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System Degeneration of the Thalamus*

A Clinico-Neuropathological Study

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Summary. A case of essential degeneration of the thalamus is reported. The patient was a 43-year-old Japanese male, who, a few weeks after mild head trauma, suffered from forgetfulness, psychomotor slowing, and Korsakoff's syndrome. Four to five months later, there were optical hallucinations and delirium and he died 9 months after the onset of symptoms.

Neuropathological examination revealed symmetrical thalamic degeneration, whose distribution corresponded to phylogenetically younger subunits of the thalamus. In addition, there was olivovermian degeneration.

These findings are identical to those of eleven cases hitherto reported. Five of these were Japanese, including the present one.

The syndrome thalamic degeneration may now be classified as a special type of "system degeneration".

Key words: Thalamic degeneration – Thalamic dementia – System degeneration of thalamus – Korsakoff's syndrome

Zusammenfassung. Es wird über einen Fall von essentieller Systemdegeneration des Thalamus berichtet. Ein 43jähriger Japaner zeigte nach leichtem Kopfstoß eine langsam progrediente Vergeßlichkeit; nach 2 Monaten eindeutiges Korsakoff-Syndrom, 4–5 Monate nach dem Initialsymptom optische Halluzinationen, nächtliche Delirien und starke Abmagerung. Der Tod trat 9 Monate nach dem Kopftrauma ein.

Neuropathologisch ergab sich eine symmetrische Thalamusdegeneration, deren Intensität und topographische Verteilung mit der phylogenetisch

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jüngeren Kerngruppe des Thalamus übereinstimmen. Als Nebenbefund fand sich eine olivovermale Degeneration.

Der neuropathologische Hauptbefund ist weitgehend identisch mit den bisher berichteten 11 Fällen; 5 davon betreffen Japaner, einschließlich unseres Falles.

Das Syndrom „Thalamusdegeneration" kann als besondere Form einer „Systematrophie" klassifiziert werden.

Schlüsselwörter: Thalamusdegeneration – Thalamische Demenz – Systemdegeneration des Thalamus – Korsakoff-Syndrom

Introduction

Degeneration of the thalamus may occur in the context of various degenerative diseases, or as a secondary change (Martin 1970, 1975). Essential systemic degeneration of the thalamus, however, has rarely been described. Clinically, it is marked by a presenile organic dementia of acute or subacute course and associated with various neurological defects. The clinical picture is similar to Creutzfeldt-Jakob disease, and the disease has been considered, even in neuropathological terms, as a "thalamic form" of the Creutzfeldt-Jakob disease (Garcin et al. 1963). Four of eleven known cases have been reported from Japan. The patient described here was also Japanese.

Case Report

H.M., male, 43 years of age, had never been seriously ill. His father had been bedridden for 2 months following a stroke. His mother's brother was an alcoholic and committed suicide at 42 years of age. Our patient worked as a farmer and, occasionally, in a factory; he had married at the age of 24 and had two healthy sons.

His illness began after a minor car accident, when he struck his head against the windscreen. There was no loss of consciousness, nor injuries, and upon reporting to the police he did not act abnormally. He complained of a mild headache the same evening. During the next few days, he appeared slow and drove his car erratically, then a week later developed clear signs of forgetfulness. His physician recorded amnesia, disorientation, confabulation, and a change in personality including uninhibited and shameless behavior. Examination of cerebrospinal fluid, angiography, and pneumoencephalography gave normal results. Eleven weeks after the accident, nocturnal delirium made admission to the psychiatric clinic necessary, where he was found to be apathetic, slow, and disorientated during the day, but restless and delirious during the night. He sometimes urinated in bed. Korsakoff's syndrome, bradylalia, and bilateral hyperreflexia became evident. His body weight decreased from 51 kg to 44 kg, his height being 160 cm. Four months after his accident, his mobility was reduced; he had episodes of rage (lasting for only a few minutes) and sudden aggressiveness toward the nursing staff. He experienced optical hallucinations. Stereotypic movements of the lower extremities caused skin ulcers on his heels, though without signs of pain. He also had mydriasis and oculogyric crisis. Six months after his accident his weight was down to 31 kg and he was permanently bedridden and was irritable when awakened. He showed oral tenderness, difficulty in swallowing, and hypersalivation during the last vegetative state. Finally, he developed general edema, hypoalbuminemia, central hyperpyrexia, and oliguria. He died 9 months after his head trauma. During the entire course there were neither convulsions, tremor, nor signs of remission.

