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Case Report

Chorea and Dystonia: A Remote Effect of Carcinoma[1]

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Summary: A 45-year-old woman with an acquired multifocal neurologic syndrome, including chorea, dystonia, cerebellar dysfunction, multiple cranial neuropathies, and pure sensory neuropathy, was found at autopsy to have oat cell carcinoma. Neuropathologic examination revealed several features typically associated with remote effects of malignancy on the nervous system. We believe that this is the first described case of chorea as a remote effect of malignancy. **Key Words:** Chorea—Dystonia—Remote effect of malignancy.

Chorea and dystonia are commonly encountered in clinical practice. The majority of cases of chorea are usually secondary to neuroleptic drugs, L-Dopa intoxication, or Huntington's disease. Cases of chorea not attributable to the above causes are sometimes seen, and the enormous differential diagnosis for other causes of chorea demands an extensive evaluation (for a comprehensive review, see ref. 1). Dystonia, on the other hand, is usually idiopathic, though an extensive list of inciting conditions has been compiled (2).

We have recently encountered a patient who manifested both chorea and dystonia during the course of a long illness. The pattern of her other neurologic symptoms and signs, and neuropathologic examination were consistent with a paraneoplastic syndrome. We believe that this is the first description of chorea as a remote effect of malignancy.

[1] A videotape segment accompanies this article.

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HISTORY

The patient was a 45-year-old right-handed white female admitted to the Neurology Service at the University of Michigan Hospital in April of 1985. She gave a history of several weeks of malaise, arthralgias, and myalgias. During the week prior to admission, she noted diminished sensation over the right side of her face and right temporal tenderness when brushing her hair.

Her initial examination revealed hypokinetic saccades and unsustained nystagmus on right gaze. Decreased pin prick sensation was found over the right side of her face. Bilateral upper extremity dystaxia and reduced ability to perform rapid, repetitive movements was noted. There was mild impairment of tandem gait and a mild reduction in vibratory sense in both lower extremities. Occasional truncal titubation was present.

During the course of her hospital stay she developed a left Adie's pupil, left central facial weakness, and left sensori-neural hearing loss. Her titubation and gait disorder worsened. Tandem walking became impossible. She developed diffuse mild weakness, and muscle stretch reflexes disappeared. Sensory perception decreased, and she complained of severe dysesthesiae. Orthostatic hypotension developed.

Laboratory evaluation indicated normal thyroid studies, vitamin B_{12} and folate levels, heavy metal screens, CPK, aldolase, erythrocyte sedimentation rate, ANA, complement levels, rheumatoid factor, serum protein electrophoresis, syphilis serology, leptospirosis titers, monospot, and hepatitis screen. Serum calcium, magnesium, and electrolytes were normal throughout this and subsequent hospitalizations with the exception of intermittent, mild hyponatremia (lowest values = 130, normal = 137–149). Lumbar punctures revealed normal glucoses and cell counts with proteins varying from 200 to 600 mg%. Cerebrospinal fluid VDRL was nonreactive, and multiple inspections showed no malignant cells. Four oligoclonal bands were present. Radiological studies including serial cranial CT scans, cerebral angiography, and bilateral mammography were all normal. Magnetic resonance imaging showed a high signal aberration suggestive of a soft tissue suprasellar mass. Temporal artery biopsy was normal. Electroneuromyography was initially normal, but later studies revealed evidence of a pure sensory neuropathy. EEG showed diffuse slowing, and visual and somatosensory evoked potentials were normal. She was discharged to home on May 31, 1985.

While at home she continued to decline with progressive loss of strength, greater dysesthesiae, and worsening dysarthria. She was readmitted June 24, 1986.

Examination at that time revealed mild impairment of attention, memory, and concentration. Her pupils were 8 mm in diameter, regular in shape, and reacted more to accommodation than to light. Facial sensation was decreased bilaterally. Left central facial weakness and sensori-neural hearing loss were present. She was mildly dysarthric. Motor impersistence of the tongue was present. She was diffusely and symmetrically weak. There was marked appendicular dystaxia. All modalities of sensation were diminished to the level of the clavicle bilaterally. Muscle stretch reflexes were absent.

