Cortical vein thrombosis in Wegener's granulomatosis

Case report

J. PARKER MICKLE, M.D., JAMES E. MCLENNAN, M.D., JE G. CHI, M.D., AND CRAIG W. LIDDEN, M.D.

Departments of Neurosurgery, Neuropathology, and Medicine, Children's Hospital, Boston, Massachusetts

A patient with Wegener's granulomatosis is reported in whom a life-threatening cortical vein thrombosis was identified as the process causing acute neurological deterioration. The literature dealing with the neurological and neuropathological manifestations in Wegener's granulomatosis is reviewed.

Key Words • cortical vein thrombosis • Wegener's granulomatosis

Wegener's granulomatosis is a chronic disease process consisting of a disseminated, necrotizing vasculitis with granulomatous lesions of the upper and lower respiratory tracts and glomerulonephritis. The disease was first described by Klinger in 1931, and defined as a clinical entity separate from the other vasculitides by Wegener in 1936.

Initially the nervous system was thought to be only rarely involved by this disease process. As more experience accrued, however, over half of all cases examined clinically were found to have central or peripheral nervous system lesions.

The mean survival time of patients with untreated Wegener's granulomatosis is 5 months. With the addition of cytotoxic agents to the therapeutic regimen, longer survival times have been reported. The present report summarizes a case of prolonged survival of a patient with Wegener's granulomatosis complicated by cortical vein thrombosis with cerebral infarction which necessitated emergency arteriography and craniotomy.

Case Report

This 15-year-old girl was admitted on December 6, 1974, after persistent vomiting of 2 weeks' duration, frontal headache, and inability to walk or talk for 12 hours.

Past History. At 12 years of age she was first evaluated for weight loss and epistaxis. A chest film revealed a cavitating lesion in her right lung. A right lower lobectomy was performed and showed multifocal granulomas with necrotizing vasculitis compatible with a diagnosis of Wegener's granulomatosis. She was discharged on prednisone and isoniazid but was readmitted 2 months later with abdominal pain. She was found to have a decreased creatinine clearance and microscopic hematuria. A renal biopsy revealed focal necrotizing glomerulitis with crescent
Cortical vein thrombosis in Wegener's granulomatosis

Formation. A course of Imuran (azathioprine) was begun and her renal function improved. At 13 years of age she developed nasal discharge secondary to a chronic *Staphylococcus aureus* maxillary sinusitis resulting in a saddle-nose deformity. The sinus was drained surgically.

Except for a brief episode of aseptic necrosis of the right hip, she did well on a regimen of Imuran, prednisone, dicloxacillin, and nasal decongestants.

For 2 weeks before the present admission the patient complained of intermittent, severe bifrontal headache with marked purulent nasal discharge. On the morning of admission she was found banging her head on the floor saying, “I’m going crazy.” One hour later, although awake, she was unable to stand or talk and was brought to the hospital.

**Examination.** The patient was somnolent, and had multiple bruises over her arms and chest. Her pulse was 64 and blood pressure 140/90. There was moderate neck stiffness. She demonstrated a global aphasia with a right hemiparesis, blurred optic discs, and a flame-shaped hemorrhage in the left optic fundus. Electrolytes, blood urea nitrogen, platelets, partial thromboplastin time, and prothrombin time were normal. An electroencephalogram showed left posterior slowing. Within 12 hours of her admission she became increasingly somnolent although large doses of dexamethasone had been given. A left internal carotid angiogram revealed a large left frontal mass with nonfilling of the anterior 8 cm of the sagittal sinus (Fig. 1).

**Operation.** A left frontal craniotomy was performed. The frontal cortex was swollen and black with several thrombosed superficial cortical veins. The arachnoid was opened, and dark necrotic brain exuded. No pus or blood could be aspirated from the mass. Necrotic brain tissue was removed to provide an adequate decompression and the bone flap was loosely replaced.

**Postoperative Course.** Two days following operation the patient began talking and the right hemiparesis was much improved. Two weeks postoperatively she was normal neurologically except for some flatness in her affect detected only by her family. The dexamethasone dosage was tapered and stopped, and she was discharged on Imuran and nasal decongestants. Four weeks following surgery she returned with severe headache and was found to have early, bilateral papilledema, a mild right hemiparesis, and an expressive aphasia. These complaints and findings disappeared 12 hours after dexamethasone was started. Again the dosage was tapered and she was discharged on Imuran without further relapse. One year postoperatively she remains without neurological deficit.

