Case Report

Cerebellar Degeneration with Hodgkin's Disease

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Abstract

A 24 year old man with symptoms and signs of cerebellar degeneration for 17 months (etiology unknown) presented with a neck swelling. A biopsy revealed Hodgkin's disease. The cerebellar degeneration observed in this patient was believed to be a remote effect of his Hodgkin's disease.

The association of cerebellar degeneration and cancer is a well recognized but infrequent entity. The literature is reviewed. Only a few cases of cerebellar degeneration with Hodgkin's disease have been reported—to our knowledge, the literature contains only six cases. What is interesting about this patient is that the cerebellar symptoms preceded the diagnosis of Hodgkin's disease by a long interval. The etiology is unknown, but the possibility of viral infection or autoimmune mechanism has been studied.

Report of a Case

A 24 year old construction worker was in good health until February 1976, when he noted unsteadiness of lower extremities and frontal headache. By April 1976, the unsteadiness had increased; the patient had difficulty walking and blurring of vision as well. During the three months he had lost approximately 20 pounds but had had no night sweats. He was admitted to a local hospital, where an admission lumbar puncture showed the spinal fluid pressure to be normal. The fluid was clear, with 10 lymphocytes per cubic millimeter; protein level 116 mg/dl; glucose 49 mg/dl. The patient was referred to a large midwestern medical center for further diagnostic evaluation.

On admission, physical examination revealed a tall, thin, white male who appeared chronically ill. General examination was unremarkable but neurologic examination revealed anisocoria, end gaze nystagmus, mild dysarthria, ataxia of the upper extremities, a wide-based ataxic gait and marked trunkal ataxia.

Routine laboratory examinations were unremarkable. EEG, nerve conduction velocities, EMI scan, radionuclide brain scan, skull and chest x-rays, urine screen for heavy metals, serum copper and ceruloplasmin all were within normal limits. Lumbar puncture revealed
an opening pressure of 160 mm H$_2$O, protein 160 mg/dl, glucose 56 mg/dl. Protein electrophoresis of the CSF showed increased albumin. CSF cytology, serology, cultures and fungal studies were all normal as were titers for influenza A and B, adenovirus, herpes, CMV, mumps and mycoplasma.

The patient was given a therapeutic trial of dexamethasone; his symptoms did not improve. He was discharged with a diagnosis of midline cerebellar syndrome, etiology undetermined.

Over the next two months, the patient's condition remained unchanged and in June 1976, he was evaluated at a second referral hospital. Physical exam again revealed nystagmus, anisocoria and gross trunkal and limb ataxia. Routine laboratory examinations, repeat EEG, CT scan, skull and chest x-rays were again within normal limits. A pantopaque myelogram of the posterior fossa, including the fourth ventricle aqueduct and posterior third ventricle, was normal. Spinal fluid contained 40 lymphocytes and 10 polymorphonuclear cells per cubic millimeter with a total protein of 128 mg/dl and glucose of 68 mg/dl. CSF cytology, cultures and fungal studies were normal. No etiology was found for the patient's symptoms and he was placed on high dose steroids.

Follow-up six weeks later found the patient essentially unchanged. Repeat lumbar puncture was performed and his CSF protein was 79 mg/dl with a glucose of 70 mg/dl. A consulting hematologist found no evidence of underlying lymphoproliferative disease. High dose steroid therapy was continued for another month and then gradually tapered.

The patient's condition remained stable until October 1977, when his right neck swelled. Biopsy of a large anterior cervical lymph node was performed at a local hospital. He was then referred for further evaluation to the Department of Human Oncology, University of Wisconsin Hospital.

Physical examination revealed several small lymph nodes in the right submandibular region. No other peripheral lymphadenopathy was noted; there was no hepatosplenomegaly. Significant neurologic findings again included anisocoria, nystagmus, dysarthria and limb and trunk ataxia.

Review of the biopsy slides revealed nodular sclerosing Hodgkin's disease. Routine urinalysis, CBC, differential, chemistry panel and electrolytes were within normal limits. In the course of staging workup, mediastinal tomography revealed adenopathy above the transverse aortic arch. Whole lung tomograms, bilateral iliac crest bone marrow biopsies, radioisotope bone scan, lymphangiography and IVP were all negative. The PPD skin test was negative, but Candida skin test was positive. Because of the patient's severe neurologic disease, it was decided not to perform staging laparotomy; however, laparoscopy, with two biopsies from each lobe of the liver, was done. The liver and spleen appeared normal and the biopsies showed only normal liver tissue. Lumbar puncture was performed, showing a normal opening pressure and crystal clear fluid. The protein was 36 mg/dl and glucose 62 mg/dl. Cell count revealed six mononuclear cells and one red blood cell. Protein electrophoresis of the CSF revealed 73.4 percent albumin and 5.8 percent globulin. CSF cytology, cultures, fungal studies, toxoplasmosis and indirect fluorescent antibody tests were all negative. CSF titers for measles and rubella were less than 1:8. EEG was normal and photic stimulation revealed a normal VECCA profile. Review of a CT scan from October 1977 revealed reduced density to the right of the fourth ventricle without mass effect. Four-vessel cerebral arteriogram was within normal limits.

The patient was considered to have stage IIa Hodgkin's disease, nodular sclerosing, and the cerebellar degeneration was felt to be a remote effect of his Hodgkin's disease. The patient was discharged to receive radiation therapy in his home city and tolerated this relatively well. Follow-up in our outpatient clinic in May 1978 revealed no further...
progression of his disease, and no lymphadenopathy or hepatosplenomegaly. A repeat chest x-ray was now considered to be normal. The patient felt that both his speech and walking ability had improved, although the cerebellar signs were believed to be unchanged on neurologic examination.