Involuntary movements of the limbs were first apparent at this time. These were present in the arms to a greater extent than the legs, and occurred spontaneously at rest. Choreic movements (videotape segment 1) were continually present and mildly worse with voluntary movements. They were of low amplitude, jerky and rapid in character, involved both proximal and distal portions of the arms, and seemed to flow from one portion of the limb to another. There was a slower, writhing, athetoid component that also was continuous, spontaneous, and present at rest. The movements were absent during sleep. They were identical with the eyes closed or open. The movements bore a striking resemblance to the choreoathetosis seen in moderately advanced Huntington's disease.

Repeat lumbar puncture revealed a protein of 225 mg% with normal glucose and cell count. Three oligoclonal bands were present. Conjunctival biopsy was normal. Sural nerve biopsy revealed evidence of ongoing axonal degeneration with segmental demyelination and remyelination. Urine prophyrin screen was normal. Pelvic and abdominal CT scans were normal. Chest CT scan revealed a 1.5–2.0 cm left hilar mass. Broncoscopy with transbronchial biopsy and serial washings was not diagnostically helpful. Bone marrow showed normal cellular elements.

Her hospital course was complex. She suffered seizures on two separate occasions and required subsequent ventilatory support after each of these seizures. She was placed on phenytoin, and no further seizures were noted. She had an episode of *Legionella* pneumonia. Her mental status gradually declined. Repeat EEG revealed a greater degree of diffuse slowing.

The character of her involuntary movements changed over the course of her hospitalization. The changes were not associated with institution of phenytoin. The choreoathetoid movements slowly diminished and were replaced by dystonic posturing. The latter involved the arms, leg, trunk, and neck. These movements also were spontaneous, present at rest and exacerbated by motion (videotape segment 2). They consisted of torsional or twisting movements of the extremities, trunk, or neck, usually sustained for seconds to minutes. These also were absent during sleep.

Consideration was given to thoracotomy and open biopsy of the hilar mass, but her medical condition was felt to preclude general anesthesia. A course of methylprednisolone (60 mg per day) failed to halt the progression. She was transferred to a hospital closer to her home on July 5, 1985. She died on July 26, 1985 after a respiratory arrest and 2 days of ventilatory support.

At autopsy a small cell undifferentiated (oat cell) carcinoma was found in a left hilar lymph node. No endobronchial primary was identified. There was evidence of bronchopneumonia. There was no evidence of systemic metastasis. Gross examination of the brain and spinal cord showed only evidence of diffuse edema. Microscopic examination of cerebral cortex revealed small, angulated, pyknotic nuclei typical of hypoxic encephalopathy. Sections of the medulla revealed marked perivascular infiltration of lymphocytes and focal chromatolysis of neurons in the nuclei of cranial nerves ten and twelve. Cerebellar cortex was found to have marked loss of Purkinje cells and atrophy of the granular layer (Fig. 1). Sections of cervical, thoracic, and lumbar cord revealed striking loss of myelin-

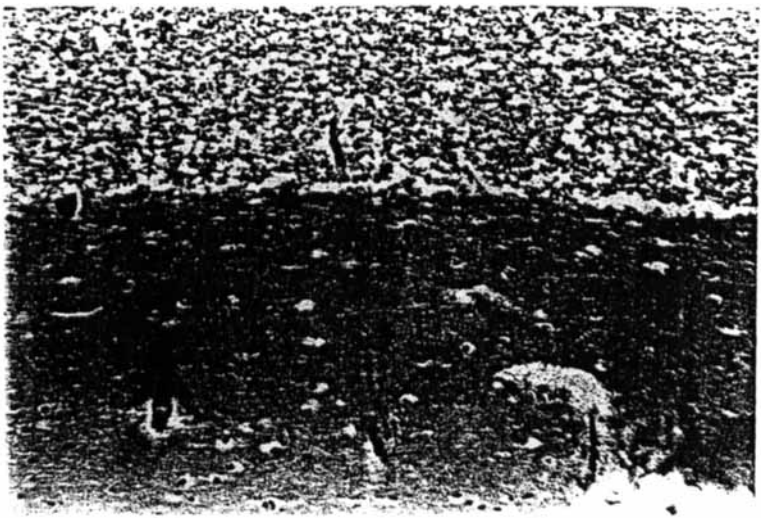

FIG. 1. Cerebellum. There is a marked loss of Purkinje cells and atrophy of the granular layer (hematoxylin and eosin, ×100).

ated fibers and gemistocytic astrocytosis in the posterior columns (Figs. 2 and 3). Perivascular lymphocytic infiltrates were also noted. Sections of the dorsal root ganglia showed marked neuronal loss and nodules of Nageotte (Fig. 4). Sections of striatum, pallidum (Fig. 5), substantia nigra, and midbrain were normal.

