The Turkish Journal of Pediatrics 33:49 - 54, 1991

ACUTE HEMORRHAGIC LEUKOENCEPHALITIS*

*Safiye Göğüş MD***, *Kalbiye Yalaz MD****, *Nurten Koçak MD*****

SUMMARY: Göğüş S, Yalaz K, Koçak N. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Acute hemorrhagic leukoencephalitis. Turk J Pediatr 33: 51-56, 1991.

The clinical and pathological findings of a ten-year-old girl, diagnosed as having acute hemorrhagic leukoencephalitis at postmortem examination, are presented.

The diagnosis of this disease is usually established at autopsy. In this paper, emphasis is given to the diagnosis of acute hemorrhagic leukoencephalitis, and the possibility of its clinical recognition is discussed. *Key words: acute necrotizing hemorrhagic leukoencephalitis, acute necrotizing hemorrhagic leukoencephalopathy.*

Acute hemorrhagic leukoencephalitis (AHL) is a rare hyperacute, inflammatory and demyelinating disease of the white matter with an abrupt onset and catastrophic course[1-6]. These characteristics make diagnosis difficult during life but diagnosis and early institution of therapy may be life-saving. Computed tomography (CT) contributes to the rapid diagnosis of AHL, nevertheless cerebral biopsy may be the only way of clarifying the diagnosis[3,5-11].

In the past twenty years, we have had only one autopsy-proven case of AHL at the Hacettepe University Children's Hospital. The clinical and pathological findings of this case are described below.

Case Report

A ten-year-old girl was admitted to the Hacettepe University Children's Hospital because of paralysis on the right side and loss of consciousness, which occurred on the way to the hospital. Past history revealed that five days prior to admission the patient had developed a nasal discharge and intermittent fever but, otherwise, she had been in good health. Twenty-four hours prior to admission, the child vomited twice and progressive weakness of the right arm and leg were observed during the next 12 hours.

* From the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.

** Professor of Pediatrics and Pediatric Pathologist, Hacettepe University Faculty of Medicine.

*** Professor of Pediatrics and Pediatric Neurologist, Hacettepe University Faculty of Medicine.

**** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

Physical examination revealed a comatose girl. The temperature was 36 C, pulse 86/min, respiration rate 28/min and blood pressure 120/70 mmHg. She responded to painful stimuli by moving her left extremities. Her pupils were of equal size, slightly dilated and reacted poorly to light. The margin of the left optic disc was blurred and the veins were engorged bilaterally. There was right central facial paralysis. Deep tendon and abdominal reflexes were absent on the right side but Babinski's sign was noted.

Laboratory findings revealed a white blood cell count of 7000/mm^3 with 79% neutrophils and 21% lymphocytes. Hemoglobin, erythrocyte sedimentation rate, serum glucose, nonprotein nitrogen and electrolytes were all within the normal range. There was 1+ protein in the urine.

An EEG on admission showed irregular background activity on the left side and epileptic discharges initiating from the left parieto-occipital region. CT findings suggested an ischemic process centrally located in the left hemisphere. Skull X-rays were normal.

Dexamethasone and diphenylhydantoin were given for a prospective diagnosis of an acute cerebrovascular accident or an intracranial lesion. After the first 18 hours, the patient was able to respond to verbal stimuli by opening her eyes. Alternating spasticity developed in her arms and legs. Her vital signs deteriorated and she died 73 hours after admission. The cerebrospinal fluid obtained after death contained 60 red blood cells/mm^3, sugar 90 mg/dl and protein 540 mg/dl. Smears and cultures were negative.

Post-mortem examination was restricted to the head. The brain was swollen and weighed 1400 g (expected weight, 1226 g). There was bilateral cerebellar herniation. Coronal sections showed numerous petechial hemorrhages and reddish-brown discoloration in the white matter of the cerebrum. There was a large hemorrhagic necrotic area near the left lateral ventricle which mainly occupied the internal capsule but also spread into surrounding tissue (Fig. 1). Brain involvement was asymmetrical, with strong predilection for the white matter. On microscopic examination there was damage to many vessel walls. Perivascular necrosis, edema, hemorrhages, focal demyelination and intense neutrophilic exudation were noted around the vessels which were spreading throughout the tissue (Fig. 2, 3, 4).

