

(0.6) during late pregnancy and 1.7 (0.9) at 6 months postpartum (mean (SD), $p = 0.27$). Table 1 shows the CSF parameters in samples taken before (diagnostic lumbar puncture), during and after pregnancy. Notably, the IgG-Index was significantly higher during pregnancy than before pregnancy or after the delivery in all patients ($p = 0.0390$), but no difference was observed in the number of oligoclonal bands (table 1). Enhanced clinical disease activity was associated with a higher number of CSF cells, as expected (table 1), but no alteration was observed in the subtypes of CSF lymphocytes during versus after pregnancy (data not shown).

To study whether the increased intrathecal IgG production was associated with a systemic Th2 shift, we measured intracytoplasmic IFN- γ and IL-4 production in peripheral blood monocyte cells after phorbol myristate acetate and ionomycin stimulation both during and after pregnancy. The percentage of IFN- γ -secreting cells within the peripheral blood lymphocyte pool was significantly lower during pregnancy than in the postpartum period (2.8 (0.7)% (mean (SEM)) IFN- γ -producing cells during pregnancy and 7.6 (0.8)% during postpartum, $p = 0.003$). The difference in IL-4-producing cells during and after pregnancy was less pronounced (1.0 (0.16)% (mean (SEM)) during pregnancy and 1.8 (0.15)% during postpartum, $p = 0.028$). This resulted in a Th2:Th1 ratio of 0.36 during pregnancy and 0.24 after delivery.

Discussion

This study describes, for the first time, that the production of intrathecal antibodies in patients with multiple sclerosis is higher during late pregnancy than in the postpartum period. A shift towards humoral (Th2)-type immune responses was shown during pregnancy, and it is the most accepted theory to explain the amelioration of Th1-type diseases such as multiple sclerosis and rheumatoid arthritis during pregnancy. Most of the data supporting the Th2 shift during pregnancy are derived, however, from mouse experiments, and the corresponding *in vivo* phenomena in pregnant women are poorly documented. Our finding of non-altered oligoclonal bands is in line with previous studies, which have shown that oligoclonal banding in the CSF of patients with multiple sclerosis is persistent, and not affected by treatment, whereas the rate of IgG production is more susceptible to alterations.⁴

The CNS parenchyma is not a physiological site for B-cell responses and antibody production, but, in multiple sclerosis, B cells are demonstrable in inflammatory infiltrates and in the CSF.⁵ Antibodies are indicative of chronic CNS inflammation and probably contribute to demyelination and axonal damage.⁵ Our data imply that factors other than intrathecal antibodies are crucial in the pathology leading to multiple sclerosis relapses in the postpartum period, as a reduction in the IgG-Index was associated with an increase in the relapse rate. Our data suggest that the consequences of alterations in the immune system leading to a Th2 shift in the periphery reach beyond the blood-brain barrier and strengthen the humoral immune responses within the CNS.

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M Saraste, J Ryyänen

MediCity Research Laboratory, University of Turku, Turku, Finland

A Alanen

Department of Gynecology and Obstetrics, University of Turku

J Multanen, M Färkkilä

Department of Neurology, University of Helsinki, Helsinki, Finland

R Kaaja

Department of Gynecology and Obstetrics, University of Helsinki

L Airas

MediCity Research Laboratory, Department of Neurology, University of Turku

Correspondence to: Dr Laura Airas, Department of Neurology, University of Turku, PO Box 52, 20521 Turku, Finland; laura.airas@utu.fi

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Severe amnesia after a restricted lesion in the left hippocampal body

Severe amnesia is caused by bilateral damage to the medial temporal lobe, specifically cornu ammonis (CA)1 of the hippocampal body.¹ Although some authors have reported that profound amnesia results from a unilateral temporal lobe stroke,² the part of the hippocampus that causes severe amnesia remains unknown. Here, we report the case of a patient who developed severe anterograde amnesia and minimal retrograde amnesia after a focal haemorrhage in the hippocampal body.

A 72-year-old right-handed man was admitted to the International Medical Center of Japan, Tokyo, Japan, in May 1999 because of acute memory impairment. A few days before admission, he started forgetting what he had done and said several minutes earlier, and he could no longer name nearby objects. On admission, he was disoriented as to the year, month and day, and could not recall the names of objects that he had been told to remember a few minutes earlier. His symptoms continued and were persistent 1 month later. MRI T1-weighted images

1 month after onset showed a haemorrhage in the left hippocampal body and in part of the hippocampal tail. The lesion included CA1, CA2 and CA3, the dentate gyrus and subiculum (fig 1), and extended subcortically in the parahippocampal gyrus.