DISCUSSION

Our patient suffered from a progressive multifocal neurologic disorder involving both the central and peripheral nervous systems. Several aspects of this case, notably the pure sensory neuropathy and cerebellar degeneration are characteristic of what are considered to be remote effects of malignancy (3). As is typical of these syndromes, this patient had multifocal disease, and the malignancy was a carcinoma, most likely of lung origin (3,4).

Chorea has not previously been described as a remote effect of carcinoma. There is one case report of dystonia occurring in a patient with a paraneoplastic brainstem encephalitis (5), and myoclonus has been described in several other cases (6).

This patient had no family history of neurologic disease, exposure to neuroleptic drugs, L-Dopa, or oral contraceptives. Several other potential causes of chorea including thyrotoxicosis, systemic lupus erythematous, polycythemia, and sarcoidosis were excluded in the course of her extensive evaluation. The association of her movement disorder with several typical manifestations of a paraneoplastic syndrome (sensory neuropathy and cerebellar degeneration) made it likely that a remote effect of malignancy is the etiology of this patient's chorea and dystonia. We do not believe that the movement disorder was pseudoathetosis from peripheral nerve degeneration because her choreoathetosis was identical with her eyes both closed and open (7). The movements also had a rapid compo-

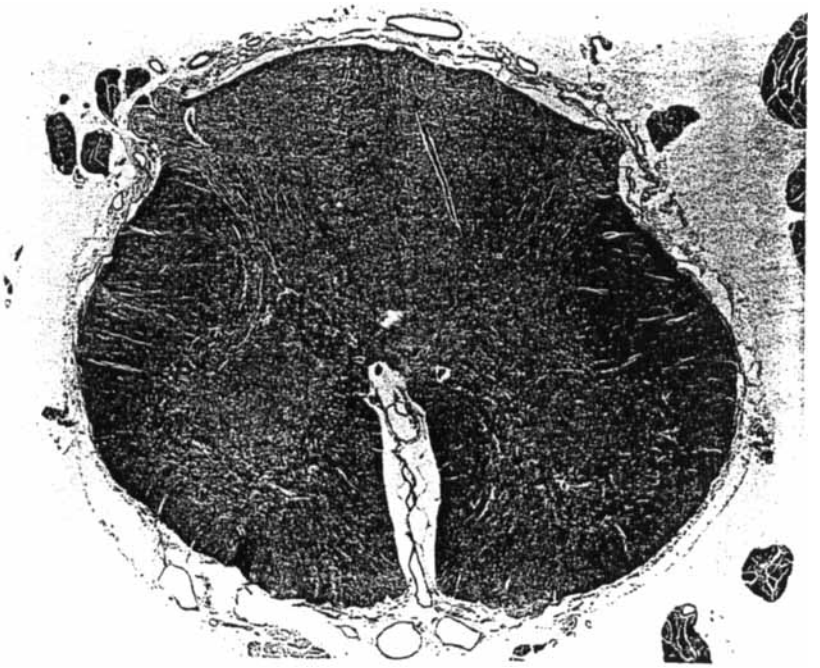

FIG. 2. Lumbar spinal cord. Degeneration of the dorsal columns. Note the loss of myelin secondary to degeneration of the nerve fibers. This was a prominent finding throughout the entire length of the spinal cord (luxol fast blue PAS, ×8).

