

## Cerebral amyloid angiopathy with attenuation of the white matter on CT scans: subcortical arteriosclerotic encephalopathy (Binswanger) in a normotensive patient

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**Summary.** Subcortical arteriosclerotic encephalopathy was diagnosed in a 56-year-old female normotensive patient with gradually progressing dementia, pseudobulbar palsy and motor deficits. CT scan showed white matter low attenuation in the frontal and parietal lobes. Neuropathological examination revealed degeneration of the white matter. Amyloid was found in walls of small cortical vessels. The walls of small vessels in the white matter showed severe thickening, fibrosis and hyalinization but not amyloid. Cerebral amyloid angiopathy may be responsible for subcortical arteriosclerotic encephalopathy.

**Key words:** Subcortical arteriosclerotic encephalopathy – Cerebral amyloid angiopathy – Normotensive subject

The term subcortical arteriosclerotic encephalopathy (SAE) was introduced by Olszewski [13] for the disease whose clinical picture was described by Binswanger [1]. Olszewski defined its pathological features as extensive hyalinization and intimal fibrosis in the long penetrating arteries and arterioles, multiple small infarcts in basal ganglia and subcortical white matter and diffuse loss of myelinated fibres in the latter with sparing of U-fibres.

The clinical picture of SAE is non-specific [4]. The diagnosis in life became possible with computed tomography (CT) [10, 14]. CT in SAE reveals low attenuation of deep hemispheric white matter. SAE is usually related to systemic hypertension [4]. Its emergence in normotensive patients with a typical clinical and CT picture should be carefully evaluated.

### Case report

A female patient had worked in a nickel-plating workshop before she retired prematurely at age 52. At that time frequent falls, dropping objects out of her hands, and worsening memory were noted. Intellectual deterioration with periods of transient improvement progressed gradually. Two years later the patient became house bound and unable to prepare a meal. Her speech was slow. At age 54 she was found to have CSF protein 160 mg/dl and an abnormal EEG with bilateral delta slowing. <sup>99m</sup>Tc brain scans were normal. There were no focal neurological deficits. A slight temporary improvement in intellectual function occurred and lasted some months. Later the patient became dysarthric and had a series of grand mal seizures. CT scan showed severe symmetrical hypodense lesions of the white matter.

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At age 56 she was admitted to the Department of Neurology, Medical Academy in Łódź. She was oriented and gave her date of birth but did not know her age. She demonstrated temporal disorientation. She could find her way to bed and the toilet and feed and dress herself. She was not incontinent. Psychomotor retardation, apathy and difficulty in sustaining attention were prominent. The score on the Dementia Scale [2] was 14 and that on Information-Memory-Concentration Test [2] was 19. There was bilateral palatal weakness, worse on the left, and right central facial weakness. She was dysarthric but had no difficulty swallowing. A slight weakness of the right arm was associated with mild hyper-reflexia. The strength of the lower extremities was preserved with exaggerated ankle tendon reflexes. The right plantar response was extensor. The gait was apraxic. The blood pressure was 140/85 on admission and there was no previous documentation of hypertension.

Laboratory data, including complete blood count, VDRL test, glucose tolerance test and total cholesterol level, were normal. ECG showed mild ischaemic changes without any evidence of left ventricular hypertrophy. Doppler ultrasonography revealed a symmetrically reduced flow in the carotid arteries. EEG revealed diffused slowing of background activity with bilateral periodic delta waves. CT scan (Figs. 1, 2) revealed diffuse decreased attenuation of deep white matter in the frontal and parietal lobes on both sides. There was only slight widening of the sulci and no ventricular enlargement (Evans index 0.29). The CT white matter changes had progressed when compared with the scans made 5 months earlier.

