness. There was neither bladder or bowel complaint nor any past history of diabetes mellitus, hypertension, tuberculosis, or cardiovascular conditions.

General physical examination revealed poor built and nutrition, PR 76/min, BP 128/78 mmHg with normal CVS and respiratory system. The results of cranial nerve examination were normal. The results of motor examination were found to normal; all reflexes were 2+ except for absent ankle jerks and plantar reflexes were flexor bilaterally; she had decreased sensations below the ankles. Her gait was ataxic. There was a large pelvic mass of size corresponding to 26 weeks gravid uterus, which was firm, non-tender with restricted mobility.

Her baseline investigations were normal; her CA-125 was 63.9 IU/ml and CEA was 2 ng/ml. USG (TAS & TVS) and CECT of abdomen showed a large solid and cystic lesion of 15 × 10 cm in dimension arising from the left adnexa (Fig. 1). MRI brain with contrast showed confluent chronic demyelinating changes in subcortical and periventricular white matter of bilateral frontoparietal region with diffuse age-related atrophy (Fig. 2). Neurologists were consulted and her CSF anti-neuronal antibody testing was performed which was negative for TB but positive for anti-YO.

Probable diagnosis of cerebellar degeneration secondary to ovarian neoplasm was made.

Staging laparotomy was performed, and total abdominal hysterectomy with bilateral salpingo-oophorectomy and infracolic omentectomy were performed. A 15 × 10 cm multilocular ovarian mass composed of solid tissues with capsule intact and papillary projections on the inner aspect was observed (Fig. 3).

Peritoneal cytology revealed numerous mesothelial cells and giant cells with few lymphocytes and neutrophils. The

Fig. 2 CT of abdomen: 15 × 10 cm of solid and cystic left ovarian mass

Fig. 1 MRI brain with contrast: confluent chronic demyelinating changes in subcortical and periventricular white matter of B/L frontoparietal region with diffuse age-related atrophy

Fig. 3 a Gross and b cut section of ovarian mass

histology of lesion revealed high-grade serous adenocarcinoma of the left ovary, consistent with FIGO stage I A.

Her postoperative period was uneventful and she received chemotherapy. She had some improvement in her gait and speech. she is currently under the follow-up of physiotherapist, speech therapist, oncologist, and neurologist.

Discussion

Paraneoplastic syndrome is broadly classified into four types: endocrinal, hematological, mucocutaneous, and neurological. PCD belongs to a neurological variety. An association between PCD and occult gynecologic cancers (breast or ovarian) was first identified in 1938. It is characterized by cerebellar atrophy with a diffuse loss of Purkinje cells, mediated by a cross reaction of antibodies with tumor antigens and cerebellar tissue [3].

Paraneoplastic cerebellar degeneration can be classified according to the presence of an antibody that reacted with an antigen present in both the tumors and in cerebellar Purkinje neurons obtained from these patients [4].

PCD-related autoantibodies, which include Anti-Hu (small cell lung ca), Anti-Ri/Nova (breast cancer), and Anti-Yo also called Purkinje cell cytoplasmic antibody type 1 (PCA-1), are usually associated with ovarian and other gynecologic cancers. It is an immunoglobulin (Ig)G directed against the cytoplasmic antigen cerebellar degeneration-related protein 2 (CDR2), detected in the central nervous system and tumor tissue. Intracellular antigens are not accessible to immune attack in situ, but peptides derived from intracellular proteins are displayed on upregulated major histocompatibility complex (MHC) class-I molecules in a proinflammatory cytokine milieu following proteasomal degradation, and are thus accessible to peptide-specific cytotoxic T cells. Antibodies targeting nuclear or cytoplasmic antigens are serum markers of T-cell effector-mediated injury. PCA-1 targeting these intracellular antigens is detected in serum and cerebrospinal fluid (CSF), but is not directly involved in the pathogenesis of neural tissue damage. CDR2 displayed in upregulated MHC class-I molecules is then accessible to peptide-specific cytotoxic T cells. Emigration of expanded populations of MHC class-I-restricted molecules and CD8⁺ onconeural peptide-specific cytotoxic T lymphocytes from tumor-draining lymph nodes to the systemic circulation, and thence to the CNS, is a plausible mechanism for neuronal degeneration in patients with PCA-1 autoimmune PCD [2]. More recently, anti-cdr2L antibodies have been identified which are involved in PCD emergence. In contrast to the cdr2, a cytoplasmic protein, cdr2L antigen is present in the cell membrane which may make it more accessible for antibody-mediated cytotoxicity. When

both anti-cdr2 and anti-cdr2L antibodies are present, they had much higher avidity than when detected alone. Patients with both antibody types developed definite PNS in contrast to individuals with either anti-cdr2 or anti-cdr2L. Cdr2L antigen is expressed both in Purkinje cells in cerebellum and in ovarian tumor tissue [5].

Symptoms of paraneoplastic neurological disorders may include ataxia, dizziness, nystagmus, difficulty in swallowing, loss of muscle tone, loss of fine motor coordination, slurred speech, memory loss, vision problems, sleep disturbances, dementia, seizures, and sensory loss in the limbs.

There are no established protocols for the treatment of most PNSs with ovarian cancer. Only mild to moderate neurological improvements have been achieved following a combination of treatment, including surgery, chemotherapy, intravenous Ig, and corticosteroids for the underlying malignancy [6].

Symptomatic relief is the mainstay for the treatment of patients with PCD. Rehabilitation, speech therapy, and psychological supports are also fruitful in the functional recovery [7].

Our patient had slight improvement in walking and speech 2 months after her surgery. she is currently undergoing speech therapy and physiotherapy.

The low success rate in our patient may be associated with neuronal loss, which was irreversible. However, it has been demonstrated that early diagnosis and therapy of PCD may improve neurological status.

Conclusion

The onset of symptoms of cerebellar degeneration indicates the presence of an occult malignancy. Early diagnosis and therapy of PCD may improve neurological status. Although PNSs form only a fraction and a rare manifestations of ovarian neoplasia, this disease is an example of how gynecological disorders are relevant to a wide range of specialists from neurologist to oncologist, physiotherapist, and psychologist.

Conflict of interest The authors declare that there is no conflict of interest.

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