Laboratory findings were not remarkable, neither were the electrolytes. Hypoalbuminemia and anemia were observed in the final stage. EEG examination was impossible because of the irritability of the patient except once during the initial stage, when a slight slowing of the alpha activity was recorded.

General necropsy was not performed and there was no indication of malignant neoplasm on clinical grounds.

Neuropathological Findings

The brain weighed 1450 g; there were no concussions. On dissection there was mild atrophy of the middle part of the thalamus with corresponding slight enlargement of the lateral ventricles.

Microscopic lesions were found throughout the thalamus, consisting of subtotal loss of nerve cells accompanied by astrocytic gliosis of varying intensity.

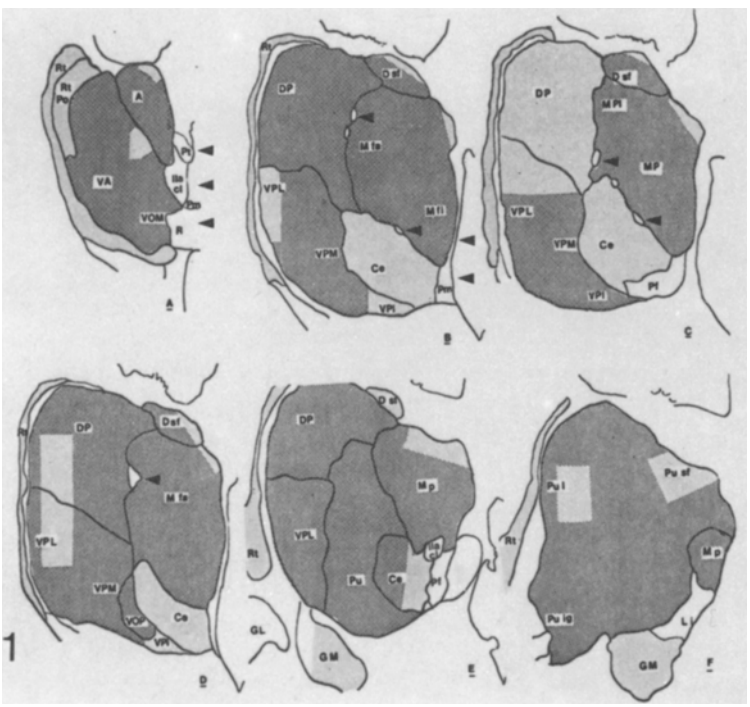

Fig. 1. Schematic drawings of degeneration in the thalamus. Black, grey, white represent severe, moderate, and no changes, respectively. Arrow heads indicate intralamellar and midline structures. *A*: Ncl. anterior, *Ce*: Ncl. centralis; *DP*: Ncl. dorsalis posterior; *Dsf*: Ncl. dorsalis superficialis, *GL*: Ncl. geniculatus lateralis, *GM*: Ncl. geniculatus medialis; *Ila*: Ncl. intralamellaris, *Ila cl*: pars centralis lateralis of *Ila, Li*: Ncl. limitans, *Mfa*: pars fasciculosus of the ncl. medialis, *Mfi*: pars fibrosa of the ncl. medialis, *Mpl*: pars paralamellaris of the ncl. medialis, *Pf*: Ncl. parafascicularis, *Pm*: Ncl. paramedianus, *Pu*: Ncl. pulvinaris, *Pu ig*: Ncl. pulvinaris intergeniculatus, *Pul*: Ncl. pulvinaris lateralis, *Pu sf*: Ncl. pulvinaris superficialis, *R*: Ncl. reuniens, *Rt*: Ncl. reticularis, *Rt po*: Ncl. reticularis polaris, *VA*: Ncl. ventralis anterior, *VOM*: pars posterior of the ncl. ventralis oralis, *VOP*: pars posterior of the ncl. ventralis oralis, *VPI*: Ncl. ventralis posterior inferior, *VPL*: pars lateralis of the ncl. ventralis posterior, *VPM*: pars medialis of the ncl. ventralis posterior. Nomenclature after Dewulf (1971)

