CASE IN POINT

Nodular Sclerosing Hodgkin Lymphoma With Paraneoplastic Cerebellar Degeneration

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Background: There are a variety of paraneoplastic syndromes associated with Hodgkin lymphoma including paraneoplastic cerebellar degeneration (PCD), which is associated with unique autoantibodies such as anti-Tr antibody. Most of these autoimmune phenomena involve older adult patients with abrupt, acute presentations.

Case Presentation: We report an atypical case of a young adult female patient with slow progressive onset of PCD symptoms with subsequent detection and treatment of Hodgkin lymphoma.

Conclusions: Early detection of PCD is critical, as treatment of the underlying malignancy decreases overall morbidity and disability.

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Paraneoplastic syndrome is a rare disorder involving manifestations of immune dysregulation triggered by malignancy. The immune system develops antibodies to the malignancy, which can cause cross reactivation with various tissues in the body, resulting in an autoimmune response. Paraneoplastic cerebellar degeneration (PCD) is a rare condition caused by immune-mediated damage to the Purkinje cells of the cerebellar tract. Symptoms may include gait instability, double vision, decreased fine motor skills, and ataxia, with progression to brainstem-associated symptoms, such as nystagmus, dysarthria, and dysphagia. Early detection and treatment of the underlying malignancy is critical to halt the progression of autoimmune-mediated destruction. We present a case of a young adult female patient with PCD caused by Purkinje cell cytoplasmic–Tr (PCA-Tr) antibody with Hodgkin lymphoma.

CASE PRESENTATION

A 20-year-old previously healthy active-duty female patient presented to the emergency department with acute worsening of chronic intermittent, recurrent episodes of lightheadedness and vertigo. Symptoms persisted for 9 months until acutely worsening over the 2 weeks prior to presentation. She reported left eye double vision but did not report seeing spots, photophobia, tinnitus, or headache. She felt off-balance, leaning on nearby objects to remain standing. Symptoms primarily occurred during ambulation; however, occasionally they happened at rest. Episodes lasted up to several minutes and occurred up to 15 times a day. The patient reported no fever, night sweats, unexplained weight loss, muscle aches, weakness, numbness or tingling, loss of bowel or bladder function, or rash. She had no recent illnesses, changes to medications, or recent travel. Oral intake to include food and water was adequate and unchanged. The patient had a remote history of mild concussions without loss of consciousness while playing sports 4 years previously. She reported no recent trauma. Nine months before, she received treatment for benign paroxysmal positional vertigo (BPPV) with the Epley maneuver with full resolution of symptoms lasting several days. She reported no prescription or over-the-counter medications, herbal remedies, or supplements. She reported no other medical or surgical history and no pertinent social or family history.

Physical examination revealed a nontoxic-appearing female patient with intermittent conversational dysarthria, saccadic pursuits, horizontal nystagmus with lateral gaze, and vertical nystagmus with vertical gaze. The patient exhibited dysdiadochokinesia, or impaired ability to perform rapid alternating hand movements with repetition. Finger-to-nose testing was impaired and heel-to-shin motion remained intact. Romberg test was positive, and the patient had tandem gait instability. Strength testing, sensation, reflexes, and cranial nerves were otherwise intact. Initial laboratory testing was unremarkable except for mild normocytic anemia. Her infectious workup, including testing for venereal disease, HIV, COVID-19, and *Coccidioidies* was negative. Heavy metals analysis and urine drug screen were negative. Ophthalmology was consulted and workup revealed small amplitude downbeat nystagmus in primary gaze, sustained gaze evoked lateral beating jerk nystagmus with rebound nystagmus R>L gaze, but there was no evidence of afferent package defect and optic nerve function remained intact. Magnetic resonance imaging of the brain

demonstrated cerebellar vermis hypoplasia with prominence of the superior cerebellar folia. Due to concerns for autoimmune encephalitis, a lumbar puncture was performed. Antibody testing revealed PCA-Tr antibodies, which is commonly associated with Hodgkin lymphoma, prompting further evaluation for malignancy.

Computed tomography (CT) of the chest with contrast demonstrated multiple mediastinal masses with a conglomeration of lymph nodes along the right paratracheal region. Further evaluation was performed with a positron emission tomography (PET)–CT, revealing a large conglomeration of hypermetabolic pretracheal, mediastinal, and right supraclavicular lymph that were suggestive of lymphoma. Mediastinoscopy with excisional lymph node biopsy was performed with immunohistochemical staining confirming diagnosis of a nodular sclerosing variant of Hodgkin lymphoma. The patient was treated with IV immunoglobulin at 0.4g/kg daily for 5 days. A central venous catheter was placed into the patient's right internal jugular vein and a chemotherapy regimen of doxorubicin 46 mg, vinblastine 11 mg, bleomycin 19 units, and dacarbazine 700 mg was initiated. The patient's symptoms improved with resolution of dysarthria; however, her visual impairment and gait instability persisted. Repeat PET-CT imaging 2 months later revealed interval improvement with decreased intensity and extent of the hypermetabolic lymph nodes and no new hypermetabolic foci.

DISCUSSION

PCA-Tr antibodies affect the delta/notch-like epidermal growth factor–related receptor, expressed on the dendrites of cerebellar Purkinje cells.[1] These fibers are the only output neurons of the cerebellar cortex and are critical to the coordination of motor movements, accounting for the ataxia experienced by patients with this subtype of PCD.[2] The link between Hodgkin lymphoma and PCA-Tr antibodies has been established; however, most reports involve men with a median age of 61 years with lymphoma-associated symptoms (such as lymphadenopathy) or systemic symptoms (fever, night sweats, or weight loss) preceding neurologic manifestations in 80% of cases.[3]

Our patient was a young, previously healthy adult female who initially presented with vertigo, a common concern with frequently benign origins. Although there was temporary resolution of symptoms after Epley maneuvers, symptoms recurred and progressed over several months to include brainstem manifestations of nystagmus, diplopia, and dysarthria. Previous reports indicate that after remission of the Hodgkin lymphoma, PCA-Tr antibodies disappear and symptoms can improve or resolve.[4,5] Treatment has just begun for our patient and although there has been initial clinical improvement, given the chronicity of symptoms, it is unclear if complete resolution will be achieved.

CONCLUSIONS

PCD can result in debilitating neurologic dysfunction and may be associated with malignancy such as Hodgkin lymphoma. This case offers unique insight due to the patient's demographics and presentation, which involved brainstem pathology typically associated with late-onset disease and preceded by constitutional symptoms. Clinical suspicion of this rare disorder should be considered in all ages, especially if symptoms are progressive or neurologic manifestations arise, as early detection and treatment of the underlying malignancy are paramount to the prevention of significant disability.

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Ethics and consent

Written informed consent was obtained from the patient.

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