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E E Duda, P R Huttenlocher and N J Patronas

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CT of Subacute Sclerosing Panencephalitis

Eugene E. Duda[1]
Peter R. Huttenlocher[2]
Nicholas J. Patronas[1]

Subacute sclerosing panencephalitis is a progressive, frequently fatal slow virus infection of the brain attacking children and young adults and caused by measles virus. Computed tomography (CT) of the brain in 15 patients with this disease was normal in seven and abnormal in eight. CT demonstrated varying degrees of cortical atrophy associated with focal and multifocal low density lesions of the white matter. Two cases demonstrated low density lesions of the caudate nuclei. The CT lesions were seen in chronic cases and reflect the gliosis and atrophy that occur in this disease. Differential diagnoses include other viral infections and demyelinating and dysmyelinating diseases. Diagnostic laboratory evaluation includes serum and cerebrospinal fluid titers for measles antibodies, cerebrospinal fluid protein electrophoresis, electroencephalography, and cranial CT.

Subacute sclerosing panencephalitis (SSPE) is a progressive, frequently fatal disease of the brain attacking children and young adults. It has been known by other names including Dawson's inclusion body encephalitis [1, 2], van Bogaert's subacute sclerosing leukoencephalitis [3], and the panencephalitis of Petté and Döring [4]. Subsequent research clearly established that SSPE is a slow virus infection of the brain caused by measles virus [5].

We discuss computed tomographic (CT) characteristics in 15 patients proven to have this disease.

Materials and Methods

The seven male and eight female patients were 11–21 years old. All patients were proven to have subacute sclerosing panencephalitis by the accepted criteria [6, 7] of elevated titers of measles antibody in both the serum and cerebral spinal fluid and an electroencephalogram characterized by synchronous, periodic, high voltage complexes. We reviewed the patients' charts and assigned a clinical stage of disease according to the method of Jabbour et al. [8], classifying the patient into one of four clinical stages. Changes in mental abilities and behavior characterize stage 1 patients. Myoclonic seizures, which often occur at regular intervals of 5–10 sec, and motor signs herald stage 2, when the patient usually comes to the attention of a physician. Ataxia and choreiform movements are seen. One-half of the patients have ocular signs including cortical blindness, optic atrophy, and chorioretinitis [9]. Coma, opisthotonous, decerebrate rigidity, impaired autonomic nervous function, and deranged temperature homeostasis are among the alarming signs of stage 3. Stage 4 patients display loss of cortical function. Death soon occurs and is usually caused by vasomotor collapse or infection.

We reviewed cranial CT scans of all 15 patients with proven SSPE. All but two (cases 9 and 12) had repeat cranial CT with intravenous iodine infusion of a solution of meglumine diatrizoate (52%) and sodium diatrizoate (8%) administered over 4 min at a dose of 2 ml/kg body weight. The ventricular diameter was measured at the level of the caudate nucleus

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[1] Department of Radiology, University of Chicago, 950 E. 59th St., Chicago, IL 60637. Address reprint requests to E. E. Duda.

[2] Departments of Pediatrics and Neurology, University of Chicago, Chicago, IL 60637.

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TABLE 1: **Clinical Data and Cranial CT Findings in Subacute Sclerosing Panencephalitis**

Case No.	Clinical Stage [8]	Disease Duration (Months)	CT Data			
			VCR	Sulci Visible	Subarachnoid Space	Lesion Description
1	2	5	0.08	No	Normal	No lesions
2	3	3	0.09	No	Normal	No lesions
3	2	6	0.10	No	Normal	No lesions
4	2	6	0.11	No	Normal	No lesions
5	2	6	0.11	No	Normal	No lesions
6	2	60	0.12	No	Normal	No lesions
7	2	15	0.13	No	Normal	No lesions
8	2	8	0.13	Yes	Enlarged	Diminished density of left basal ganglia
9	2	24	0.13	Yes	Normal	Diminished density of caudate nuclei
10	2	36	0.13	Yes	Enlarged	Focal atrophy of frontal lobes
11	1	86	0.19	Yes	Enlarged	Diffuse cerebral cortical atrophy with multifocal bifrontal and right parietal, low density white matter lesions
12	3	84	0.20	Yes	Enlarged	Diffuse cerebral atrophy with multifocal parietal, low density white matter lesions
13	2	48	0.26	Yes	Enlarged	Diffuse cerebral atrophy; no white matter lesions
14	4	68	0.30	Yes	Enlarged	Profound, diffuse cerebral cortical atrophy; atrophic pons; focal diminished density of white matter of temporal and parietal lobes
15	2	82	0.31	Yes	Enlarged	Moderate cerebral atrophy; multifocal diminished density of centrum semiovale

Note.—VCR = ventriculocephalic ratio of Banna. Normal = 0.08–0.15.