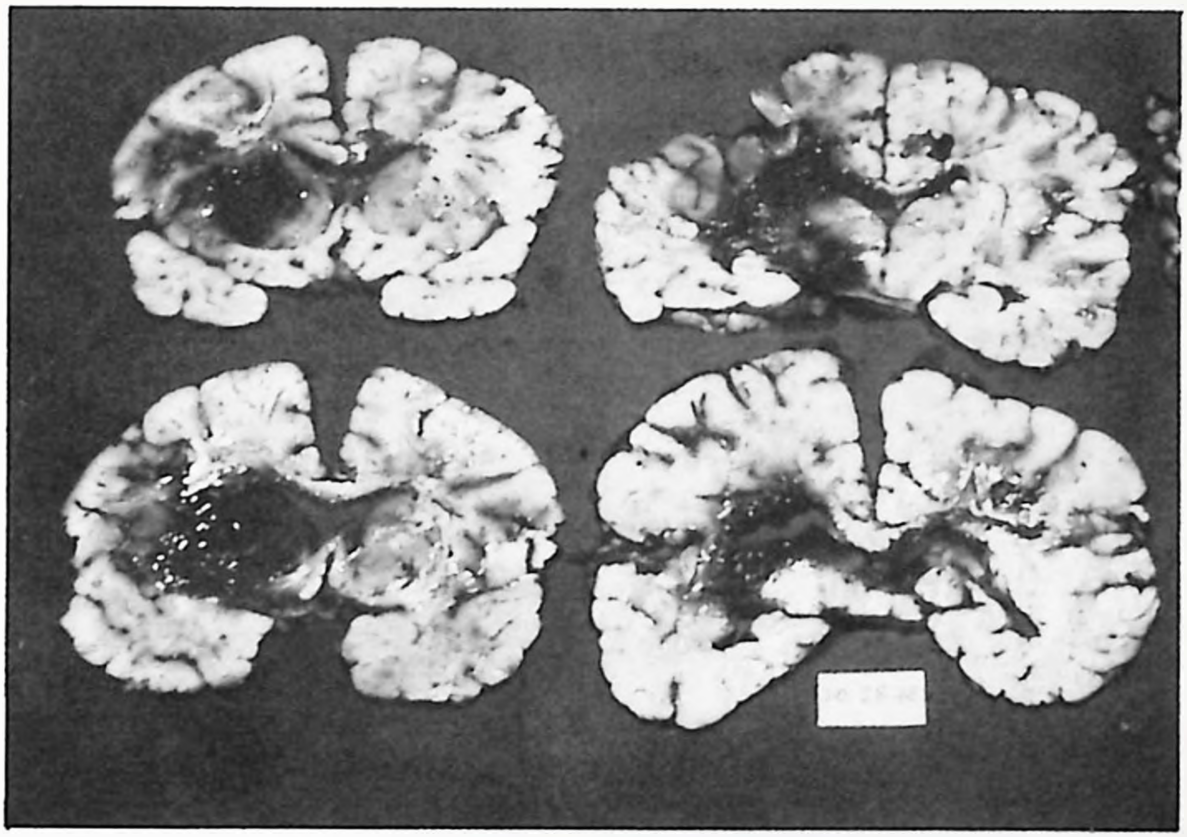

Fig. 1: Macroscopic appearance of the lesions.