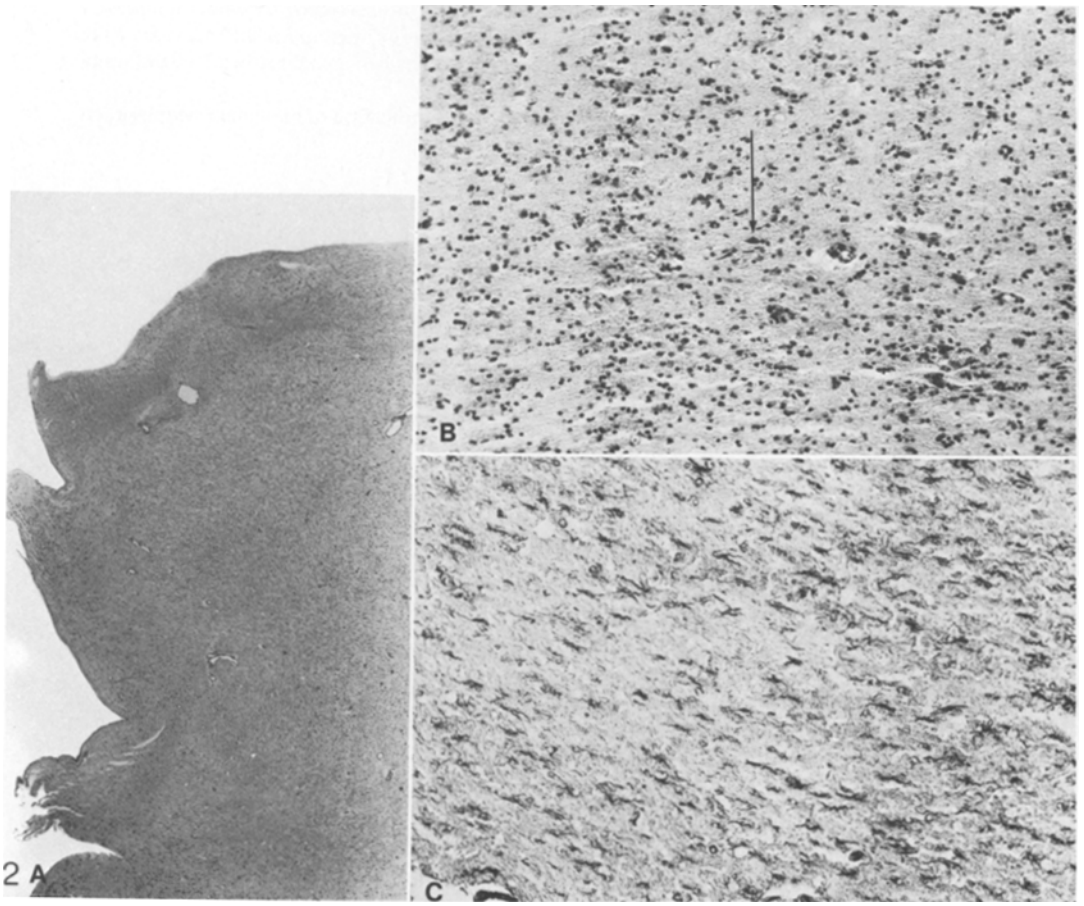

Fig. 2. A Medial parts of the thalamus in Nissl's stain (×5). Note the well-preserved nerve cells near the ventricle. **B** Ncl. anterior. Only one neuron is visible in the whole picture (*arrow*) (Nissl's stain, ×100). **C** Ncl. anterior, showing marked reactive fibrillary astrocytosis (Holzer's stain, ×40)

