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S El-Tatawy, N Badrawi and A El Bishlawy

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Cerebral Atrophy in Infants with Protein Energy Malnutrition

Samir El-Tatawy,[1] Nadia Badrawi,[2] and Amal El Bishlawy[2]

Central nervous system manifestations are common in infants suffering from protein energy malnutrition. Computed tomography was used to search for pathology in the brain that might explain these symptoms. Subjects were 40 infants with protein malnutrition. All had mental symptoms. The bifrontal index was taken as the best parameter for measuring central atrophy, and the width of the sylvian fissure was used as the parameter for cortical atrophy. Ventricular dilatation and widened sylvian fissure of various degrees were found in every patient. The severity of atrophy correlated with the duration of the illness.

Protein energy malnutrition is one of the most serious health problems in Egypt. It is found predominantly in infants whose requirements for protein have not been met for some time. The age of peak incidence is 6–30 months [1]. As the human brain grows rapidly from the 11th week of gestation to the second year of life, malnutrition during this period would be expected to impair the growth and functioning of the brain. Children with protein energy malnutrition manifest such symptoms as listlessness, apathy, irritability, weakness, and inactivity [2]. The bases for these profound disturbances are complex and poorly understood.

Computed tomography (CT) provides us with a convenient and noninvasive method of examining the morphology of the human brain in vivo. We used this technique to search for abnormalities that might relate to the symptoms seen in infants suffering from protein energy malnutrition.

Subjects and Methods

Subjects were 40 infants aged 12–30 months with protein energy malnutrition. The duration of the disease at the time of the study was 10–70 days. All infants had central nervous system manifestations of the disease (listlessness, apathy, irritability). Cases were divided into three groups according to the duration of the disease, as follows: group 1, less than 1 month (11 cases); group 2, 1–2 months (10 cases); group 3, more than 2 months (19 cases). A fourth group of 10 normal controls was included.

All cases were subjected to CT head scan using the ACTA 200FS scanner at Cairo University Hospital. Central atrophy (dilatation of the ventricles) was evaluated by the bifrontal index (bifrontal diameter/transverse diameter of the brain at the same level). Cortical atrophy was evaluated by the width of the sylvian fissure at its anteroposterior diameter. The CT measurements were scaled to the actual dimensions. Other criteria for detection of cortical atrophy were widening of the interhemispheric fissure (6–11 mm), widening of the cortical sulci (3–7 mm), and the number of visible cortical sulci (3–12/hemisphere).

Results

The results are presented in tables 1–3. Central and cortical atrophy of various degrees was found in 100% of cases, the severity correlating with the duration of protein deficiency. Representative CT scans of infants suffering from protein energy malnutrition are shown in figures 1–5.

In four cases with severe cortical atrophy, the atrophy was locally prominent in the frontal region, resulting in an appearance identical to localized frontal hygroma (fig. 4). These cases had an especially severe clinical presentation.

The bicaudate index (bicaudate diameter/transverse diameter of the brain at the same level) had a mean value of 0.2 (range, 0.15–0.27 ± 0.03), substantially higher than that of the normal controls (0.14); however, it did not show significant correlation with the duration of the disease.

TABLE 1: **Evaluation of Central Atrophy (Dilatation of the Ventricles) by the Bifrontal Index**

Degree of Atrophy	Range	Mean	Standard Deviation
Normal	<0.28	0.26	0.054
Mild	0.28–0.32	0.30	0.013
Moderate	0.33–0.37	0.35	0.017
Severe	>0.38	0.41	0.034

Note.—The bifrontal index is the bifrontal diameter of the brain divided by the transverse diameter at the same level. Values obtained are expressed as ratios.

TABLE 2: **Evaluation of Cortical Atrophy by the Width of Sylvian Fissure**

Degree of Atrophy	Range (mm)	Mean (mm)	Standard Deviation (mm)
Normal	0–6	4.7	1.16
Mild	6–9	7.8	0.68
Moderate	9–11	10.4	0.96
Severe	>11	14.7	2.40

[1] Department of Radiology, Faculty of Medicine, Cairo University, 166, 26 July St., Dokki, Cairo, Egypt. Address reprint requests to S. El-Tatawy.
[2] Department of Pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt.

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Discussion

Although mental changes are one of the diagnostic criteria in protein energy malnutrition, few studies have examined the underlying pathologic changes in the brains of affected infants. Electroencephalographic (EEG) studies are few. Taori and Pereira [3] found normal EEG readings in a group of 20 patients with the disease. Slowing of the electrical patterns, particularly over the temporal lobes, was reported in acute protein energy malnutrition by Hansen et al. [2]. Engsner et al. [4] studied the cerebral ventricles by sonography and found a significant dilatation of the ventricles in protein energy malnutrition. In our study, the results of CT head scan were striking. Central and cortical atrophy, present in 100% of cases, were found to have a significant correlation with the duration of the illness ($p < 0.05$).