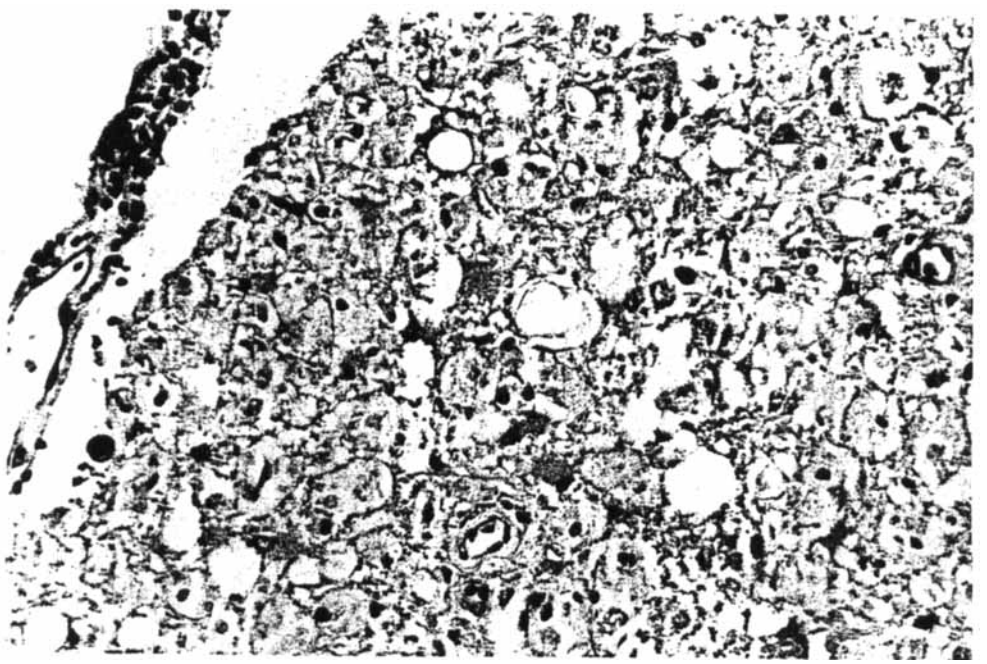

FIG. 3. Dorsal column of spinal cord. There is a marked loss of nerve fibers. Notice the large numbers of lipid-laden macrophages, presumably phagocytizing debris from nerve fibers, and numerous gemistocytic astrocytes. There is a perivascular infiltrate of lymphocytes (left upper corner) (hematoxylin and eosin, ×250).

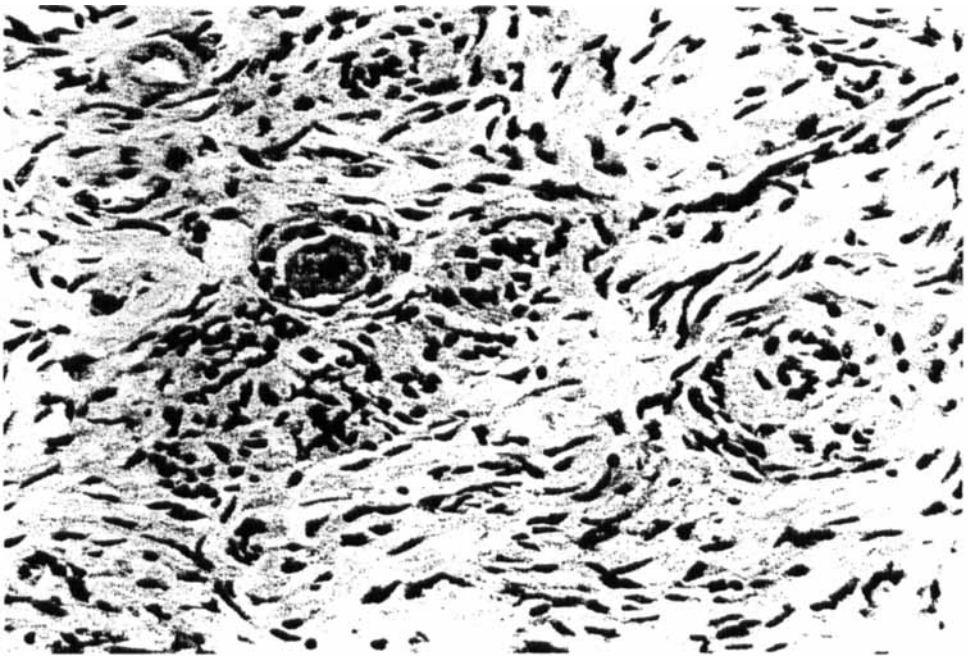

FIG. 4. Dorsal root ganglia. There is a prominent loss of neurons. There are tight clusters of lymphocytes which replace the degenerative neurons, i.e., nodules of Nageotte (hematoxylin and eosin, ×250).