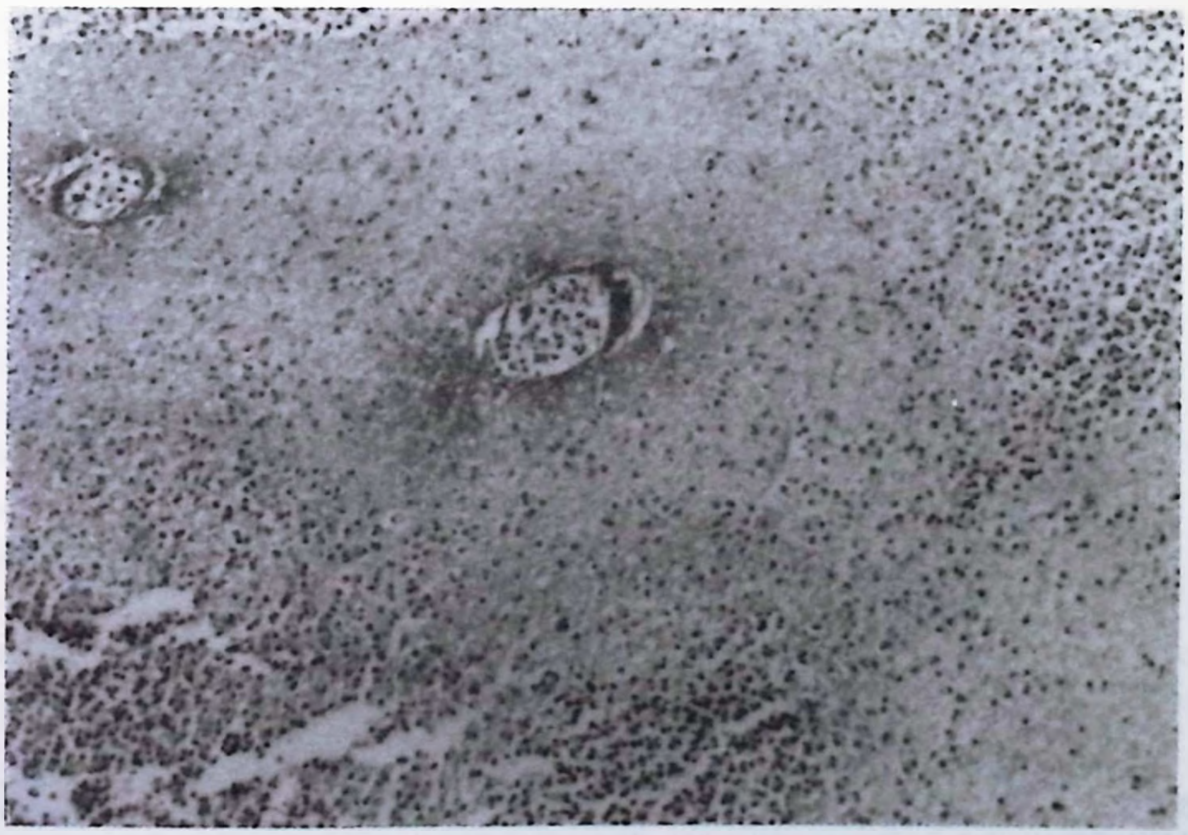

Fig. 2: Necrosis in the vessel walls and inflammatory cells in the tissue PAS × 115.

