Ballistic-Choreic Movements as the Presenting Feature of Renal Cancer

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Background: The paraneoplastic syndromes can involve multiple areas of the central nervous system and result in a variety of neurological symptoms. To our knowledge, severe, rapidly progressive, and drug-resistant ballistic-choreic movements have not been previously described as the presenting feature of renal cell carcinoma.

Patient and Methods: A previously healthy 55-year-old man developed limb ballismus and involuntary choreic movements of his face over several weeks. Extensive laboratory, diagnostic, and radiographic studies failed to reveal a cause, until an abnormality on a chest x-ray film prompted a search for a primary neoplasm and a final diagnosis of renal cell carcinoma. High doses of medications traditionally used to treat choreic disorders had no effect on the abnormal movements. A biopsy specimen of the basal ganglia showed focal encephalitic changes but no malignant neoplasm.

Conclusions: Whereas prior cases of paraneoplastic syndromes with chorea have been reported in other forms of cancer, our case was significant because, to our knowledge, renal cell carcinoma has not been previously reported in association with this syndrome. Furthermore, the chorea was categorically resistant to pharmacological treatment, and the movement disorder was the initial and only focal neurological feature of the primary illness.

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THE DIFFERENTIAL diagnosis of chorea, which is extensive, includes hereditary (Huntington disease and Wilson disease), infectious (Sydenham chorea), metabolic (abnormal sodium, glucose, and magnesium levels), endocrine (hyperthyroidism), inflammatory (vасculitis, lupus, and sarcoidosis), cerebrovascular (arteriovenous malformations, stroke, and polycythemia), levodopa intoxication, and neurodegenerative disorders (Hallervorden-Spatz disease). Although neuroleptic and anticonvulsant medications are used in the treatment of chorea, these drugs can also induce chorea. Rarely, chorea can occur as a form of paraneoplastic central nervous system disease. We describe a patient who presented with severe, disabling, and drug-resistant ballistic-choreic movements that represented the first and isolated focal neurological symptom of renal cell carcinoma.

REPORT OF A CASE

A 55-year-old white man was referred for evaluation and treatment of ballistic and choreiform movements. He was in his usual state of health until 6 weeks before admission, when he first noted shortness of breath, insomnia, and anxiety. The results of routine blood tests, chest radiography, transthoracic echocardiography, and an exercise stress test were normal. Over the next week, the patient developed mild involuntary movements of his face and limbs, and his family noted slurred but appropriate speech. He then rapidly developed more severe involuntary movements, difficulties with his balance, light-headedness, and a mild frontal headache. He was first admitted to a community hospital but was transferred to our university hospital for further evaluation approximately 3 weeks after the initial onset of involuntary movements.

The patient’s medical history was significant for a traumatic amputation of the right middle finger and pneumonia. He was not taking any prescription medications. He was married and had an adult son and a developmentally delayed daughter. He was employed full-time as a truck driver transporting organic solvents but had no history of accidental exposure. The pa-
tient had stopped smoking 20 years ago, drank alcohol on social occasions, and denied the use of illicit substances. His parents were alive and well, and there was no family history of neurological illness or movement disorder.

On general examination, the patient was a moderately obese man in no apparent distress. His vital signs, including temperature, respiration rate, blood pressure, and pulse rate, were normal. His cardiac, lung, and abdominal examinations revealed no abnormalities. A non-palpable petechial rash was noted over his neck, shoulders, and back. His neurological examination revealed moderately severe involuntary movements of his extremities, which were more pronounced in his arms, neck, and face. These movements were random and unpredictable at rest and had a choreic and ballistic quality that increased when the patient was stimulated or speaking. He was alert and able to follow commands but was not oriented to time and place. His speech was appropriate but markedly dysarthric, with intact naming and repetition. The results of his cranial nerve and muscle strength testing were normal. Pin sensation was symmetrically diminished distally to his elbows and ankles. He was areflexic, with bilateral Babinski responses. He could sit upright, but gait testing could not be completed owing to the severity of the involuntary movements. Finger-to-nose and heel-to-shin testing evoked ballistic movements of the active extremity.

