

Cerebral vasculitis in Wegener's granulomatosis

Fred V. Lucas, M.D.
Sanford P. Benjamin, M.D.
Marta C. Steinberg, M.D.

Department of Pathology

Wegener's granulomatosis is a necrotizing granulomatous vasculitis of the respiratory tract associated with a focal glomerulonephritis.¹⁻⁴ Disseminated necrotizing angiitis involving large, medium, and small-sized vessels also comprises a part of the clinical and pathologic spectra. Although the specific pathologic features are well described by Godman and Churg,¹ several recent reviews have clarified the renal² and pulmonary⁵ histologic findings and discussed improved aspects of treatment.^{3,4} There has been less emphasis on the neuropathologic manifestations of Wegener's granulomatosis. The frequency of nervous system involvement, based upon clinical and pathologic criteria, varies from 22%⁴ to 54%.⁶ The purpose of this report is to emphasize neuropathologic involvement in a case of fulminant Wegener's granulomatosis at autopsy.

Case report

A 53-year-old man was transferred to the Cleveland Clinic Hospital with diffuse abdominal pain, fever, and pedal edema of 3 weeks' duration. Proximal muscle weakness and bilateral pedal edema were found on physical examination. Blood pressure was 110/70 mm Hg. The patient was alert and oriented. Roentgenographic examination demonstrated two

discrete nodular shadows in the upper right lung field. Urinalysis revealed proteinuria, microhematuria, and numerous granular casts. Hemogram included hemoglobin, 9.3 g/dl; hematocrit, 29.5%; and white blood cell count, 14,800/ μ l, with a normal differential count. Results of laboratory studies revealed the following values: blood urea nitrogen (BUN), 69 mg/dl and serum creatinine, 5.5 mg/dl. Studies from the referring hospital had included electrocardiogram, electroencephalogram, brain scan, skull films, and complete gastrointestinal barium x-ray series. All were normal. During the week following admission, right epididymo-orchitis, increasing weakness, lethargy, and progressive renal failure (serum creatinine 10.2 mg/dl) developed. A renal biopsy specimen on the 6th hospital day was interpreted as an acute cortical infarct compatible with arterial occlusion. Lethargy persisted, and on the 8th hospital

day, the patient suddenly became comatose, areflexic, and apneic. Mechanical ventilatory therapy was initiated. An atraumatic lumbar puncture revealed xanthochromic fluid with 24,000 red blood cells. Dexamethasone (Decadron) therapy, 24 mg four times a day, was instituted. Complete electrocerebral silence was noted on the 10th hospital day. The patient died on the 11th hospital day.

Postmortem examination. Necropsy examination revealed multiple organ involvement with necrotizing vasculitis and granulomatous inflammation of lungs (*Fig. 1*), kidneys, spleen, and prostate; necrotizing vasculitis without granulomatous inflammatory component was noted in the coronary arteries, liver, testes, right epididymis and spermatic cord, periadrenal fat, and skeletal muscle. Multifocal thromboses of small, medium, and large-sized vessels were associated with recent massive infarction of both kidneys;