**Pathological Examination.** The surgical specimen revealed acute, necrotizing thrombophlebitis with early necrosis of the underlying cortex (Fig. 2). The arterioles were only minimally involved by the acute inflammatory reaction. No evidence of granuloma formation was identified, no organisms were seen on Gram stain, and there was no blood clot. Cultures of the specimen were sterile.
Discussion

Wegener's granulomatosis has two forms. The focal or restricted type involves the upper and lower respiratory tracts, sparing most other organ systems. The generalized form is marked by focal glomerulitis or fibrinoid glomerulonephritis. All organ systems are susceptible to the granulomatous and vasculitic lesions in the generalized variety.

The disease affects males more frequently than females in a ratio of 2 to 1. The peak incidence is in the fourth decade, but cases occurring in childhood have been reported. There is good evidence to suggest an autoimmune reaction as the basic mechanism in Wegener's granulomatosis.

Drachman reported clinical nervous system involvement in 56 of 104 cases found in the literature. Wolff, et al., reported an incidence of 24%. The nervous system lesions are of three types: 1) destruction of nervous elements by direct invasion of the granulomatous process from contiguous nasal and paranasal sinuses; 2) granulomatous lesions arising within the central nervous system remote from the sinuses; and 3) complications of the diffuse vasculitis. The last is the most common cause of neurological complaints. It is felt that involvement of the vasa nervorum is responsible for most cases of peripheral neuropathy which is commonly a mononeuropathy multiplex. The intracranial vessels may be affected by the vasculitis resulting in intracerebral and subarachnoid hemorrhage. Fahey, et al., reported a case in which thrombosis of the lateral sinus was found at autopsy. Small areas of hemorrhage and necrosis are commonly found on careful neuropathological examination.

The present case represents several interesting clinical and pathological aspects. Our patient presented with an acute exacerbation...
Cortical vein thrombosis in Wegener's granulomatosis

tion of her disease primarily involving her central nervous system. It is important that this crisis occurred while she was being treated chronically with Imuran and prednisone and doing well without active renal involvement. To our knowledge, necrotizing cerebral thrombophlebitis leading to local infarction and acute mass lesion in Wegener's granulomatosis has not been previously reported. The recommended treatment for patients with Wegener's granulomatosis is the persistent use of cytotoxic agents until the patient has been asymptomatic for 1 year without evidence of active renal disease. At this point dosage of the immunosuppressive agent is tapered. Steroids are added to the therapeutic regimen during acute exacerbation but are rapidly tapered. Dramatic improvement in renal function has been obtained with heparin in patients with chronic renal failure in Wegener's granulomatosis. This was an intriguing consideration in our patient since the lesion was well defined as thrombophlebitis with a poor prognosis. This aspect of therapy remains theoretical as far as the central nervous system is concerned.

The vasculitis of Wegener's granulomatosis tends to be disseminated and usually involves both small arteries and veins. The lesion in our patient was clearly nonseptic thrombophlebitis and sagittal sinus thrombosis resulting in a venous infarct in the left frontal lobe. One case reported by Fahey, et al. (their Case V), demonstrated a lateral sinus thrombosis at postmortem examination. The small arteries in the present case appeared not to be involved. The two forms of therapy used to treat the acute neurological deterioration of the patient were high dose dexamethasone and surgical decompression. It is impossible to say what would have been the result if only one of these modes of therapy had been used. The recurrent neurological signs and symptoms of our patient 2 weeks after discharge completely abated with a course of dexamethasone. It appears valid then to treat this life-threatening central nervous system complication of Wegener's granulomatosis with high dose dexamethasone and Imuran with the option to surgically decompress the brain if needed.

In summary, we have presented a case of cortical vein thrombosis in a patient with Wegener's granulomatosis resulting in a cortical infarct that required surgical intervention for survival. High dose dexamethasone may well have had a limiting effect on the basic pathological process. We anticipate that with the improved survival obtained using cytotoxic agents, more of these patients will be seen and followed for long periods by their physicians. Perhaps, as in our patient, isolated complications threatening to life and yet reversible will become a major problem in this group of patients.

References


Address reprint requests to: J. Parker Mickle, M.D., Box 147, Children's Hospital Medical Center, 300 Longwood Avenue, Boston, Massachusetts 02115.