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BRIEF COMMUNICATION

Paraneoplastic cerebellar degeneration as a presenting manifestation of non-Hodgkin's lymphoma

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Abstract

Background Paraneoplastic Cerebellar degeneration (PCD) is one of the classical paraneoplastic syndromes (PNS) which is characterised by subacute onset, progressive cerebellar ataxia and is usually associated with small cell lung carcinoma, adeno carcinoma of breast and ovary followed by Hodgkin's lymphoma.

Objective We herein report a case of subacute onset, progressive cerebellar ataxia in a 37-year-old female, who on evaluation was found to have non-Hodgkin's lymphoma and experienced good clinical response to treatment.

Discussion As compared to solid tumours, chances of association of PNS with Lymphomas is quite low and there are only few case reports in the literature showing association of PCD with non-Hodgkin's lymphoma. As PCD is one of the classical PNS, it is very important to identify subtle cerebellar manifestations in an otherwise apparently normal individual, as early diagnosis and aggressive treatment can immensely improve the mortality and morbidity associated with this syndrome.

Conclusion This case signifies the importance of suspecting PNS as an important differential diagnosis in a young patient presenting with subacute onset progressive cerebellar ataxia and evaluating her extensively for malignancy in spite of no paraneoplastic antibody been detected as early diagnosis and treatment can lead to gratifying response. We do agree that 2 weeks follow up is a short time interval to determine whether the response was sustained or not, for which a long term follow up is required.

Keywords Paraneoplastic neurological syndrome · Paraneoplastic cerebellar degeneration · Non-Hodgkin's lymphoma · Lymphoma · Paraneoplastic syndromes

Introduction

Although direct invasion of cancer cells or metastasis is the most common mechanism by which nervous system is involved in patients with malignancy, less than 1% of cancer patients present with paraneoplastic neurological syndrome (PNS) which is characterised by immune mechanism, triggered against antigens expressed on the tumour cells which are normally present in the nervous system [1]. Paraneoplastic cerebellar degeneration (PCD) is one of the classical paraneoplastic syndromes which is characterised by subacute onset, progressive cerebellar ataxia and is usually associated with small-cell lung carcinoma, adeno carcinoma of the breast and ovary, and Hodgkin's lymphoma [2, 3]. As compared to solid tumours, the chances of association of PNS with lymphomas are quite low, and there are only few case reports in the literature showing association of PCD with non-Hodgkin's lymphoma (NHL) [4]. We herein report a case of subacute onset, progressive cerebellar ataxia in a 37-year-old female, who on evaluation was found to have non-Hodgkin's lymphoma and experienced good clinical response to treatment.

Case report

A 37-year-old female was admitted with chief complaints of subacute onset and progressive gait instability (swaying towards either side) and double vision since 1 month, associated with intermittent vertiginous sensation. Over time, the patient's husband noticed a change in her voice due to which certain

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words were not clear. The patient was initially able to walk independently with instability mainly during traversing narrow path, but over next 1 month, the instability progressively increased and the patient now had to take support of the walls to even go to the washroom. Patient did not have a history of fever, decreased appetite, or significant weight loss. There was no history of similar illness in the family. On examination, the patient was hemodynamically stable with no postural drop in blood pressure. Neurological examination revealed staccato speech, gaze evoked nystagmus to either side, and limb and gait ataxia with tendency to fall towards either side. There was no other neuraxial involvement clinically and the rest of the systemic examination was normal with no palpable lymphadenopathy. Routine investigations including complete blood count and liver and kidney function tests were normal except mildly reduced serum albumin levels. Serum lactate dehydrogenase (LDH) levels, vitamin B 12, and vitamin E levels were normal. Contrast-enhanced magnetic resonance imaging (MRI) of the brain showed no abnormal lesion or contrast enhancement. Cerebrospinal fluid (CSF) examination was normal with no malignant cells (normal immunophenotyping among the cell population studied). Paraneoplastic antibody panel (anti Ri; Yo; Hu; GAD65; Tr; CV2; Ma2/Ta; Amphiphysin; Recoverin; SOX1; Titin; Zic4) was negative. Tumour markers (CA 19.9; alpha-fetoprotein; carcino embryonic antigen) and serum viral markers including human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV) antibody were negative. Ultrasound (USG) of whole abdomen including the pelvis revealed a right adnexal mass, and thus, a contrast-enhanced MRI of abdomen was advised which showed a well-defined, lobulated lesion in the right adnexal region, abutting the right ovary and the anterior aspect of the uterus with another altered signal intensity lesion involving the proximal appendix and mildly thickened fluid filled appendix distally. To confirm the aetiology, an USG-guided tru-cut biopsy was taken from the right iliac fossa lesion. The histopathology was suggestive of non-Hodgkin's lymphoma which was followed by immunohistochemistry which further classified it to diffuse large B cell lymphoma: germinal centre type (Figs. 1 and 2). Whole-body positron emission tomography-computed tomography (PET-CT) done for initial staging showed evidence of metabolically active disease involving supra- and infradiaphragmatic lymph nodes with no evidence of increased metabolic activity elsewhere in the body. Thus, a final diagnosis of paraneoplastic cerebellar degermation secondary to non-Hodgkin's lymphoma was made. She was given IV steroids (methylprednisolone 1 g/day for 5 days), and chemotherapy was started for NHL as advised by the medical oncologist. The patient was discharged after 5 days of steroids, and at 2 weeks follow-up, she showed good neurological improvement in her gait and speech as she was now able to walk without support with mild imbalance only during turning, and her speech appeared clearer. She was advised to follow-up with the medical oncology department for further chemotherapy.