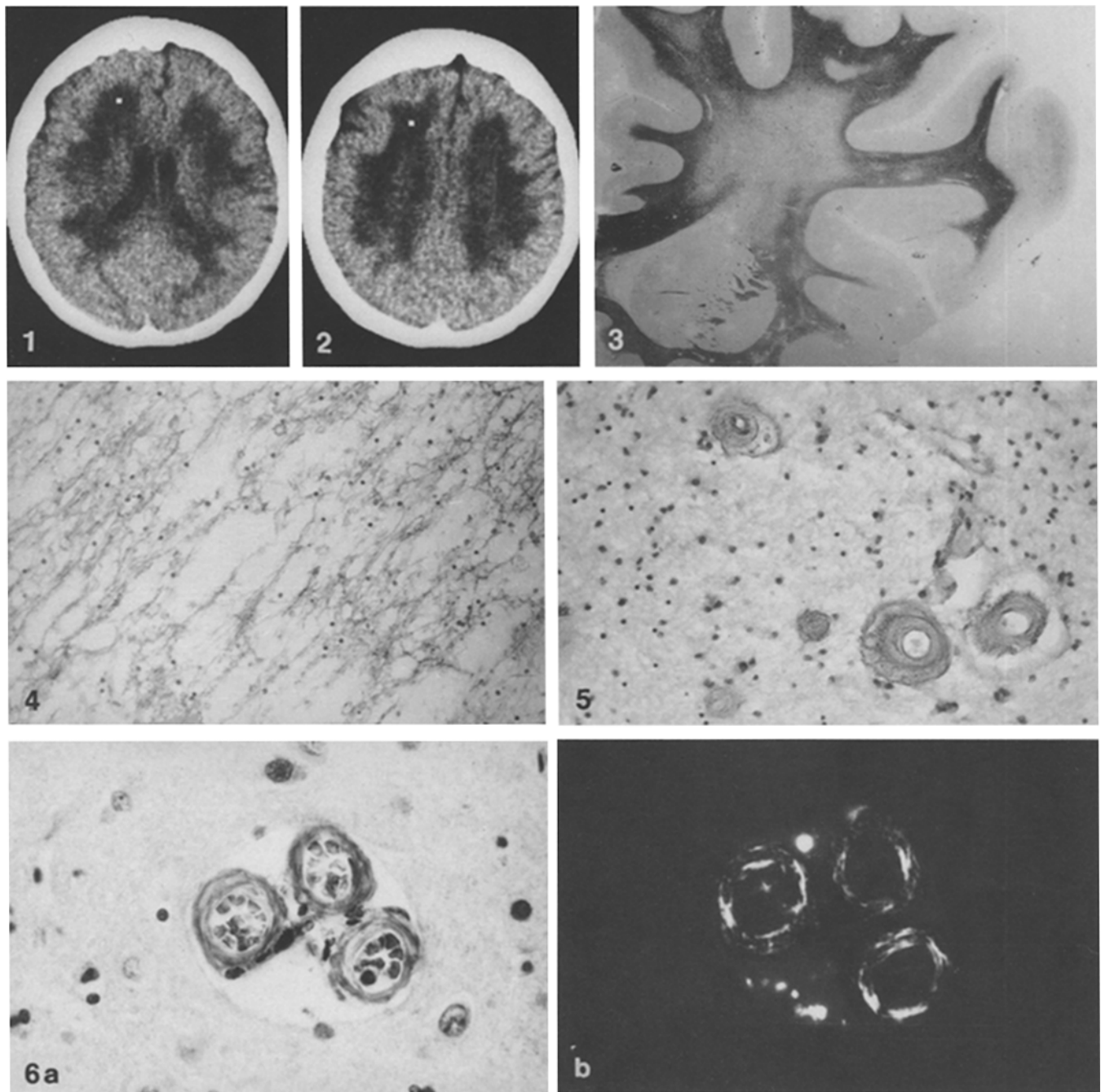
On the 10th day of hospitalization the patient suddenly became immobile, incontinent and more dysarthric. Prominent dysphagia developed and she had to be fed by stomach tube. She died 9 days later of bilateral bronchopneumonia.

### Pathology

Autopsy revealed bronchopneumonia of the lower lobes and moderate atherosclerosis of the aorta and coronary arteries. There was no left ventricular hypertrophy. Only slight atherosclerosis was found in the carotid and vertebral arteries.

The brain after fixation weighed 1190 g. Slight, diffuse fibrosis of the leptomeninges was observed. Coronal slicing showed a small cystic defect (3 × 6 mm) in the white matter of the left frontal lobe. There were no lesions in the brain stem, cerebellum and spinal cord.

Histological slides were stained with haematoxylin-eosin, Congo-red and according to the methods of Bodian, van Gieson, Gordon-Sweet, Kluver-Barrera and Heidenhain.