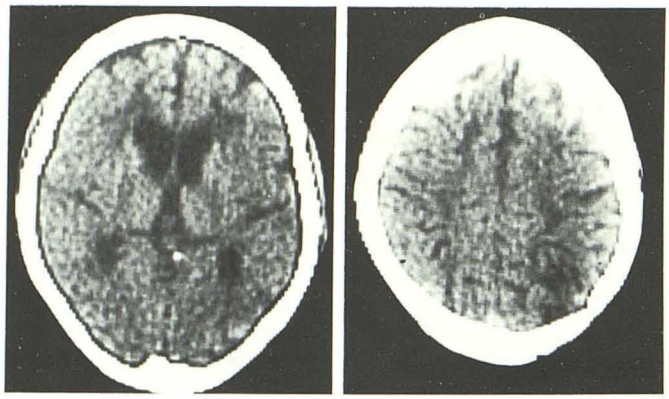

Fig. 1.—Case 11, 17-year-old girl with symptoms for 86 months. Focal areas of diminished density in paraventricular frontal white matter and in white and gray matter of right parietal lobe. Diffuse cortical atrophy.

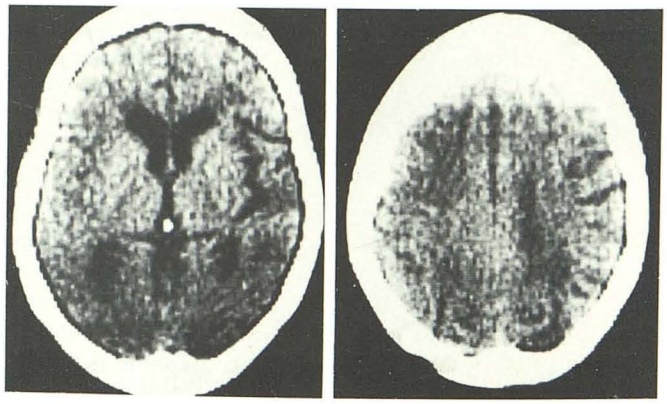

Fig. 2.—Case 12, 17-year-old girl. Mild diffuse cortical atrophy and focal areas of diminished density in central white matter.

and expressed as a ratio of the inner table diameter measured at the same level, the ventriculocephalic ratio of Banna [10]. The measurements were made with a millimeter rule on 4:1 minification transparencies. We also recorded the visibility of cortical sulci and made subjective estimates of the size of the subarachnoid space including the cisterns, fissures, and sulci.

Results

Table 1 compares the clinical data with the CT findings. The CT findings were abnormal in those cases following a chronic course. Cases 1–5 and 7 had rapidly progressive disease and reached late stage 2 or stage 3 within a few months after onset. No lesions were found in this group. Cases 9, 10, and 12–15 were chronically progressive and in some the disease had been quiescent for several months. These patients had diffuse cerebral atrophy and multifocal low density lesions of white matter.

Varying degrees of morphologic abnormalities typically

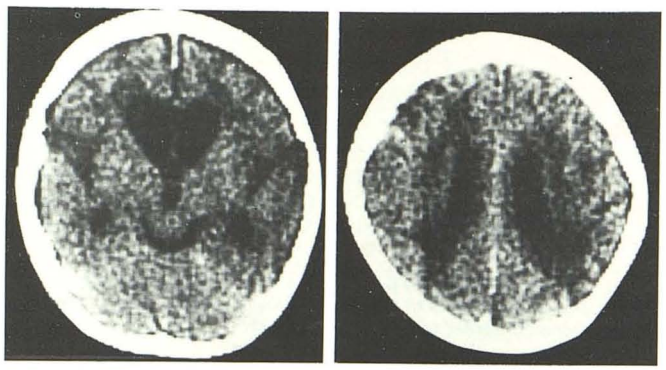

Fig. 3.—Case 15, 12-year-old boy. Moderate diffuse cortical atrophy and diminished paraventricular density involving frontal and parietal lobes.

