Case Report

Paraneoplastic cerebellar dysfunction in Hodgkin's lymphoma

Kazi Sazzad Manir, Swapnendu Basu[1], Rahul Bhowmik, Debanti Banerjee

Department of Radiation Oncology, R. G. Kar Medical College and Hospitals, Kolkata, [1]Department of Radiation Oncology, Medica Cancer Hospital, Siliguri, West Bengal, India

ABSTRACT

Paraneoplastic cerebellar degeneration (PCD) is a rare presentation of Hodgkin's Lymphoma (HL) manifests as acute/sub-acute nature. We report a case of 21 yr old male presented with acute cerebellar signs along with underlying HL.MRI brain was normal. CSF study was unremarkable. Patient was treated with six cycles of chemotherapy followed by radiotherapy. Neurological manifestations remarkably improved along with complete resolution of underlying HL. Anti-cancer therapy of underlying HL is the main strategy of treating associated PCD.

Key words: Cerebellar degeneration, Hodgkin's lymphoma, paraneoplastic syndrome

INTRODUCTION

Paraneoplastic cerebellar degeneration (PCD) is a rare manifestation of systemic malignancy. It presents with acute or subacute cerebellar ataxia. It is most commonly associated with small cell carcinoma of the lung, breast cancer, and ovarian cancer and rarely with Hodgkin's lymphoma (HL).[1] By definition, PCD occurs neither by direct involvement of tumor nor by infection, ischemia, metabolic and nutritional abnormalities, or any form of anti-malignant therapy.[2] It was first described by Rewcastle in the year 1963.[3] Early diagnosis is essential because anti-malignant therapy targeting primary tumor controls PCD manifestations also.

CASE REPORT

A 21-year-old young college student with no comorbidity presented with gradually increasing swelling at left inguinal area from June 2014. After 3 weeks, he had progressive worsening unsteadiness with generalized clumsiness, vibrating vision on left lateral gaze, and poor articulation of phonemes during speech. These symptoms worsened rapidly. He had no history of headache and fever. There is no family history of such illness. On general examination, he was normal except multiple lymph nodes at left inguinal area that are matted with one another and firm in consistency. On central nervous system examination, he had normal higher mental functions, normal pupillary reflexes. He had bilateral, horizontal, and gaze-evoked nystagmus with an upbeat component on gaze to the left. On cerebellar testing, he had a pronounced intention tremor and dysdiadochokinesia of the left upper extremity. His gait was wide-based and unsteady. Marked truncal ataxia with inability to stand without the support was observed. His speech was mildly dysarthric. He had no cranial neuropathy. Upper and lower limb power was 5/5 with brisk tendon reflexes. Magnetic resonance imaging (MRI) of brain showed no abnormality. Antinuclear antibody, anti-dsDNA, anti-neutrophil cytoplasmic antibody, and

Address for correspondence: Dr. Kazi Sazzad Manir, Department of Radiation Oncology, R. G. Kar Medical College and Hospitals, Kolkata - 700 004, West Bengal, India.
E-mail: kazi.dr@gmail.com

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rheumatoid arthritis factors were negative. Serum protein electrophoresis was normal with no evidence of an M band. Cerebrospinal fluid (CSF) examination did not reveal any abnormalities. CSF cytospin was negative for malignant cells. CSF polymerase chain reaction tuberculosis was negative. 18-fluro deoxy glucose-positron emission tomography (FDG-PET) showed increased FDG avidity in multiple lymph nodes at left inguinal level (maximum size 10.4 cm × 4 cm × 2.7 cm) and mediastinum. Excision biopsy from left inguinal lymph node showed nodular sclerosis type of classical HL. Immunohistochemistry profile showed CD 15+, CD 30+, PAX 5+, CD45-, and CD20- cells. The patient was staged as stage IIIA classical HL.

The patient was treated with 6 cycles of injection doxorubicin, bleomycin, vinblastine, and dacarbazine. His neurological signs and symptoms started disappearing from the 2nd cycle onward. After completion of systemic chemotherapy, the patient was re-evaluated by PET computed tomography scan at the 6th week follow-up. It showed disappearance of all nodal masses. Detail clinical examination showed no neurological abnormality except mildly dysarthric speech. The patient underwent involved-field radiation therapy (IFRT) in left inguinal lymph node area. Dose was 30 gray in 2 gray per fraction 5 days a week. In first followed up after 4 weeks of completion of IFRT, he was completely normal in clinical examination, having no neurological signs or symptoms.

DISCUSSION

The patient's clinical presentation was typically of HL associated PCD. Small cell carcinoma of lung, ovarian cancer, and breast cancer are other malignancy associated with PCD. Cause of HL associated PCD is not well-understood but seems to be autoimmune in nature.[4-8] Trotter *et al*. showed strong association with the presence of anti-Tr antibody in serum and CSF in suspected HL associated PCD patients.[5] Arkenau *et al*. reported association with anti-Yo antibody, anti-HU, and anti-CV2 antibody.[1]

Although rare, this disease entity is well-documented.[1-8] Several aspects of this case bear emphasis. First, PCD was not associated with any other clinical or biochemical abnormalities except underlying HL. Second, MRI brain finding was absolutely normal unlike few other case reports. Suri *et al*.[4] reported hyperintensities in MRI T2 and fluid attenuation inversion recovery sequences in vermis and cerebellar hemispheres. Third, remarkable improvements with systemic chemotherapy were an interesting clinical observation, which coincided with resolution of underlying nodal disease. This finding emphasizes treatment of underling HL is the key management of PCD.

The prognosis of PCD associated with HL seems to be very poor. Of 28 patients described by Bernal *et al*., 86% suffered irreversible damage to the cerebellum.[9] The patients who recovered from their symptoms were all relatively young, under 40 years (as is the case in our patient). No relation to type or stage of the Hodgkin's disease is known. If treatment of the underlying neoplasm is successful, the antibody disappears in most of the cases.[9] There is also no evidence that a decrease of the antibody titer by means of treating the underlying Hodgkin's disease predicts better outcome.[8] In general, early recognition and intensive treatment of the underlying malignancy is advocated in most paraneoplastic neurological conditions. Other therapeutic interventions such as intravenous immunoglobulin, plasmapheresis, and immunosuppressive therapy (prednisolone, cyclophosphamide) have been attempted with variable results.[10] An improvement of PCD is possible if treatment is started before irreversible neuronal damage occurs (as in our case). It is a rare achievement; therefore, the central nervous system condition can be a considerable prognostic factor in PCD.

HL associated PCD presents with acute/subacute cerebellar dysfunction. Patients presented with florid cerebellar symptoms with paucity of other systemic features needs careful evaluation of lymphatic system for associated HL. Treatment of underlying HL is main management strategy of PCD.

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Department of Radiotherapy, R. G. Kar Medical College and Hospitals, Kolkata.

Conflicts of interest

There are no conflicts of interest.

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