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Computed Tomography of Wilson Disease

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Computed tomography (CT) was performed on 25 patients with Wilson disease (hepatolenticular degeneration). The diagnosis was confirmed biochemically. CT was normal in seven patients, five of whom presented clinically with the hepatic form of the disease. In 10 patients, CT abnormalities were graded as mild: there were atrophic changes around the basal ganglia and in the cortex and cerebellum. In eight patients, besides areas of atrophy there were low absorption areas subcortically in the frontal lobi and in the cerebellar hemispheres, as well as brainstem atrophy. Hypodense lesions in the lentiform nucleus and the area of the dentate nucleus were also noted, although mathematical analysis in terms of decrease of Hounsfield units failed to demonstrate significant differences from normal values.

Hepatolenticular degeneration (Wilson disease) is an autosomal recessive disease due to an inborn error of ceruloplasmin metabolism, which results in the abnormal deposition of copper in the liver and brain. The diagnosis of Wilson disease has been based mainly on decreased serum ceruloplasmin concentration (below 80 μg/100 ml), low serum copper levels (below 80 μg/100 ml), and copper diuresis after chelation with penicillamine. Pathologic findings are located in the lentiform nucleus, cerebral cortex, thalamus, dentate nucleus of the cerebellum, brainstem nuclei and elsewhere [1, 2]. Atrophies have been described macroscopically, predominantly in the insula. Histologic examination demonstrates reduced numbers of neurons, demyelination of nerve fibers, and, later, areas of cavitation and glial scarring. Several papers have been published [3–5] demonstrating computed tomographic (CT) abnormalities (areas of low density) involving the basal ganglia and the cerebellar nuclei. As the patients with Wilson disease in Czechoslovakia are concentrated at our institution, we have had an opportunity to examine a relatively large number.

Materials and Methods

The CT brain scans of 25 patients with Wilson disease were reviewed. (There were 19 cases of the cerebral form and six cases of the hepatic form, but since patients with the hepatic form can demonstrate electroencephalographic (EEG) changes, we do not think these two forms should be distinguished.) All 25 patients had low serum ceruloplasmin and/or low serum copper concentrations. Follow-up examinations were performed after 1 year in 12 patients, all of whom were treated with penicillamine. CT scans of 5 and 10 mm slice thickness were obtained with and without intravenous contrast enhancement using a Siemens 2000 unit. Slices at the levels of the dentate and lentiform nuclei were analyzed using a special software program that permitted evaluation of densities in Hounsfield units (H) in one line.

Results

CT studies were normal in seven patients, including five of the six cases with the hepatic form of the disease. In 10 patients CT abnormality was mild, and characterized by atrophic changes in the region of the basal ganglia (fig. 1A). Frontal horns were dilated, in some cases predominantly adjacent to the head of the caudate nucleus. There were signs of atrophy in the insular region; the sylvian fissure was widened, the cerebral sulci were impressively dilated, and the gray matter of the lentiform nucleus was reduced in size. Areas of slightly diminished density in the lenticular nuclei and the anterolateral portion of the head of the caudate nucleus were noted in several patients, although mathematical evaluation failed to demonstrate significant reduction in Hounsfield units (22 ± 7 H). The results of measurements in this region showed in 20 healthy cases values of 29 ± 4 H. The fourth ventricle and the vermian cistern were enlarged (figs. 1B–1D).

In eight patients the CT abnormalities were impressive. Cortical atrophy (predominantly but not only in the frontal region) was extensive. Enlarged cerebral sulci and impressively enlarged ventricles were apparent (fig. 2A). In the frontal region, there were areas of low absorption of 13–15 H in three patients (fig. 2B). Posterior fossa abnormalities were characterized by atrophic changes with reduction in width of the brainstem predominantly in the cerebral crura (eight patients). The ambient and intercrural cisterns were enlarged, and stripes of low absorption in the cortex and white matter of the cerebellar hemisphere were seen (figs. 2C and 2D). Enlargement of the fourth ventricle was pronounced in all eight patients. While areas of low density were identified in the dentate nuclei, measured values (27 ± 5 H) were not significantly below the range of normal for these areas. All eight patients with impressive CT findings suffered from motor defects and resting tremor. There were only slight rigidity and tremor in the 10 patients with unimpressive CT.

Discussion

Twelve patients were examined both before penicillamine therapy and after they had been taking 1 mg of the drug daily for 12 months. In six cases CT atrophic changes worsened, five remained unchanged, and one improved.