**Figs. 1, 2.** CT scan. Low white matter attenuation in frontal and parietal lobes. Slight widening of the sulci without ventricular dilatation

**Fig. 3.** The frontal lobe. Diffuse pallor of the white matter with relatively spared U-fibres. Heidenhain,  $\times 1.5$

**Fig. 4.** Pallor and rarefaction of the white matter. Kluver-Barrera,  $\times 100$

**Fig. 5.** The frontal white matter. Sclerosed walls and narrowed lumina of small arteries. H & E,  $\times 100$

**Fig. 6. a** Small arteries of the cerebral cortex. Thickening of the walls. H & E,  $\times 250$ . **b** The same arteries: amyloid birefringence under polarized light. Congo red,  $\times 250$

There was diffuse reduction of myelinated nerve fibres in the white matter of the cerebral hemispheres (Fig. 3) and to a lesser extent also in the cerebellum. Some pallor of the lateral and anterior funiculi of the spinal cord was present. The U-fibres were relatively well preserved. Microscopically the white matter rarefaction resembled the late effect of oedema (Fig. 4). Minimal sclerotic changes were seen in large arteries, whereas many small arteries and arterioles of the brain, cere-

bellum and their leptomeninges showed severe thickening (fibrosis and hyalinization) of their walls (Figs. 5, 6a). The walls of the majority of these arteries in the meninges and cortex showed amyloid (Fig. 6b). Some affected cortical vessels were occluded with thrombi (usually old-organized ones) and surrounded by small areas of incomplete necrosis. In some places perivascular spaces contained few erythrocytes, haemosiderin-laden macrophages and/or lymphocytes. The latter

were also seen in the leptomeninges. Blood vessels of the brain stem and spinal cord were generally free of changes except that some leptomeningeal arteries showed slightly fibrotic walls.

The cerebral cortex showed both focal and mild diffuse loss of neurons and small, dispersed areas of perivascular scarring. Senile plaques or neurofibrillary tangles were not present. The grey matter of the basal ganglia, cerebellum, brain stem and spinal cord was not involved.

## Discussion

The pattern of illness of the presented case was typical for SAE. The patient had been exposed to cyanide for several years but her health worsened even after she retired and the neuropathological picture of white matter lesion in cyanide intoxication is different from that found.

Dementia, white matter degeneration and cerebral amyloid angiopathy (CAA) coexist in some neuropathological conditions. CAA is a common finding in Alzheimer's disease [5] and the amyloid  $\beta$ -protein has been identified in both cerebrovascular and plaque amyloid [15, 16]. In Alzheimer's disease, besides congophilic angiopathy in the cerebral cortex the fibrohyaline degeneration may be observed in subcortical arterioles. It occurs in normotensive subjects and is associated with diffuse loss of myelin and scattered infarction in the white matter [3].

Leukoencephalopathy similar to that observed in SAE may be found in elderly normotensive patients with CAA leading to cerebral haemorrhage. In such cases congophilic deposits were seen in small arterial vessels of leptomeninges and cerebral cortex but the arterioles of the white matter did not contain amyloid [9]. We suggest that amyloid deposits in cortical segments of the long penetrating arterioles may be partially responsible for hypoperfusion and hypoxaemia of the deep white matter in our case.

Arteriosclerotic thickening of deep perforating vessels with prominent medial hypertrophy is typical of SAE pathology. Vascular changes are presumed to be related to the systemic hypertension and they are similar to those observed in hypertensive encephalopathy. However, hypertrophy of the media of small white matter arteries was found by Okeda [12] to be more pronounced in SAE. In some well-documented cases, however, hypertension was never found [4, 6, 11] and probably other factors were responsible for severe arteriosclerosis.

White matter degeneration is the most characteristic pathological feature of SAE. Its pathogenesis remains unknown. It is unclear why the ischaemia in SAE causes diffuse loss of myelinated fibres as well as lacunes. The following hypotheses were proposed by Caplan and Schoene [4]: (1) SAE represents a special type of vascular disease (as suggested by Okeda's study [12]); (2) arteriosclerotic changes reduce the blood flow in subcortical regions and a fall from a raised blood pressure may cause partial ischaemia in wide areas; (3) SAE is a form of hypertensive encephalopathy and local fluid transudation in which focal cerebral oedema and hypoxia are responsible for the white matter changes (as proposed by Feigin et al. [7, 8]).