Distribution and intensity of the thalamic degeneration are shown in Fig. 1. Degenerative changes generally showed a symmetrical distribution. Using the nomenclature of Dewulf (1971), the nucleus anterior and medialis were damaged most severely, as were parts of the formatio lateralis and posterior. In the nucleus anterior, there was an especially marked astrogliosis and distinct rarefaction of the tissue (Fig. 2 B, C). In contrast to these areas, the formatio intralamellaris (Figs. 1 and 3 A), paraventricularis (Figs. 1 and 2 A), and epithalamica were entirely spared (Fig. 1).

In the periventricular region of both the nucleus anterior and dorsalis superficialis, some nerve cells were preserved. The nucleus geniculatus medialis was moderately degenerated while the geniculatus lateralis was intact. The degree of cell loss occasionally varied within one given subnucleus (for example, in the nucleus centralis).

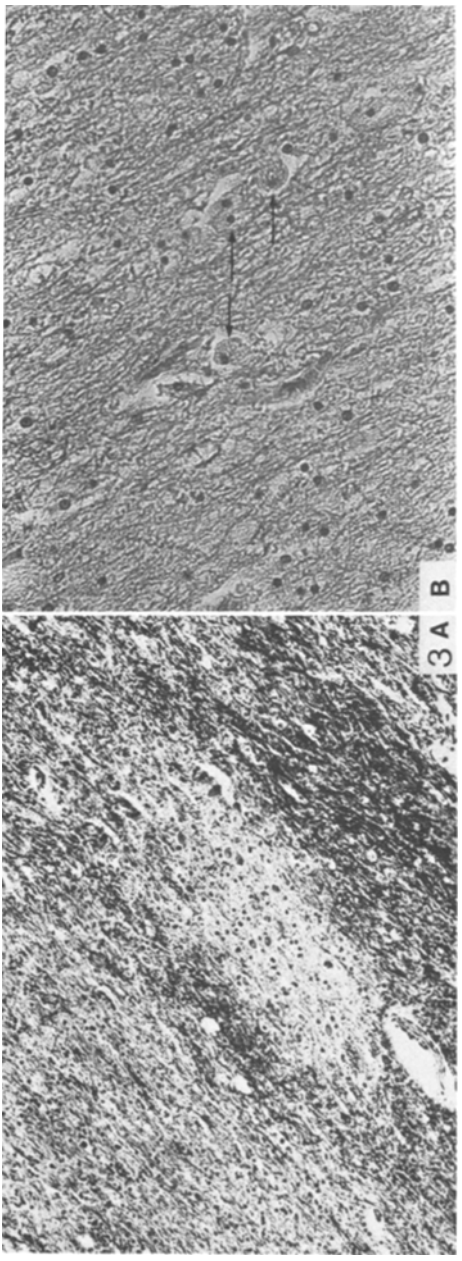

Fig. 3. A Island-like perfectly preserved ncl. intralamellaris. Compare with Fig. 1 (Klüver-Barrera's stain, ×40). **B** Fat granule cells in the corona radiata (*arrows*) (H.-E., ×100)

The neurons in the cerebral cortex, especially in the gyrus cinguli, were slightly reduced. Betz cells were well preserved, only a few showed chromatolysis. Neither astrogliosis nor status spongiosus was encountered in the cerebral cortex. Ammon's horn was normal except for focal capillary calcification. There was slight and diffuse pallor of the cerebral white matter. Isolated fat granule cells were encountered along the fibers of the corona radiata (Fig. 3 B).