High-density lesions on CT reflecting basal ganglionic copper deposition do not seem to occur in Wilson disease [3–5]. The mean

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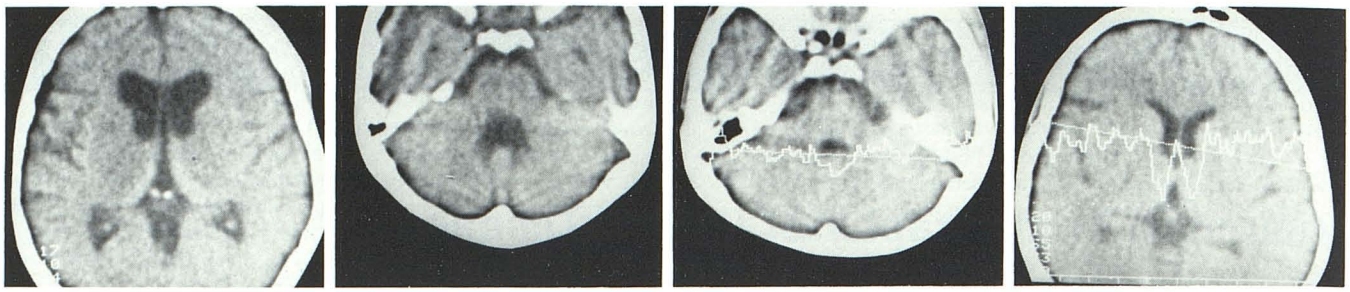

Fig. 1.—**A**, Atrophic changes around basal ganglia. **B**, Widening of fourth ventricle. **C** and **D**, Line where absorption values were analyzed.

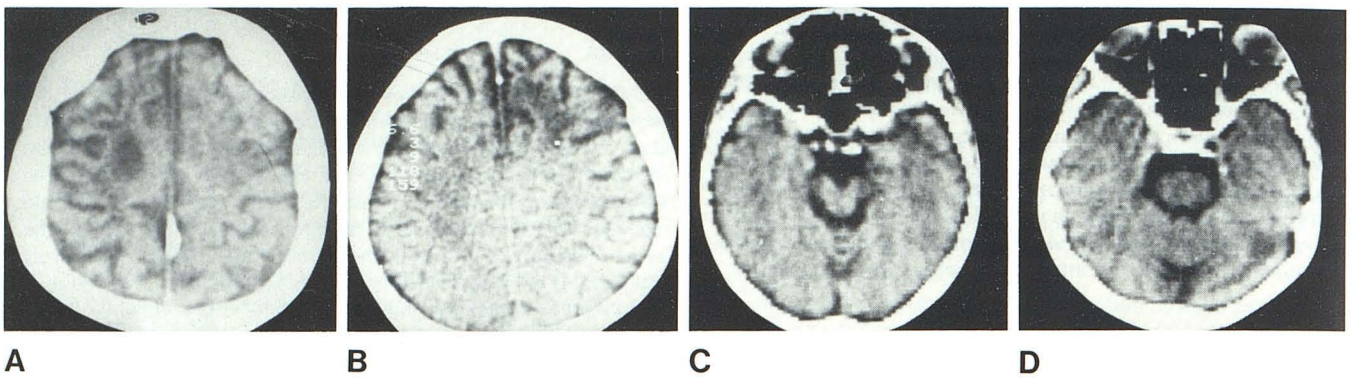

Fig. 2.—**A**, Brainstem atrophy. **B**, Area of low density in right cerebellar hemisphere. **C**, Cortical atrophy and areas of hypodensity in frontal lobe. **D**, Diffuse cortical and subcortical atrophy.

copper concentration assessed by Cummings [1] in lentiform nuclei of healthy males was 9.3 mg/100 mg dry tissue, while in patients with Wilson disease it was 37 mg/100 mg. Increased copper concentration values were also found in the white matter of the cerebral hemispheres, in the thalamus, and in the brainstem. These concentrations are far too low to be detected by CT.

Microscopically, focal degeneration and cavitation are frequently found in the anterior putamen and the caudate in Wilson disease. On CT, areas of hypodensity in the lateral part of the putamen in the area of distribution of the lenticulostriate artery were noted in four patients. Moreover, indirect signs of lesions in the lentiform nuclei area were found in eight patients. CT atrophic changes in the insula and around the frontal horns also correlate with anatomic findings.

Histologically proved lesions, predominantly cortical and subcortical in the frontal lobe, are also manifest on CT images, which demonstrate diffuse and localized hypodensities in this region with widening of sulci and shrinkage of gyri. Similar changes in the dentate nucleus, red nucleus, and cerebellar cortex are described by pathologists.

In correlation, in our study CT abnormalities were identified in 13 patients, and included dilatation of the fourth ventricle, widening of cerebellar sulci, and areas of hypodensity. We also noted narrowing of brainstem in eight of these cases. The CT abnormalities did not change with contrast enhancement, suggesting no increase in capillary permeability or in vascularity. We found correlation between the severity of clinical symptoms and CT abnormalities, but during penicillamine therapy the CT changes worsened, while the overall neurologic condition of the patients improved.

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