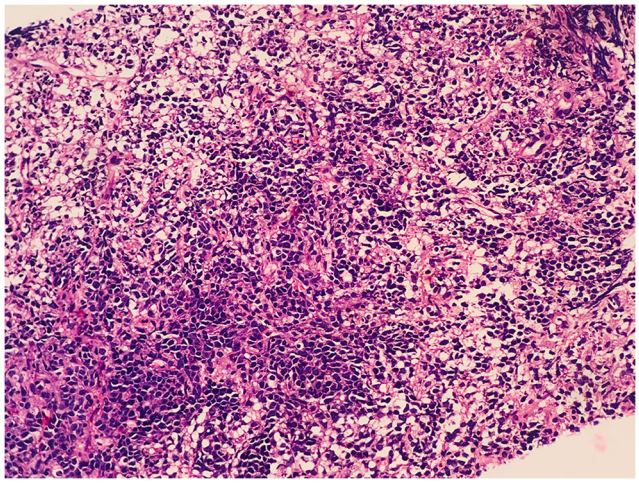

Fig. 1 × 100 H&E-stained slide showing diffuse infiltration by malignant small round cell tumour

Discussion

Graus et al. classified PNS into definite and possible depending on the type of neurological syndrome, detection of onconeuronal antibodies, and presence of malignancy. Classical neurological syndromes are considered almost pathognomonic of underlying malignancy, and detection of onco-neuronal antibodies or presence of cancer will further classify them into definite PNS [5]. The association of PNS with lymphomas is quite uncommon, and a study conducted by Briani et al. reported NHL in only 5 out of 21 patients with PCD [6]. The absence of onco-neuronal antibodies (except Tr and metabotropic glutamate 5), no antigens on the tumour cells, and extensive involvement of tumour at the time of diagnosis are

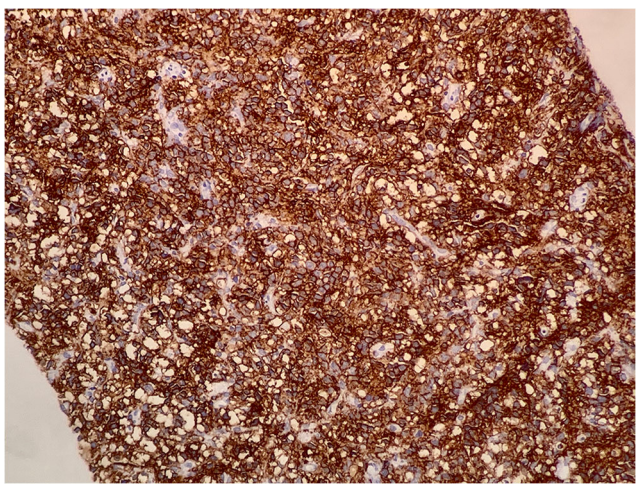

Fig. 2 × 100 immunohistochemistry (IHC) for CD20 immunopositivity - diffuse and strong membranous

some of the unique characteristic features seen in PNS associated with lymphoma. The target of damage is most commonly found to be Purkinje cells with relative sparing of other cerebellar neurons [2]. Clinically, PCD presents initially with giddiness and then usually progresses to gait ataxia and diplopia [4]. Our patient too presented with severe diplopia and gait ataxia enough to incapacitate her daily routine activities. Radiologically, initial MRI may be normal and later imaging may show cerebellar atrophy. Fluorodeoxyglucose positron emission tomography (FDG-PET) on the other hand may initially show cerebellar hypermetabolism but eventually with cerebellar atrophy setting in shows cerebellar hypometabolism [7, 8].

Appropriate management of PCD is a three-pronged strategy involving the removal or treatment of the tumour, immunotherapy, and rehabilitation. Although, progression of malignancy is the main reason of mortality, persistent neurological deficits cause high morbidity, and thus, rehabilitation plays an important role in improving quality of life in patients with PCD. Prognosis of PCD associated with lymphoma is reported to be poor, with younger age (less than 40 years) and absence of paraneoplastic antibody identified as relatively good prognostic indicators [1, 3]. Possible reasons for our patient's good response to treatment could be younger age and absence of any paraneoplastic antibody, although it is too early to be certain about the improvement to be persistent and not transient.

Conclusion

As PCD is one of the classical PNS, it is very important to identify subtle cerebellar manifestations in an otherwise apparently normal individual, as early diagnosis and aggressive treatment can immensely improve the mortality and morbidity associated with this syndrome. This case signifies the importance of suspecting PNS as an important differential diagnosis in a young patient presenting with subacute onset progressive cerebellar ataxia and evaluating her extensively for malignancy in spite of no paraneoplastic antibody has been detected, as early diagnosis and treatment can lead to gratifying response. We do agree that a 2-week follow-up is a short time interval to determine whether the response was sustained or not, for which a long-term follow-up is required.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The Ethics committee of our hospital was informed about the case report. As it didn't involve any trial or any new treatment to be tried and neither was it a study its approval was not required. It only involves reporting of a case.

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