seen in the chronic cases of subacute sclerosing panencephalitis were demonstrated. Figures 1–3 show varying degrees of cortical atrophy and multifocal low density lesions of the subcortical and periventricular white matter. All

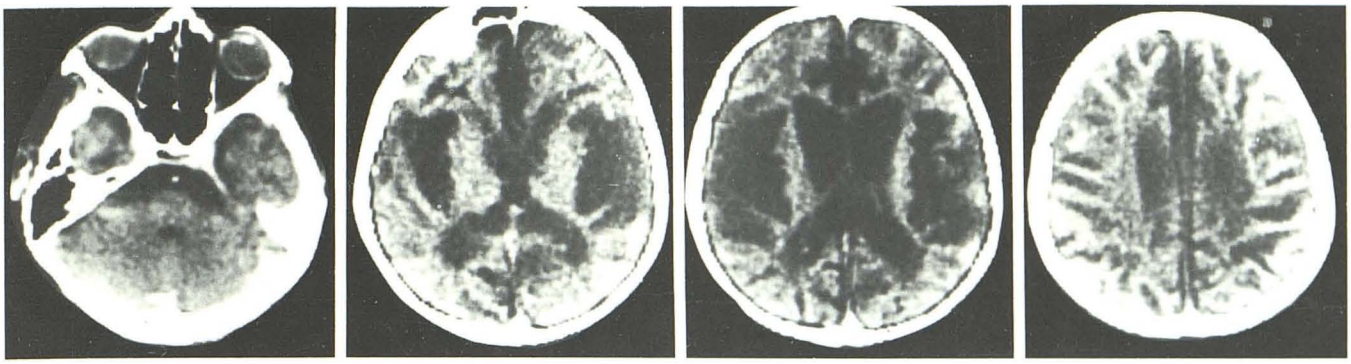

Fig. 4.—Case 14, 14-year-old boy. Extensive atrophy affecting both white and gray matter of cerebral hemispheres, especially of temporal lobes. Pontine atrophy.

lobes were randomly affected. Figure 4 shows the most extensive changes of atrophy in our series. Both cerebral hemispheres were severely affected. The temporal lobes in particular showed striking atrophy. The pons showed mild atrophy.

Case 8 experienced a rapidly progressive clinical course but the CT was abnormal, showing diminished density in the left basal ganglia. Cases 6 and 11 were atypical in that they experienced a rapidly progressive early clinical course followed by prolonged remission with remarkable recovery of both intellectual and motor functions. Both of these cases were treated with an experimental antiviral agent, isoprinosine [11], before CT.

There was no correlation between clinical stage and the location or severity of the brain lesions. No abnormal areas of iodine contrast enhancement could be discerned.

Discussion

Subacute sclerosing panencephalitis (SSPE) is an uncommon disease with an incidence of 1:1,000,000 in the United States [12] and a possible male preponderance [8]. One-half of the patients have clinical measles before age 2 [12] and clinical signs are usually manifest after a latent period of 6 years [13]. Although earlier reports indicated that most patients died within 9 months [14], subsequent reports have shown many cases with a chronic course of several years [15, 16]. Although uncommon, spontaneous remissions do occur; they most often begin during clinical stage 2 [15] and may last for years [17].

It is still unclear what circumstances cause the rare patient with measles to experience this progressive, insidious slow virus infection. Although the host lymphocytes are probably immunologically competent [18], a measles-specific inhibitory substance that blocks expression of cellular immunity has been suggested [19]. Although three patients in our series (cases 2, 4, and 5) were immunized with live measles vaccine, no increase of SSPE has been noted after mass immunization in the United States [20].

The best proof of the SSPE diagnosis is recovery of measles virus from brain tissue. However, diagnosis is usually firmly established by clinical criteria including a high cerebrospinal fluid gamma globulin level, elevated serum and cerebrospinal fluid measles titers, and an abnormal encephalographic pattern of "suppression, burst" [8].