A neuropsychological evaluation was carried out from 34 to 40 days after onset. The Wechsler Memory Scale-Revised score showed that verbal and delayed memory indices were markedly low, whereas the visual memory index was relatively preserved (attention and concentration 79, verbal memory 61, visual memory 79, general memory 65 and delayed recall 55). A comparison of the delayed test raw score total (II) with the first test raw score total (I) implied that both encoding and retrieval were impaired for verbal memory (II/I 0/6, full score 58/58), whereas retrieval was mainly impaired for visual memory (II/I 6/33, full score 47/47). The Benton Visual Retention Test score showed that both immediate figure reproduction (7/10) and reproduction after a 15 s delay (3/10) were impaired. Delayed reproduction was also poor in the Rey-Osterreith Complex Figure Test (copying 36/36, 30 min delay 6/36). Conversely, scores for the Wechsler Adult Intelligence Scale-Revised were normal (verbal intelligence quotient (IQ) 105, performance IQ 121 and full-scale IQ 114). Subtest scores for digit span (9/19; forward 4 and backward 4) and arithmetic (6/19), however, were relatively low. Digit span forward was also 4 when presented visually on a personal computer. These findings suggested impaired short-term memory or working memory.

Remote memory was assessed with an autobiographical memory interview and with the specific questions as described below. The patient could recall autobiographical episodes well, but could not remember public events 2 years before onset. For example, he remembered the British royal wedding of Princess Diana and Prince Charles in 1985, but did not remember Diana's death in August 1997. Furthermore, he remembered the Nagano Winter Olympics in February 1998, the Kobe earthquake in January 1995 and the Tokyo subway sarin gas attack in March 1995. To determine whether there was a temporal gradient in his past memory loss, we gave the patient an 80-question multiple-choice questionnaire on public events during the four decades from 1950 to 1989, divided into four sections with 20 questions for every 10 years.⁴ He showed a slight temporal gradient in these sections, but all these scores were above the normal mean (percentage correct (normal mean for ≥ 70 -year-olds, SD)⁴: 1950s, 95 (53.7, 5.45); 1960s, 85 (55.3, 4.83); 1970s, 75 (58.5, 5.05); 1980s, 70 (66.8, 4.94)).

The patient profile was rated as follows: (1) severe anterograde amnesia that affected verbal memory more than visual memory; (2) minimal retrograde amnesia for the occurrence of public events over the 2 years before onset, with temporally graded event memory loss over the preceding 20 years; and (3) impaired short-term memory.

This patient showed severe encoding and retrieval deficits in verbal memory. This can occur because of a unilateral left hippocampal lesion. A comparison of the reported cases shows that bilateral lesions of the hippocampus or medial temporal lobe can cause moderate to severe anterograde amnesia.¹ Examination of our patient suggested that damage to the unilateral (left) hippocampal