The results of the following laboratory investigations were normal or negative: glucose, electrolytes, complete blood cell count, urinalysis, coagulation studies, erythrocyte sedimentation rate, porphyrins, toxicology screen, genetic testing for Huntington disease, ceruloplasmin, heavy metals, thyroid function, rheumatoid factor, rapid plasma reagin test, human immunodeficiency virus, serum protein electrophoresis, and Lyme, thyroid, antiphospholipid, and anti-Hu antibodies. The following values were abnormal: ammonia, 38 mg/dL (27 µmol/L) (reference range, 11-35 mg/dL [8-25 µmol/L]); antistreptolysin antibody, 599 IU/mL (reference range, 0-200 IU/mL); and C-reactive protein, 41 µg/mL (reference range, 0-5 µg/mL). A chest x-ray film showed mild pulmonary edema with upper lobe pulmonary vessel distention. A lumbar puncture completed with the patient under general anesthesia revealed the following values: leukocyte count, 176/µL (lymphocytes, 62%; neutrophils, 9%); erythrocyte count, 175,000/µL; protein, 2.1 g/dL; and glucose, 112 mg/dL (6.2 mmol/L). Bacterial, fungal, and acid-fast bacilli cultures were negative. The findings of magnetic resonance imaging of the brain, with and without contrast, were unremarkable. A transesophageal echocardiogram showed normal ventricular size and function, with normal valvular morphological features. There was no evidence of vasculitis on a 4-vessel cerebral angiogram. The results of nerve conduction studies were normal. A biopsy specimen of the patient’s skin lesions revealed nonspecific dermatitis. Review of a right basal ganglia stereotactic biopsy specimen showed perivascular and transmural inflammatory infiltrates, without destruction of vessel walls or necrotic debris (Figure). As these findings were suggestive but not definitive of primary vasculitis, high-dose intravenous methylprednisolone sodium succinate therapy was initiated. The results of special stains later showed parenchymal infiltration by both T lymphocytes and microglia. These findings, along with the vascular changes, suggested encephalitis rather than vasculitis, and the methylprednisolone therapy was discontinued after 4 days.

During the hospitalization, the patient’s involuntary movements persisted despite increased doses of haloperidol (60 mg/d), clonazepam (3 mg/d), and valproic acid (1800 mg/d). Tetrabenazine therapy was started, and the dosage was titrated up to 200 mg/d without significant improvement of the ballistic-choreic movements. The patient’s cognition deteriorated over several days, and he was no longer oriented to time and place. Because of increasing agitation, he required sedation with lorazepam. A low-grade fever prompted additional chest radiography, and the radiogram showed new infiltrative changes in the right hilar region. A computed tomographic scan of the chest, abdomen, and pelvis demonstrated masses in both kidneys and the omentum, right adrenal gland, mediastinal lymph nodes, and lungs. Findings of a computed tomography-guided biopsy of the omental mass confirmed the suspected diagnosis of metastatic renal cell carcinoma. The patient’s cognition continued to deteriorate without new focal neurological symptoms, and his family elected not to resuscitate him in the occurrence of a cardiovascular event. He received a single dose of chemotherapy (vinblastine sulfate and interferon), later developed respiratory failure, and died 3 weeks after diagnosis and approximately 10 weeks after the onset of the involuntary movements. At autopsy, additional metastases were found in the left adrenal gland and pancreas. Cardiomegaly, pulmonary edema, and congestive hepatosplenomegaly were present. A section of the putamen showed numerous vessels with chronic inflammation, parenchymal astrocytosis, and slight microglial proliferation, but no neoplastic cells.

The paraneoplastic syndromes are remote, nonmetastatic manifestations of cancer that can affect multiple
areas of the nervous system. These syndromes can have several presentations, including encephalitis, cerebellar degeneration, motor neuron disease, impaired neuromuscular transmission, and motor, sensory, and autonomic neuropathy. Movement disorders have also been reported as a remote complication of malignancy. The first reported case of chorea presenting as a paraneoplastic syndrome involved a 45-year-old woman with a sensory neuropathy, nystagmus, and ataxia who subsequently developed choreic movements of the extremities over a 2-month period. Her movements evolved from choreoathetoid to dystonic over the course of her hospitalization. A computed tomographic scan of her chest revealed a left hilar mass that was diagnosed as oat cell carcinoma at autopsy approximately 4 months after initial presentation. Batchelor et al later described a 67-year-old woman with dysarthria and ataxia who developed progressive choreic movements of her face, neck, and extremities 13 months after the onset of neurological symptoms. Hodgkin disease was confirmed after a biopsy specimen of a splenic lymph node was obtained 2 months later, and the patient died approximately 17 months after the initial onset of symptoms. Cases of chorea developing months after the diagnosis of lung, colon, and ovarian tube cancer have been described. Chorea was also reported as the initial presentation of acute lymphoblastic leukemia in a child who had resolution of movements after the cancer was in remission.

The inability to pharmacologically control our patient’s involuntary movements suggested the possibility of a paraneoplastic syndrome, since previously cited cases have shown only partial or transient improvement with medication. His course was rapidly progressive, with severe chorea that was resistant to multiple medications, including a neuroleptic, a benzodiazepine, an anticonvulsant, an intravenous corticosteroid, and a dopamine-depleting agent. Our case was significant for chorea as the initial and only focal neurological feature of renal cell carcinoma. The search for a primary neoplasm was conducted because of the medication-resistant chorea and because an abnormality was detected on a chest x-ray film. While not specific, the inflammatory findings in the basal ganglia biopsy specimen were typical of paraneoplastic encephalitis. Several studies, which suggested only mild pulmonary edema, had been completed over the course of the patient’s protracted hospitalization. Although Chamouard et al published a case of chorea as a complication of polycythemia in a patient with renal adenocarcinoma, we believe that the case reported herein is the first case of chorea that preceded the diagnosis of renal cell carcinoma. While the list of possible causes of chorea is extensive, a paraneoplastic syndrome should be considered in the differential diagnosis of a patient who presents with this isolated movement disorder.

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REFERENCES