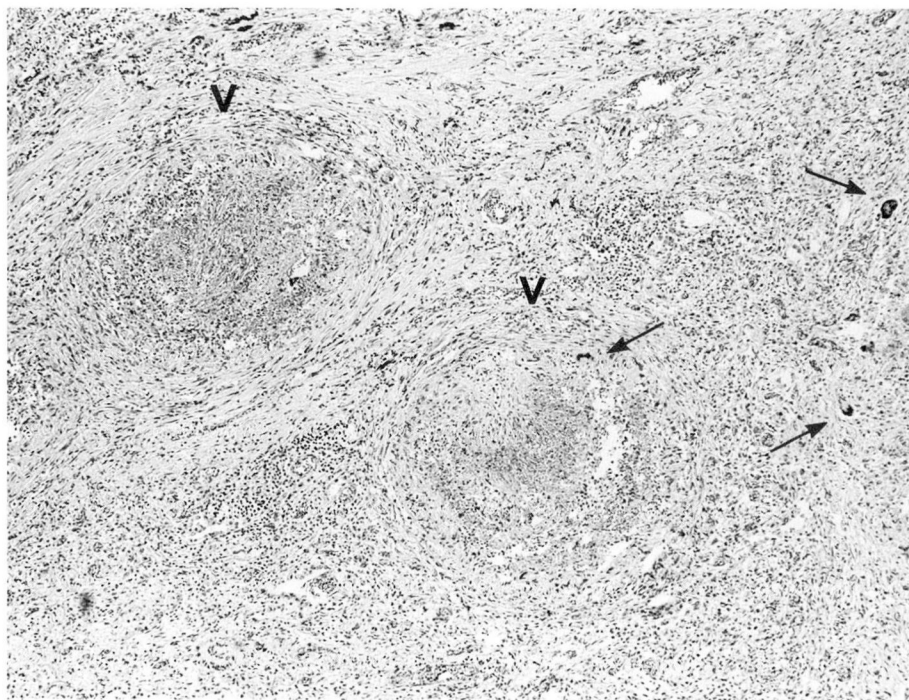


Fig. 1. Photomicrograph of lung with necrotizing granulomatous vasculitis of two vessels (V) and perivascular pulmonary parenchyma. Arrows indicate multinucleate giant cells within vessel wall and in adjacent lung tissue (hematoxylin and eosin stain, $\times 40$).

infarctions of myocardium, right testis, and right epididymis; and a focal necrotizing glomerulonephritis in the residual viable kidney parenchyma.

Neuropathologic examination. The brain was edematous, weighing 1,460 g. Both cerebellar tonsils were herniated; there was no evidence of subfascial or uncus herniation. The major cerebral and cerebellar arteries showed minimal atherosclerosis, and no aneurysmal dilations were identified. Serial coronal sections through the cerebral hemispheres revealed an intracerebral hemorrhage in the left caudate nucleus with extension into the lateral ventricles (*Fig. 2*). In the adjacent portion of the left caudate, a small thrombosed vessel was identified. Serial 1 mm sections revealed continuity between this vessel and the intracerebral hemorrhage. The ventricular system was completely filled and distended by hemorrhage which extended through the for-

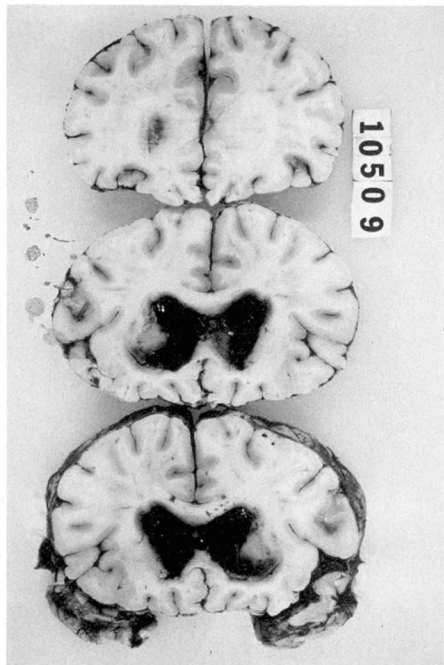


Fig. 2. Photograph of cerebral hemispheres with intracerebral and intraventricular hemorrhage. Note focal accumulations of subarachnoid hemorrhage.

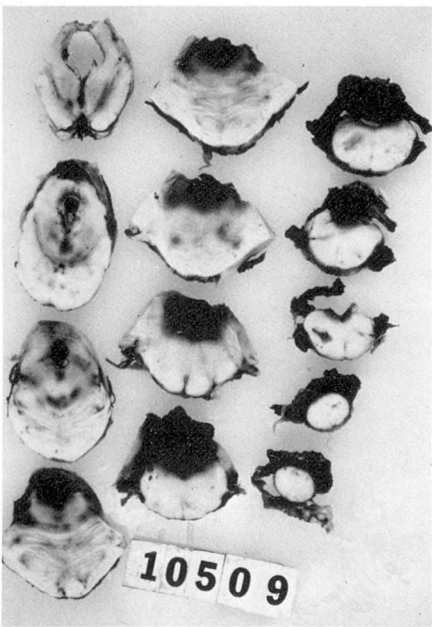


Fig. 3. Photograph of brainstem sections with intraventricular hemorrhage extending into the subarachnoid space through the foramina of Luschka. Multiple secondary pontine hemorrhages are evident.

amina of Luschka and Magendie. Moderate subarachnoid hemorrhage was noted over the ventral midbrain, pons, and medulla. Secondary midbrain and pontine hemorrhages were present in serial cross sections of the brainstem (*Fig. 3*). Focal subarachnoid hemorrhage was present over the ventral upper thoracic spinal cord segments.