Comment

The first report of a case of cerebellar degeneration with a co-existing cancer was published more than 50 years ago. However, the occurrence of these entities together was not well established until 1951 when Brain, Daniel and Greenfield reviewed the literature and added new cases of their own.

Usually, the presenting symptoms are limb ataxia, especially of the legs, with difficulty in walking. Dysarthria, nystagmus and diplopia are also common features. Symptoms of non-cerebellar origin are also seen. These include dysphagia, mental changes, muscular weakness and reflex changes. The onset is usually subacute and the clinical course is progressive over a few months until a plateau of neurologic symptoms is reached. In only one reported case has there been improvement of the cerebellar symptoms with treatment of the primary cancer. That patient had Hodgkin’s disease treated with nitrogen mustard.

In their review, Brain and Wilkinson described 10 males and nine females with cerebellar degeneration and co-existing cancer. The average age was 56.4 years, ranging from 36 to 70 years. The interval between the discovery of the tumor and the development of neurologic symptoms was three to 24 months in seven patients. In the remaining 12 patients the symptoms of cerebellar disease preceded the diagnosis of co-existing cancer. The interval in this group generally was one to 24 months; however, in one case the neurologic symptoms antedated the diagnosis of cancer by eight years.

The neoplasms most frequently associated with cerebellar degeneration are the following: carcinoma of the lung (44 percent), carcinoma of the ovary (16 percent), and lymphoma and Hodgkin’s disease (14 percent). The spinal fluid examination was abnormal in 13 of 18 cases. Spinal fluid protein was elevated in six cases; eight patients had an abnormal gold curve and in two cases, there were lymphocytes present in the spinal fluid.

On gross and microscopic examination, carcinomatos cerebellar degeneration has been more diffuse than that seen with alcohol use or nutritional deficiency. Loss of Purkinje cells is characteristic in carcinomatos cerebellar degeneration. The molecular layer is thinner and the granular layer is narrower than normal. Degeneration in the lateral and posterior columns of the spinal cord has been described in several cases and degeneration of the ganglion cells of the cranial nerve nuclei, as well as the anterior horn cells of the spinal cord, have been reported. Lymphocytic infiltration of the meninges has also occurred. These widespread changes may account for the non-cerebellar signs reported above.

The lesions do not depend on the presence of tumor infiltration anywhere in the nervous system and therefore the pathogenesis has been quite obscure. Of interest is the Gordon reaction, where lymph node suspensions from cases of Hodgkin’s disease by intercerebral injection in rabbits caused cerebellar symptoms and Purkinje cell degeneration. It was found that the encephalopathic property was related to the number of eosinophils in the suspension. Eosinophils from various sources injected by subcutaneous route have also caused the same changes. In reports on cerebellar degeneration with Hodgkin’s disease, two patients have had eosinophilia.

A remarkable parallel has been noted between carcinomatos cerebellar degeneration and both scrapie in sheep and Kuru. In these entities the clinical course and pathologic findings have been very similar, although not entirely identical. It has been speculated that a combination of viral infection and autoimmune pro-
cess may be involved in this disease.
Trotter and colleagues,6 using immunofluorescent techniques, found antibodies to Purkinje cells in serum from a patient with Hodgkin's disease. This suggests an autoimmune mechanism but further clarification is needed.

References

1. Victor M, Ferendelli JA: The cerebellum in health and disease, in Fields WS, Willis WD (eds): Nutritional and Metabolic Disease. St Louis, Warren H Green Inc, 1970, pp 412-449.
2. Malamud N: Atlas of Neuropathology. Berkeley, University of California Press, 1957, pp 118-123.
3. Rewcastle NB: Subacute cerebellar degeneration with Hodgkin's disease. Arch Neurol 9:407-413, 1963.
4. Horwich L, Buxton PH, Ryan GM: Cerebellar degeneration with Hodgkin's disease. J Neurol Neursurg Psychiat 29:45-51, 1966.
5. Brain L, Wilkinson M: Subacute cerebellar degeneration associated with neoplasms. Brain 88:465-478, 1965.
6. Trotter JL, Hendin BA, Osterland CK: Cerebellar degeneration with Hodgkin's disease. An immunological study. Arch Neurol 33:660-661, 1976.
7. Brain WR, Daniel PM, Greenfield JG: Subacute cortical cerebellar degeneration and its relation to carcinoma. J Neurol Neurosurg Psychiat 14:59-75, 1951.
8. Meyer JS Foley JM: The encephalopathy produced by extracts of eosinophils and bone marrow. J Neuropath Exp Neur 12:349-362, 1953.
9. Beck E, Daniel PM, Parry HB: Degeneration of the cerebellar and hypothalamic neurohypophysial systems in sheep with scrapie; and its relationship to human system degenerations. Brain 87:153-176, 1964.

THE LANGUAGE OF MEDICINE

Medical terminology contains many references to classic mythology. In anatomy, the otic labyrinth recalls the subterranean maze on the island of Crete, to the center of which Theseus penetrated to slay the Minotaur. Venus the love goddess is commemorated in mons Veneris as well as in venereal disease. The tendo Achillis refers to the one vulnerable spot of the Greek hero in the Iliad. Atlas, who bore the world on his shoulders, has given his name to the first cervical vertebra.

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