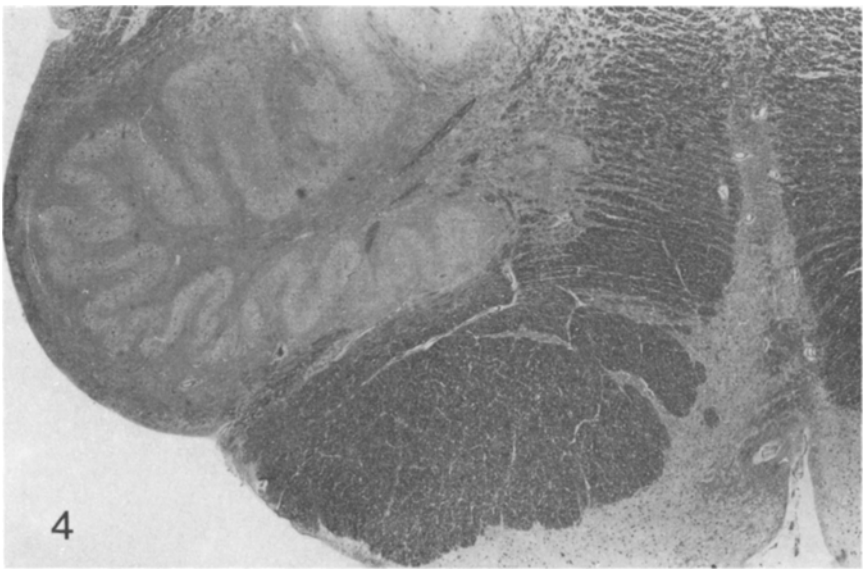

Fig. 4. Subtotal nerve cell loss and partial demyelination in the ncl. olivaris inferior (Klüver-Barrera's stain, ×3.5)

In the midbrain, the colliculus superior showed complete loss of nerve cells with gliosis. Other structures including the area pretectalis and the nucleus habenularis were preserved.

In the nucleus olivaris inferior there was severe loss of neurons; some were preserved only in the lateral aspects of the nucleus. Periolivary myelin sheath destruction and gliosis were observed (Fig. 4). In the cerebellar cortex, Purkinje and granular cell loss and astrogliosis were restricted to the vermis.

No significant changes were observed in any other area of the brain, including vascular changes or neurofibrillar degeneration.

Discussion

Clinical and Clinicopathological Aspects

A 43-year-old patient died after a 9-month course of progressive organic dementia, which began with Korsakoff's syndrome, followed by disturbances of consciousness, neurological symptoms, and severe emaciation. The illness had been triggered by a slight cranial trauma 1 week prior to the apparent onset of symptoms.

Manifestation of various dementias subsequent to cranial trauma have been noted, with the trauma seeming to be a trigger rather than a cause (McMenemey et al. 1950; Behrman et al. 1962), in contrast to the traumatic dementia seen in boxers (Grahmann and Ule 1957).

One of the main and initial clinical features of our patient was Korsakoff's syndrome. The morphological substrate of Korsakoff's syndrome is a disturbance of the Papez-ring, which is one of the essential neuronal circuits for memory.

Mnemonic failure can occur after damage to the corpora mamillaria (Gamper 1928), the fornix (Orthner 1957), or Ammon's horns (Conrad and Ule 1951; Glees and Griffith 1952). In our case, severe damage in the nucleus anterior of the thalamus, a component of the Papez-ring, with the absence of changes in Ammon's horns, fornices, and corpora mamillaria, might have caused Korsakoff's syndrome.

Other neurological symptoms including dementia may have been caused by both cerebral and severe thalamic lesions. It is difficult to attribute a particular clinical feature to specific thalamocortical lesions. The midbrain lesions, however, were responsible for the oculogyric disturbances. The cerebellar symptoms were clinically not manifest and neuropathologically the degeneration was restricted to the olivovermian region.