On hematoxylin and eosin microscopic sections, necrotizing vasculitis without granulomatous inflammation was noted in the left caudate nucleus (*Fig. 4*), the pituitary pars intermedia (*Fig. 5*), and the choroid plexus (*Fig. 6*) near both hippocampal gyri (*Figs. 4-7*). Several sections through the involved vessel of the left caudate nucleus demonstrated direct continuity with the adjacent intracerebral hemorrhage. The hemorrhage involved the caudate, putamen, and anterior limb of the internal capsule, with extension into the lateral ventricle (*Fig. 7*). A lack of glial reaction to the hemorrhage indi-

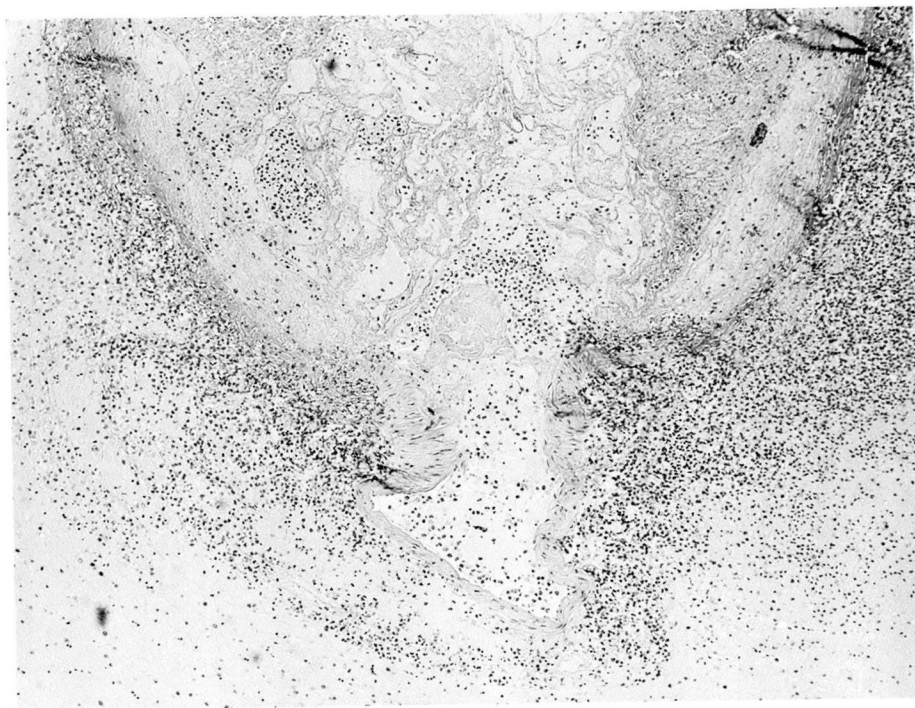


Fig. 4. Photomicrograph of thrombosed vessel from the left caudate nucleus with aneurysmal dilatation and partial destruction of vascular wall due to inflammatory process (hematoxylin and eosin stain, $\times 64$).

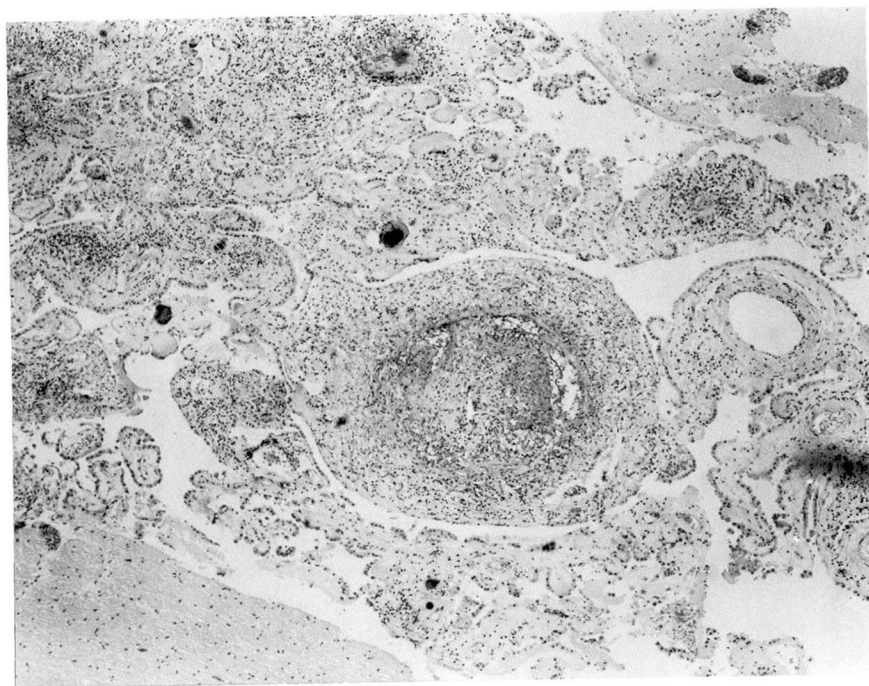


Fig. 5. Photomicrograph of necrotizing vasculitis involving the pars intermedia of pituitary gland (arrow) (hematoxylin and eosin stain, $\times 40$).