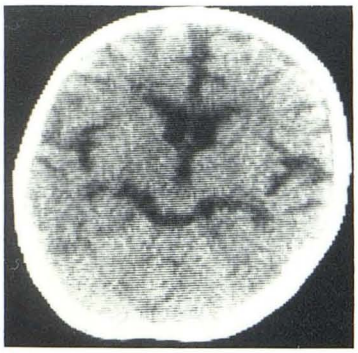
TABLE 3: **Severity of Cerebral Atrophy Related to Duration of Protein Energy Malnutrition**

Type of Atrophy: Severity	Duration of Illness (days)		
	<30 (n = 11)	30–60 (n = 10)	>60 (n = 19)
Central:			
Mild	54.5	20.0	10.5
Moderate	27.2	60.0	36.9
Severe	18.2	20.0	52.6
Cortical:			
Mild	63.6	10.0	21.0
Moderate	27.3	50.0	31.6
Severe	9.1	40.0	47.4

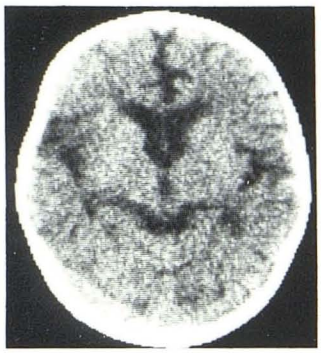
Note.—The chi-square test was used for analysis of covariance. Correlation values are expressed as percentages ($p < 0.05$).

The assessment of the normal shape and size of the infant brain and ventricles had been a problem until the advent of CT. Several authors have described different methods of evaluating the normal shape of the ventricle in infants. Hahn and Rimm [5] reported the ratio of the maximum bifrontal diameter to the maximum transverse diameter at the level of the frontal horn. Pedersen et al. [6] used the sum of the widths of the left and right anterior horns. In the present series we adopted the method of Heinz et al. [7] as a simple and accurate assessment of central atrophy or atrophic dilatation of the ventricles. They divided the bifrontal diameter at its widest dimension by the coronal diameter of the skull at the same level. Their indices of ventricular enlargement are significantly higher than ours, probably because their cases were both obstructive and atrophic while our cases are only atrophic (and presumably cause less ventricular dilatation). Dilatation of the temporal horns, more suggestive of obstructive ventricle dilatation [7], was not a prominent feature in our cases.

Cortical atrophy, on the other hand, is still very difficult to evaluate. There is no universally accepted method of measuring it. Some authors have assessed cortical atrophy by measuring the width of the cortical sulci [8–9]. Other authors [7], dismissing this method as inaccurate and variable, have suggested simple counting of the number of visible cortical sulci as an index to cortical atrophy. The sylvian fissure, being a specific anatomic entity and wide



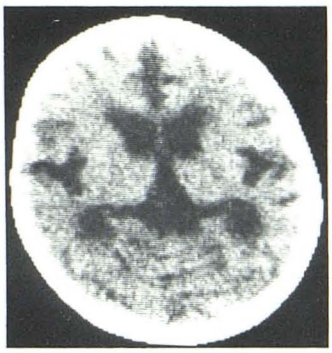
1



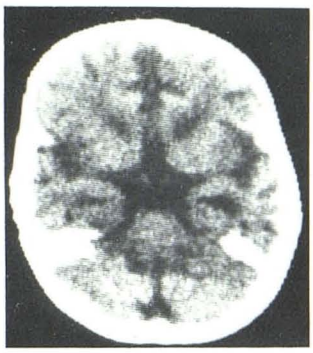
2

Fig. 1.—Mild central atrophy. Bifrontal index is at upper limit for mild ventricular dilatation, although bicaudate index is disproportionately larger. Mild cortical atrophy by width of sylvian fissure. Interhemispheric fissure and cortical sulci are also widened.

Fig. 2.—Moderate central atrophy by bifrontal index; severe cortical atrophy by width of sylvian fissure.



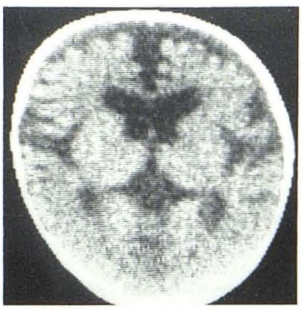
3A



3B

Fig. 3.—Severe central and cortical atrophy. **A**, Prominent cerebellar folia indicate cerebellar atrophy, uncommon in these cases. **B**, Enlarged basal cisterns indicate widened subarachnoid space. Temporal horns are not proportionately wide.

Fig. 4.—Severe cortical atrophy, locally prominent in frontal region and anterior part of interhemispheric fissure, simulating appearance of hygroma.



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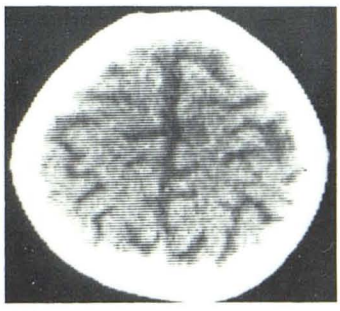
5A



5B

Fig. 5.—Slightly prominent (**A**) and markedly prominent (**B**) widening of cortical sulci and interhemispheric fissure indicate presence of cortical atrophy, but may not stage it in all cases.

enough for convenient measurement, is probably the best parameter of cortical atrophy. In our patients, its width showed a significant correlation with the duration of the disease.

Our results are in accordance with the work of Dobbing [10], who found that the mean weight of the brain in undernourished developing animals is less than in a normally nourished age-matched control group. The same author [11] found that malnourished rats show curtailment of brain development and permanent deficit in the number of brain cells and in the DNA and cholesterol content of the brain. It was also reported [12, 13] that the mean brain weight and the numbers of cells in cerebrum, cerebellum, and brainstem were significantly fewer in malnourished infants than in well nourished infants. Our observations in vivo support the postmortem findings.

The brain is presumed to be stunted because of protein energy malnutrition. However, mere underdevelopment of the brain would not be sufficient to account for the CT appearance within the relatively short course of the disease. An atrophic process with loss of cerebral tissue is probably a contributing factor. It is suggested that the morphological appearance of the brain in protein energy malnutrition depends on the relative extent of these two factors. Undergrowth can be corrected while atrophy cannot. Future studies are planned to explore and elaborate upon this theory.

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