The absence of hypertension in our case should be noted. Measured blood pressure was never elevated and no indirect pathological features of hypertension (left heart hypertrophy) were found. It is suggested that hypoperfusion and hypoxia

are the important factors responsible for development of SAE and the concept of SAE as a late effect of cerebral oedema in systemic hypertension is rather unlikely.

The pathological changes in the white matter of our case were striking but no lacunes in the basal ganglia and thalami were observed. In the literature we found one similar case: case 4 presented by De Reuck et al. [6]. Lack of involvement of deep grey structures and relatively well preserved cortex confirm the opinion that the white matter disease is responsible for progressive deterioration of intellectual functioning in SAE.

*Acknowledgement.* This paper is part of a study supported by MZ V R-30.

## References

1. Binswanger O (1894) Die Abgrenzung der allgemeinen progressiven Paralyse. *Berl Klin Wochenschr* 31: 1180–1186
2. Blessed G, Tomlinson BE, Roth M (1968) The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry* 114: 797–811
3. Brun A, Englund E (1986) A white matter disorder in dementia of the Alzheimer type: a pathoanatomical study. *Ann Neurol* 19: 253–262
4. Caplan LR, Schoene WC (1978) Clinical features of subcortical arteriosclerotic encephalopathy (Binswanger disease). *Neurology* 28: 1206–1215
5. Cosgrove GR, Leblanc R, Meagher-Villemure K, Ethier R (1985) Cerebral amyloid angiopathy. *Neurology* 35: 625–631
6. De Reuck J, Crevits L, De Coster W, Sieben G, Eecken H vander (1980) Pathogenesis of Binswanger chronic progressive subcortical encephalopathy. *Neurology* 30: 920–928
7. Feigin I, Popov N (1963) Neuropathological changes late in cerebral edema: the relationship to trauma, hypertensive disease and Binswanger's encephalopathy. *J Neuropathol Exp Neurol* 22: 500–511
8. Feigin I, Budzilovich G, Weinberg S, Ogata J (1973) Degeneration of white matter in hypoxia, acidosis and edema. *J Neuropathol Exp Neurol* 32: 125–141
9. Gray F, Dubas F, Rouillet E, Escourolle R (1985) Leukoencephalopathy in diffuse hemorrhagic amyloid angiopathy. *Ann Neurol* 18: 54–59
10. Kinkel WR, Jacobs L, Polachini J, Bates V, Heffner RR (1985) Subcortical arteriosclerotic encephalopathy (Binswanger's disease). Computed tomographic, nuclear magnetic resonance, and clinical correlations. *Arch Neurol* 42: 951–959
11. Loizou LA, Jefferson SM, Thomas Smith W (1982) Subcortical arteriosclerotic encephalopathy (Binswanger type) and cortical infarcts in a young normotensive patient. *J Neurol Neurosurg Psychiatry* 45: 409–417
12. Okeda R (1973) Morphometrische Vergleichsuntersuchungen an Hirnarterien bei Binswangerscherecephalopathie und Hochdruckencephalopathie. *Acta Neuropathol (Berl)* 26: 23–43
13. Olszewski J (1968) Subcortical arteriosclerotic encephalopathy: review of the literature on the so-called Binswanger's disease and presentation of two cases. *World Neurol* 3: 359–375
14. Rosenberg GA, Kornfeld M, Stovring J, Bicknell JM (1979) Subcortical arteriosclerotic encephalopathy (Binswanger): computerized tomography. *Neurology* 29: 1102–1106
15. Selkoe DJ, Bell DS, Podlisny MB, Price DL, Cork LC (1987) Conservation of brain amyloid proteins in aged mammals and humans with Alzheimer's disease. *Science* 235: 873–877
16. Tanzi RE, Gusella JF, Watkins PC, Bruns GAP, StGeorge-Hyslop PH, Van Keuren ML, Patterson D, Pagan S, Kurnit DM, Neve RL (1987) Amyloid  $\beta$ -protein gene: cDNA, mRNA distribution, and genetic linkage near the Alzheimer locus. *Science* 235: 880–884

Received September 14, 1987 /

Received in revised form March 16, 1988 / Accepted March 31, 1988