The widespread but silent cerebral mineralization: a case report

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Abstract. We present a sporadic infantile case of primary cerebral mineralization with unexpected asymptomatic clinical course. An 11 months old boy with negative familial and gestational data developed normally. He died after two days of fever and rapid course of cardiorespiratory failure due to pneumonia. Parathyroid dysfunction and somatic abnormalities were not evident clinically. Neuropathological examination revealed bilateral, diffuse or pericapillary calcifications in the striatum, cerebral and cerebellar cortex, dentate nucleus and brain stem. The mineralizations were less prominent in the cerebral hemispheres than in cerebellum. A diffuse demyelination was seen in the cerebellum where calcifications were numerous. We suggest that the intracerebral calcifications progressed gradually through a disease course and probably started in the cerebellum. We discuss the lack of clinico-pathological correlations and the nosologic position of the observed syndrome.

Key words: primary cerebral mineralization, idiopathic cerebral calcinosi
Primary cerebral mineralization of unknown origin had been defined as cerebral calcinosis, striopallido-dentate calcinosis and Fahr's disease. At present, opinion prevails, that primary cerebral mineralizations are a group of ethiologically differentiated disease entities (Razavi-Encha et al. 1988, Friede 1989). They appear in such clinically and pathologically characteristic diseases as Cockayne syndrome, may coexist with parathyroid dysfunction and form a group of idiopathic, sporadic or familial cases of intracerebral calcifications in children and adults. Previously precise term of "Fahr's disease" is presently adequate only in cases of idiopathic nonarteriosclerotic intracerebral calcifications appearing in adults. Clinically, most of this condition are characterized by neurological symptoms (mental deterioration, epilepsy, pyramidal, extrapyramidal deficit and cerebellar signs).

We report an infantile case with cerebral calcifications but an asymptomatic clinical course.

An 11 month old boy, the first child of healthy parents, was born from a full-term normal pregnancy. During perinatal period, no abnormalities were observed. His motor development was considered normal during the first months of life. At 10 months after birth he could sit unassisted and stand when supported. At the age of 11 months he presented with an onset of sudden vomiting, fever, respiratory deficiency and bradycardia. His state was severe and he required mechanical ventilation and pressor drug administration. The clinical course was complicated by hypoglicemia, thrombocytopenia and anuria. The normal serum calcium levels allowed to exclude the clinically relevant parathyroid hormone deficiency. Ultrasound scan of the brain was normal. Two days after hospitalization the child died. At autopsy pneumonia and hemorrhagic necrosis of the adrenal glands were found and considered to be the cause of death.

Macroscopic examination of the central nervous system disclosed no abnormalities of cerebral gyri. However, on coronal sections of the brain, small plaques of calcification were seen bilaterally in the cerebellar cortex and in the dentate nuclei. Representative sections were paraffin-embedded and stained by haematoxylin-eosin, cresyl-violet, Klüver-Barrera, for GFAP and von Kossa method specific for calcium compounds.

Histologically, a horizontal section through both cerebral hemispheres revealed in the basal ganglia (Fig. 1) numerous pericapillary basophilic deposits and mineralization in the media of small vessels. Focally, in the cortical layers there were pearl-like incrustations in the capillary walls. They were mainly localized at the bottom of the gyri. This granular, basophilic material was at times negative, or at other times positive for calcium. In the cerebellum numerous deposits were found bilaterally in the dentate nuclei and in the granular layer of the cortex (Fig. 2). These deposits were strongly positive for calcium and were seen in the pericapillary area or free in the tissue but not inside the cells. The cerebellar white matter stained poorly in myelin stains (Fig. 3). Slight fibrillary gliosis with GFAP positive glial cells was observed. There were also numerous blood vessels showing calcified media or diffuse thickening of walls with ring-like calcifications in the adventitia and media. Mineralizations of the same type as in the cerebral hemispheres were also seen in the basal part of the pons (Fig. 4), in the nucleus ruber and in the substantia nigra. Neuronal loss was prominent in places where calcifications were numerous. Leptomeninges were normal.
Cerebral calcifications were disclosed during neuropathological examination. Parathyroid dysfunction or somatic abnormalities were clinically excluded. Cerebral calcifications were clinically not evident probably due to the child’s age. In a few published cases of infantile intracerebral calcifications (Melchior et al. 1960, Norman and Tingley 1966, Razavi-Encha et al. 1988, Reske-Nielsen et al. 1988), slight and not characteristic symptoms were noted in the first weeks or months of life (such as tremor, truncal hypotonia, abnormal eye movements, seizures). Usually in the later period of life these symptoms evolved into a severe, progressive neurological syndromes. In these infantile cases, besides intracerebral calcifications, additionally diffuse demyelination of the cerebral white matter was observed similar to the one in sudanophilic leukodystrophies. In our case, demyelination was only prominent in the cerebellar hemispheres and may be caused by vascular obliterations due to calcification of numerous vessel walls of the cerebellar white matter (Bruyn et al. 1972). It seems, that hypomyelination was not primary in the described syndrome, because the white matter of the cerebral hemispheres and the brain stem was normally myelinized.

In the morphological appearance of the intracerebral calcifications, the calcium deposits are characteristically located in the close vicinity of the cerebral blood vessels. The chemical studies of Smyers-Verbke et al. (1975) on the cerebral calcifications enabled to demonstrate, that initially non-
calcified round bodies are formed, which contain an organic matrix composed of large quantities of protein, on which inorganic salts become deposited (calcium, iron, magnesium and copper) leading to the formation of large deposits.

Gradual appearance of the changes was most prominent in our case by simultaneous presence of old calcified deposits in the cerebellum and early uncalcified deposits in the cerebral hemispheres. Slowly progressing appearance of deposits was also noted during life on CT scans or X-rays of the skull in adult patients with neurological syndromes in the course of idiopathic cerebral calcifications (Smits et al. 1983).

In conclusion, the reported case represents an early onset of the calcifying process which progressed from the cerebellum to cerebral hemispheres with secondary demyelination of the white matter and belonging to the group of sporadic, infantile form of primary cerebral mineralization.


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