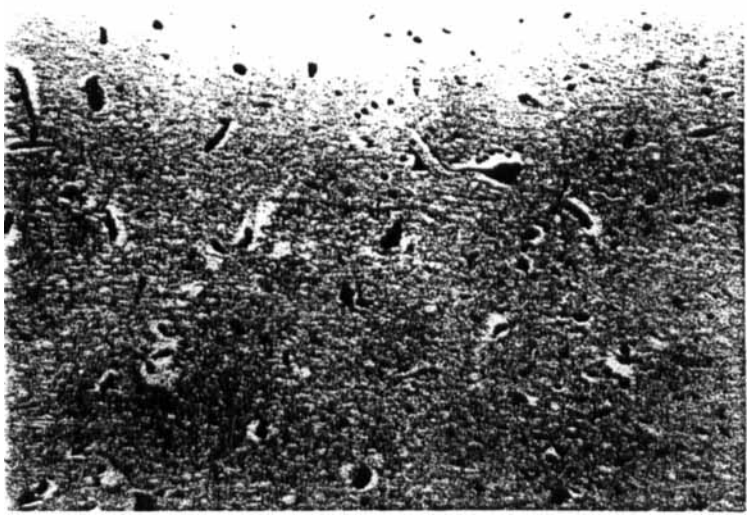

FIG. 5. Globus pallidus. This is morphologically unremarkable (hematoxylin and eosin, ×100).

nent typical of chorea, but not typical of the slower, writhing movements of pseudoathetosis (7). In addition, peripheral neuropathy would not account for her dystonia.

The pathogenesis of paraneoplastic syndromes is uncertain at this time. Speculation has mainly focused on an inflammatory or autoimmune mechanism. Inflammatory infiltrates are common in these disorders, and anti-purkinje cell antibodies have been detected in patients with the cerebellar syndrome (8). Whether or not the latter represent a primary or secondary phenomenon is unclear.

While this patient's autopsy material did reveal changes typical of a paraneoplastic syndrome, the basal ganglia were intact. Other cases have been described in which no histological correlates have been found to account for the clinical abnormalities (9,10). While most speculation regarding pathogenesis has focused on autoimmune mechanisms, Brain et al. (10) suggested that tumor-mediated toxic or metabolic factors could be a cause of paraneoplastic phenomenon. The lack of atrophy or inflammation in the basal ganglia would be more in keeping with this hypothesis. The progression from choreoathetosis to dystonia is also intriguing in that it mimics the natural history of Huntington's disease (HD). It has recently been suggested that the chorea of HD is secondary to a relatively greater loss of striatal neurons projecting to the lateral pallidum (11). Some recent evidence has emerged to support these ideas (12,13). This patient's choreoathetosis could have resulted from dysfunction of a specific pool of striatal neurons in a manner analogous to the specific degeneration of cerebellar purkinje cells and primary sensory neurons (3).

Finally, while this patient's movement disorder presented as part of a multifocal syndrome, it is conceivable that choreoathetosis could be the initial manifestation of a paraneoplastic syndrome. As in this case, remote effects are well known to have occurred in advance of the diagnosis of malignancy (4,7). When confronted with a patient with choreoathetosis without obvious cause, remote effect of carcinoma might be considered in the differential diagnosis.

LEGENDS TO THE VIDEOTAPE

SEGMENT 1: Choreoathetoid movements are present in both lower and upper limbs but are more marked in the arms. Superimposed dystonic posturing is also seen, especially as the patient moves her arms.

SEGMENT 2: Dystonia of the extremities, neck, and trunk. Mild resistance to passive manipulation without catch at wrist joints only. The dystonia has a torsional quality, is exacerbated by movement, and may persist for minutes. Dystaxia to finger-to-nose testing is present with superimposed dystonia. Rapid rhythmic movements are slow and irregular.

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