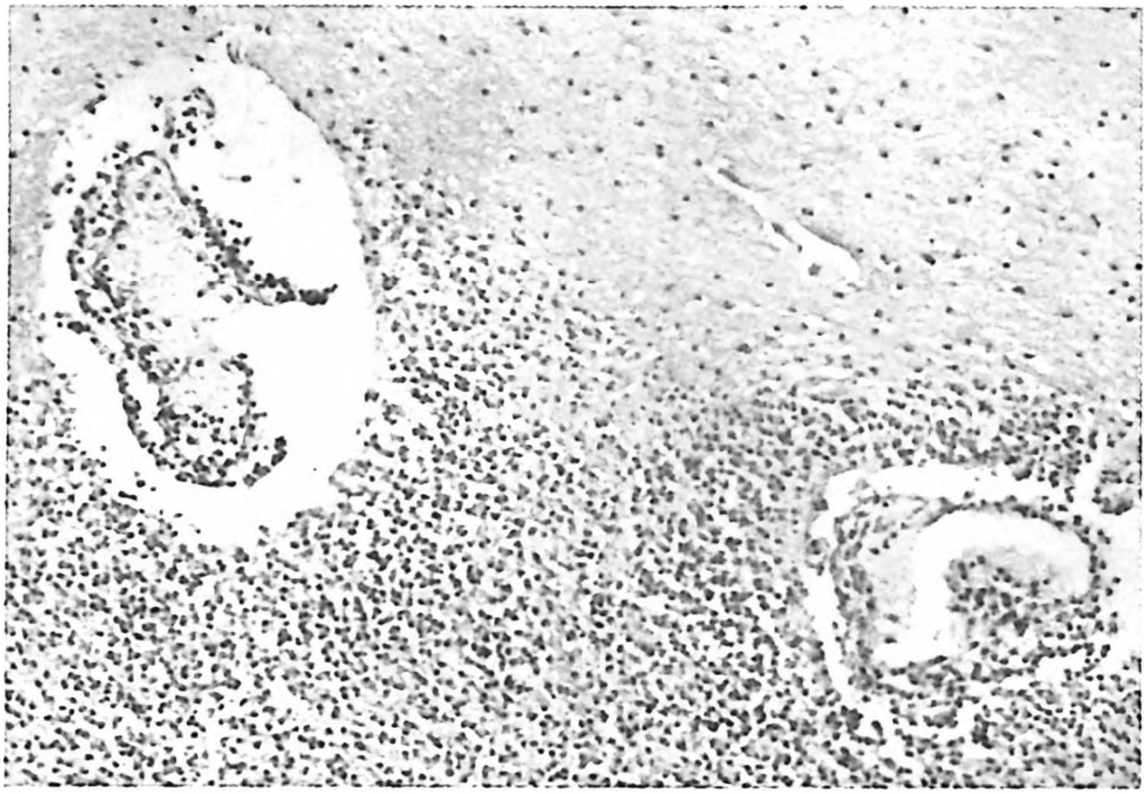

Fig. 3: Infiltration of inflammatory cells, mainly neutrophils and hemorrhage in the tissue H+E × 230.

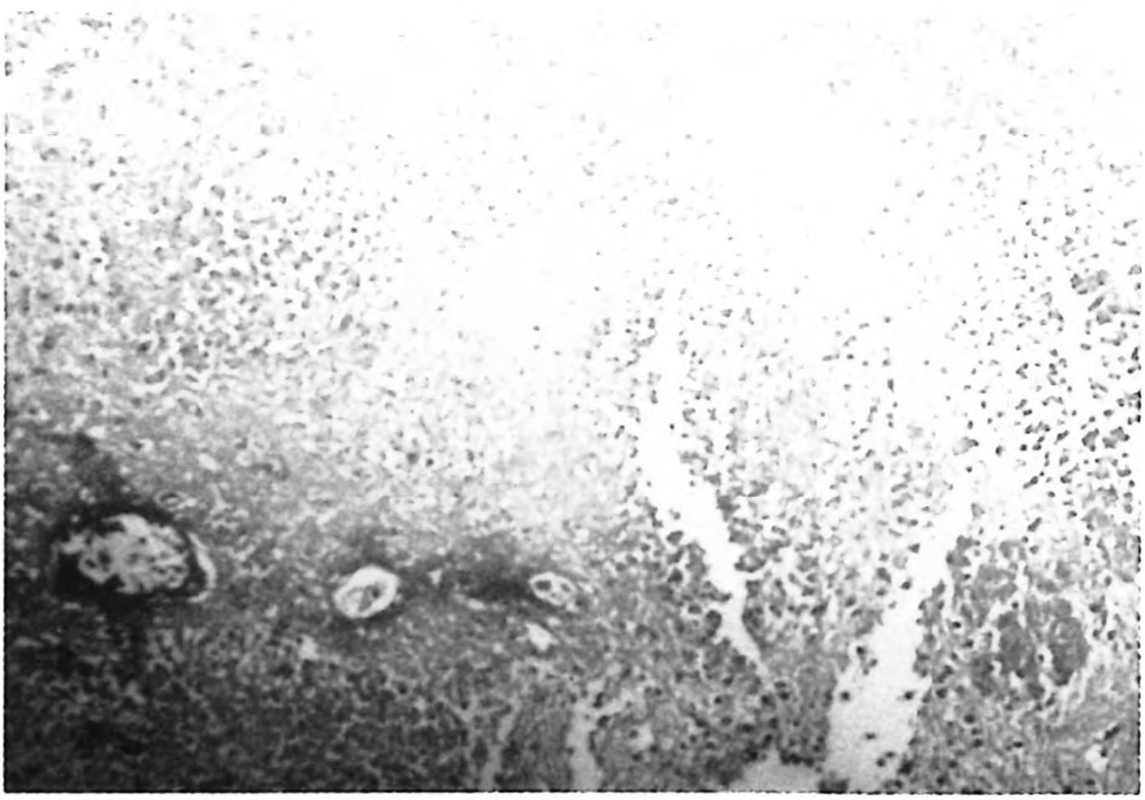

Fig. 4: Extravasation of neutrophils from the affected vessels spreading throughout the tissue. H+E × 115.