Care was taken in reviewing our data to record all medications, toxins, physical agents, or associated illnesses that may cause CT findings to resemble cerebral atrophy. Except for case 15 (neurofibromatosis), no other chronic diseases or steroid therapy was recorded. The most common drugs used were anticonvulsants, which are not known to produce CT findings resembling atrophy. Isoprinosine [11] was administered to this patient group after cranial CT scans in cases 2, 4, 5, 10, and 12–15. This agent is not known to produce atrophic changes. A search for other concurrent infections, particularly viral, failed to implicate other possible agents for the CT findings. Malnutrition and dehydration were not present in our patients.

The pathology of SSPE is variable and depends to a large extent on the rate of progression of the illness. Cases with a rapidly fatal course may have primarily cortical changes with perivascular inflammatory infiltrates and with intranuclear inclusion bodies in cortical neurons and oligodendroglia. This is the pathologic change initially described by Dawson [1] in 1933, and referred to as "subacute inclusion body encephalitis." More chronic cases may show prominent subcortical white matter lesions with perivascular infiltration by lymphocytes and plasma cells, gliosis, and demyelination. These pathologic changes, described by van Bogaert [3] as "subacute sclerosing leukoencephalitis," are often associated with neuronal loss and with astrocytic and microglial hyperplasia in cerebral cortex, thalamus, basal ganglia, and brain stem. Cases with such widespread changes gave rise to the term "subacute sclerosing panencephalitis" that is now commonly applied to all cases of subacute encephalitis related to rubeola virus.

Known pathologic changes correlate quite well with CT findings. Cases with short clinical histories and a rapidly progressive course, in which pathologic changes might be expected to be primarily intracortical and subtle (viral inclusions in neurons), had normal or minimally abnormal CT patterns. With one exception, the eight cases with abnormal CT findings had a chronic clinical course and would be expected to show the pathologic changes of sclerosing panencephalitis, including cerebral cortical and subcortical nuclear atrophy and gliosis and demyelination of the subcortical white matter. The CT patterns of cerebral atrophy, low density lesions in white matter, and basal ganglia lesions

found in these cases reflect the expected pathologic changes. The presence of discrete lesions in the caudate nuclei in two of the patients [8, 9] is interesting in view of the frequent occurrence of clinical manifestations of basal ganglia involvement in SSPE, including choreiform movements, dystonia, and parkinsonian tumor and rigidity [21].

The abnormal ventriculocephalic ratios noted in our patients indicate ventricular dilatation and are direct signs of generalized atrophy. The cortical sulci and subarachnoid space were appropriately enlarged in those patients demonstrating cerebral atrophy. The third ventricle was dilated in all cases that demonstrated lateral ventricle dilatation. The fourth ventricle was normal in all cases. The cerebellar hemispheres were normal in all cases except 14 which showed mild cerebellar atrophy but profound cerebral atrophy. Case 14 is the only case showing brainstem atrophy.

None of the CT scans of the SSPE patients exhibited abnormal areas of contrast enhancement. The lack of enhancement may be attributed to a lack of significant, acute inflammatory response.

The CT findings of SSPE may resemble other diseases. Multiple sclerosis may show focal low density lesions in the periventricular and subcortical white matter with or without cerebral atrophy. Progressive multifocal leukoencephalopathy may display prominent focal or multifocal areas of decreased attenuation of white matter, often with contrast enhancement [22]. Similarly the gender-linked adrenoleukodystrophies associated with adrenal insufficiency commonly show extensive white matter low density lesions, often accompanied by enhancement of the margins [23].

The dysmyelinating disorders tend to show a pattern of diffuse low density of the centrum semiovale without contrast enhancement. These changes reflect the pathologic findings of abnormal formation of myelin and lack of inflammatory change. They are sufficiently distinct from SSPE to avoid general confusion.

Other viral infections may be considered in the differential diagnosis. However, only herpes simplex encephalitis has been well characterized by CT and it tends to produce unilateral low density lesions of the temporal lobe, sometimes hemorrhagic, and sometimes demonstrating streaked contrast [24].

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