Neuropathological Aspects

There was widespread and severe thalamic neuronal degeneration with a distinct pattern of predilection. The neothalamus was most severely degenerated. The formatio geniculata and the nucleus ventralis posterior, which belong to the paleothalamus, were moderately to severely affected. The midline structures, i.e., the formatio paraventricularis and the formatio intralamellaris (archithalamus) were completely preserved. Hence, the phylogenetic-ontogenetically younger subnuclei were more severely affected than the older ones. This pattern suggested a "system" degeneration of the thalamus, although the degeneration within some of the subnuclei was not uniform. For example, the nucleus geniculatus medialis was mildly affected, the nucleus geniculatus lateralis was preserved; the oral and caudal parts of the nucleus centralis medialis were varyingly affected. Lack of uniformity in a subnucleus or slight asymmetry in the intensity of changes have been noted by Schulman (1957) and Oda et al. (1972) in their cases of thalamic degeneration.

In our case the thalamic changes were combined with olivovermian degeneration. Oda et al. (1973) stressed the combination of olivopontocerebellar and nigropallidal degeneration in each of their cases of thalamic degeneration. These combinations were also an important point in their argument concerning "system degeneration" in terms of multiple system atrophy. Thalamic degeneration may occur within the framework of various system degenerations, for instance, in cerebellar degenerations or Pick's disease (Martin 1970, 1975). The trivial olivovermian degeneration in our case was apparently an additional change.

Thalamic degeneration may also occur secondarily. A very similar system-like degeneration of the thalamus associated with bronchial carcinoma was described as "paraneoplastic" thalamic degeneration by Daniels et al. (1969). A report by Finlayson et al. (1973) dealt with a myelinolytic process in the thalamus and pons. In our patient, neither malignant neoplasm nor electrolyte anomalies were observed. Also, there was no evidence of vascular changes in the thalamus.

The pathology in the cerebral cortex of our patient was different from that of anoxic encephalopathy. Possibly, it was due to thalamocortical transneuronal degeneration (Pilz and Erhart 1981). Fat granule cells exclusively scattered along the corona radiata suggest this interpretation, but it is not yet clear whether

transneuronal degeneration occurs in the cortex after nerve cell loss in the thalamus.

Differential Diagnosis

There was no status spongiosus in the cerebral cortex or the thalamus. Neuronal loss in the neocortices and allocortices was considered to be transneuronal due to thalamic changes. The pathological changes may resemble the "thalamic form of the Creutzfeldt-Jakob disease" (Garcin et al. 1963; Ogasawara 1973), but the system-bound lesions of primary degeneration in the thalamus oppose this possibility (Fig. 3A).

In view of the distribution of the morphological change in the CNS, a similarity to the Steele-Richardson- Olszewski's syndrome must be considered. However, clinically no typical nuchal rigidity, supranuclear ocular palsy or other signs, except for the oculogyric crisis, were observed. Neuropathologically there were no neurofibrillar tangles in any lesion. Neuronal loss in the thalamus was lacking or obscure in the cases of Steele et al. (1964). From these aspects, the "progressive supranuclear palsy" of Steele et al. may be excluded.

Hitherto, eleven cases of essential degeneration of the thalamus have been reported (Table 1); five cases, including the present case, were Japanese. The mean age of these patients was 47.4 years. Most patients were males; the only two female patients had hereditary idiocy. These observations indicate the need for further case collections and epidemiological studies.

Table 1. Hitherto reported cases of essential thalamus degeneration

Author(s)	Age and sex of patient	Clinical course	Remarks
Stern (1939)	40 years, male	9 months	
Grünthal (1942)	61 years, female	26 years	Familial idiocy
Schulman (1957)	50 years, male	6 months	
Garcin et al. (1963)	56 years, male	9 months	
McMenemey et al. (1965)	51 years, male	13 weeks	
Martin (1970)	65 years, male	6 months	
Oda et al. 1) 1965	18 years, female	14 months	Japanese, familial idiocy
2) 1970	33 years, male	19 months	Japanese
3) 1972	57 years, male	7 years	Japanese
Ogasawara (1973)	36 years, male	2 years and 6 months	Japanese
Pilz and Erhart (1981)	61 years, male	20 years	
Hori et al. (1981)	43 years, male	9 months	Japanese, present case

At present, the syndrome "thalamus degeneration" should be classified as special form of "essential system degeneration" as proposed by Martin (1975).

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