Discussion

Acute necrotizing hemorrhagic leukoencephalitis is a rare disease which is usually diagnosed at autopsy and rarely suspected during life[1-6]. However, there have been a few reported cases with recovery, in which diagnosis was made by cerebral biopsy[3]. Cases of relapse have also been reported[3,11].

This disease usually affects young males but may also be seen in childhood. An upper respiratory infection is the most common antecedent illness. Presenting neurologic abnormalities are hemiplegia, confusion, aphasia, and seizures progressing to coma. Etiologic speculation has included infections, toxic substances and an immunopathologic mechanism[4,5]. Laboratory findings usually include urine, peripheral blood and cerebrospinal fluid abnormalities. In reports in which the results of urinalysis have been given, proteinuria has been noted. Leukocytosis appears early and is predominantly neutrophilic. Most cerebrospinal fluid specimens have a high white blood cell count composed mainly of neutrophils. Red blood cells may be present and protein is usually elevated[4,5].

Our patient had a previous undetermined illness five days prior to admission and had many of the usual clinical and laboratory findings for the diagnosis of AHL.

The pathology of AHL is striking[1-8,10,11]. There is necrotizing angiitis of the white matter. The vessel walls are necrotic with fibrinous exudate into the walls and surrounding tissue. Early in the course of the disease, there is extravasation of neutrophils found in the vessel walls and neighbouring parenchymal tissue, which is later replaced by lymphocytes. Diapedesis of red cells occurs especially around the affected vessels, forming ball and ring hemorrhages. These often become large and confluent. Demyelination within the cellular cuffs is also detected. Edema involves areas around the affected vessels which becomes diffuse. Meningeal involvement can also be seen.

Our patient had typical histopathological findings of AHL. The lesion on the left internal capsule was very severe and spread towards the basal ganglia and ventricle. Although the cortical gray matter is usually spared, basal ganglia involvement and brainstem, cerebellum and cord lesions can be detected[5].

Confirmation of diagnosis by cerebral biopsy is academically important in the evaluation of treatment, and it should be performed early in the course of the illness.

Recently, many authors have accepted the use of CT as an aid in diagnosing AHL. They claim that it would be possible to make the diagnosis of AHL during life-time on the basis of characteristic clinical and CT findings[7-10].

Corticosteroids are recommended for treatment[4,5] therapeutically of this condition. However surgical decompression has also been reported to be beneficial[3,11].

REFERENCES

1. Hurst EW. Acute haemorrhagic leucoencephalitis: a previously undefined entity. *Med J Aust* 2:1, 1941.
2. Crawford T. Acute Haemorrhagic Leuco-encephalitis. *J Clin Pathol* 7:1, 1954.
3. Cox WS, Luse SA. Acute hemorrhagic leukoencephalitis: a clinical and electron-microscopic report of 2 patients treated with surgical decompression. *J Neurosurg* 20:584, 1963.
4. Behan PD, Moore MJ, Lamarche JB. Acute necrotizing hemorrhagic encephalopathy. *Postgrad Med* 54:154, 1973.
5. Byers RK. Acute hemorrhagic leukoencephalitis: report of three cases and review of the literature. *Pediatrics* 56:727, 1975.
6. Gosztonyi G, Cervós-Navarro J. Immunohistochemical and electron microscopic techniques in the diagnosis of viral encephalitides. *Pathol Res Pract* 183:223, 1988.
7. Rothstein TL, Shaw CM. Computerized tomography as a diagnostic aid in acute hemorrhagic leukoencephalitis. *Ann Neurol* 13:331, 1983.
8. Valentine AR, Kendall BE, Harding BN. Computed tomography in acute haemorrhagic leukoencephalitis. *Neuroradiology* 22:215, 1982.
9. Reich H. Lin SR and Goldblatt D. Computerized tomography in acute hemorrhagic leukoencephalopathy: a case report. *Neurology (Minneap)* 29:255, 1979.
10. Watson RT, Ballinger WE Jr, Quisling RG. Acute hemorrhagic leukoencephalitis: diagnosis by computed tomography [letter]. *Ann Neurol* 15:611, 1984.
11. Lamarche JB, Behan PO, Segarra JM, Feldman RG. Recurrent acute necrotizing hemorrhagic leukoencephalopathy. *Acta Neuropathol (Berl)* 22:79, 1972.