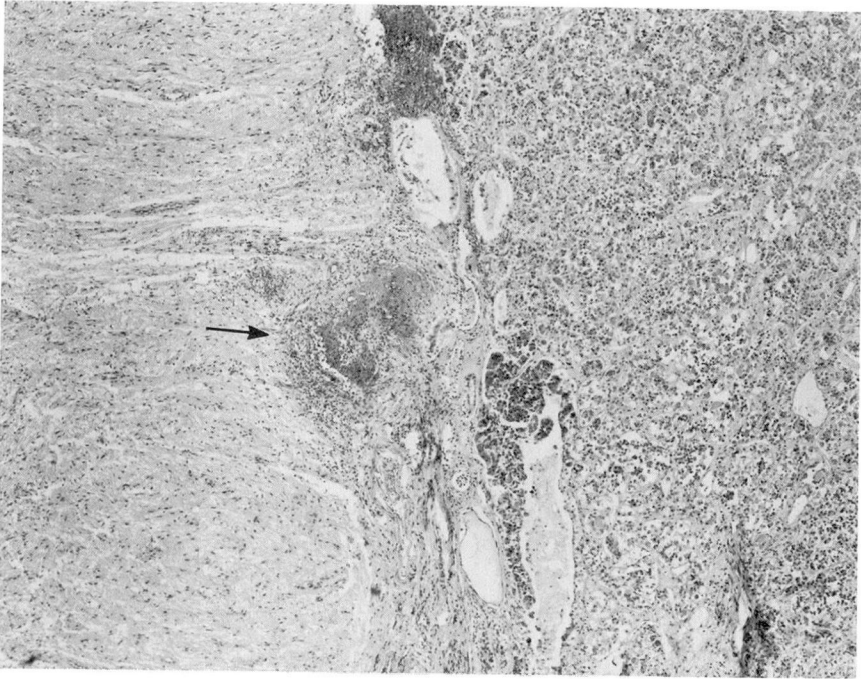


Fig. 6. Photomicrograph of necrotizing vasculitis involving right ventricular choroid plexus (hematoxylin and eosin stain, $\times 40$).

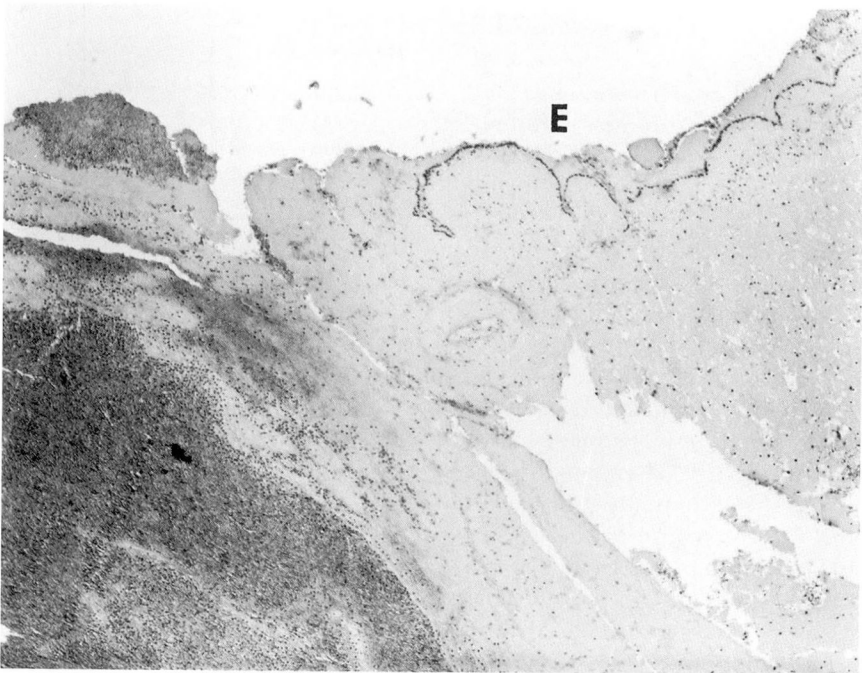


Fig. 7. Photomicrograph of extension of intracerebral hemorrhage (lower left) into the left lateral ventricular system. The ependymal ventricular lining surface is denoted by "E" (hematoxylin and eosin stain, $\times 40$).

cated the acute nature of the process. Cerebellar tonsillar necrosis and secondary brainstem hemorrhages confirmed histologically extended to the level of the pons; these changes were compatible with herniation. The cerebral cortices and right basal ganglia showed diffuse mild neuronal "dropout" without reactive glial changes. Loss of neurons was most severe in the mammillary bodies, but again no reactive astrocytosis was noted.

Discussion

The findings of necrotizing granulomatous inflammation and vasculitis in the lungs and kidneys in this patient, accompanied by a focally necrotizing glomerular lesion and widespread necrotizing vasculitis, are characteristic of Wegener's granulomatosis.¹⁻⁴ The principal cause of death was an intracerebral hemorrhage which extended into the ventricular system. Of particular interest was coexistent necrotizing arteritis with aneurysmal dilatation at the site of intracerebral hemorrhage. Further examination of this caudate lesion revealed direct communication between the necrotic vessel and the hemorrhage.

Before the advent of cytotoxic therapy, renal and respiratory failures were the most common causes of death in patients with Wegener's granulomatosis.⁷ However, sporadic reports of death caused by central nervous system involvement have been published.⁷⁻¹⁰ Drachman⁶ has described the extent and nature of nervous system symptomatology and pathologic findings in a review of 104 patients with Wegener's granulomatosis. Cases were grouped according to three patterns: (1) contiguous spread of extravascular granulomatous inflammation from the facial sinuses, orbit, and auditory canal; (2)

isolated necrotizing granulomas in skull, meninges, or brain; (3) necrotizing vasculitis of the cerebral arterial supply and peripheral nerves. Cerebral vasculitis was demonstrated histologically in only five of these cases. In a previously published series at the Cleveland Clinic, no morphologic evidence of nervous system involvement was described in four patients at autopsy, although clinical ocular, and nonspecific neurologic abnormalities were recorded in all four.^{11, 12}

We conclude that necrotizing cerebral vasculitis in Wegener's granulomatosis is an unusual pathologic finding that occasionally may be responsible for sudden death. Cerebral vasculitis represents part of the spectrum of the Wegener complex and may be heralded by clinical signs of changing levels of consciousness.

References

1. Godman GC, Churg J: Wegener's granulomatosis; pathology and review of the literature. *Arch Pathol* **58**: 533-553, 1954.
2. Horn RG, Fauci AS, Rosenthal AS, et al: Renal biopsy pathology in Wegener's granulomatosis. *Am J Pathol* **74**: 423-439, 1974.
3. Wolff SM, Fauci AS, Horn RG, et al: Wegener's granulomatosis. *Ann Intern Med* **81**: 513-525, 1974.
4. Fauci AS, Wolff SM: Wegener's granulomatosis; studies in eighteen patients and a review of the literature. *Medicine* **52**: 535-561, 1973.
5. Liebow AA: Pulmonary angiitis and granulomatosis. *Am Rev Resp Dis* **108**: 1-18, 1973.
6. Drachman DA: Neurological complications of Wegener's granulomatosis. *Arch Neurol* **8**: 145-155, 1963.
7. Fred HL, Lynch EC, Greenberg SD, et al: A patient with Wegener's granulomatosis exhibiting unusual clinical and morphologic features. *Am J Med* **37**: 311-319, 1964.
8. MacFadyen DJ: Wegener's granulomatosis

with discrete lung lesions and peripheral neuritis. *Can Med Assoc J* **83**: 760-764, 1960.

9. Kinney VR, Olsen AM, Hepper NGG, et al: Wegener's granulomatosis; report of two cases and brief review. *Arch Intern Med* **108**: 269-278, 1961.

10. Fahey J, Leonard E, Churg J, et al: Wegener's granulomatosis. *Am J Med* **17**: 168-

179, 1954.

11. O'Duffy JD, Scherbel AL, Reidbord HE, et al: Necrotizing angitis. I. A clinical review of twenty-seven autopsied cases. *Cleve Clin Q* **32**: 87-98, 1965.

12. Reidbord HE, McCormack LJ, O'Duffy JD: Necrotizing angitis. II. Findings at autopsy in twenty-seven cases. *Cleve Clin Q* **32**: 191-204, 1965.