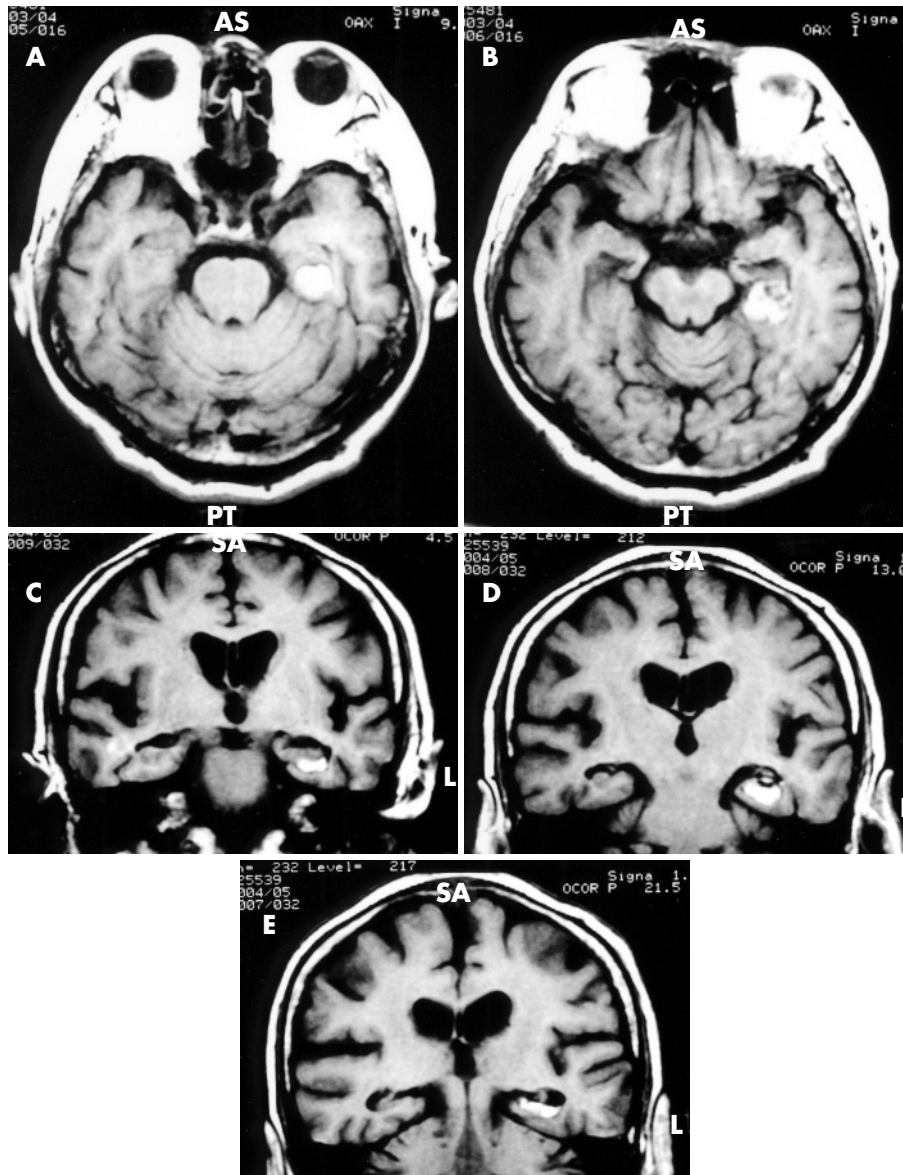


Figure 1 MRI T1-weighted axial (A,B) and coronal (C–E) images 1 month after onset showed a high-intensity area, suggesting a haemorrhage in the left hippocampus. The lesion included cornus ammonis 1–3, dentate gyrus and subiculum, and extended subcortically in the parahippocampal gyrus. The anterior part of the hippocampus—that is, amygdala, entorhinal cortex and hippocampal head—appears intact.

body (CA1–3, dentate gyrus) and subiculum was enough to result in severe anterograde amnesia. As no case report has described circumscribed damage to the amygdala, hippocampal head and entorhinal cortex, it is yet to be clarified whether these anterior lesions alone can cause severe anterograde amnesia.

Retrograde amnesia was minimal in our patient, although a detailed evaluation of his past memory showed a slight temporal gradient in the knowledge of events over the preceding 20 years. Studies on patients with reported amnesia with hippocampal lesions suggested that severe retrograde amnesia was caused by extensive damage to the hippocampal formation^{1,3} or to additional temporal lobe structures. That our patient showed minimal retrograde amnesia with sparing of the amygdala and hippocampal head is consistent with this view.

Another possibility is that the anterior part of the hippocampus (hippocampal head and

entorhinal cortex) is more associated with extensive retrograde amnesia than the hippocampal body. As the entorhinal cortex projects to the medial thalamus, whereas the subiculum (posterior hippocampus lesion in our patient) has connections to the anterior thalamic nuclei,³ it is rational to compare associated amnesic symptoms between the two lesions. Patients with a lesion limited to the anterior hippocampus would thus tend to show the involvement of this area in retrograde memory.

Our patient also showed a reduced digit span, which indicated auditory and visual-verbal short-term memory impairment. Few case reports have referred to digit span in temporal lobe amnesia. One possible explanation for the reduced digit span is that the haemorrhage affected extensive areas in the temporal and parietal lobes.

In conclusion, a comparison of the patient’s lesion and symptoms with those of previous cases with bilateral and unilateral

hippocampal lesions suggests that severe anterograde amnesia can occur after a restricted lesion in the unilateral (left) hippocampal body and subiculum, and that severe retrograde amnesia can be caused by additional damage to the anterior hippocampus.

N Arai, C Shikai, S Fuse, T Shimpo

Department of Neurology, International Medical Center of Japan, Tokyo

Correspondence to: Dr Yasuhisa Sakurai, 1 Kanda-Izumi-cho, Chiyoda-ku, Tokyo 101-8643, Japan; ysakurai-iky@umin.ac.jp

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Opercular syndrome due to non-convulsive status epilepticus in an adult

The Foix–Chavany–Marie opercular syndrome (FCMS), a severe form of pseudobulbar palsy due to bilateral anterior opercular lesions, may be congenital or acquired, persistent or intermittent.¹ FCMS due to epilepsy has been described nearly exclusively in childhood.¹ We report the case of an adult patient in whom non-convulsive status epilepticus (NCSE) manifested with opercular syndrome, and which was completely reversible with treatment for epilepsy.

Case report

A 55-year-old patient with chronic renal failure on haemodialysis was admitted to the orthopaedic surgery department for the treatment of a bilateral humerus fracture. Cognitive and mental functions of the patient were normal before admission. She started to receive oxycodone–acetaminophen four times a day and later oxycodone 10 mg twice a day (total dose of oxycodone 60 mg over 48 h) for pain control. Over the course of 3 days she

became confused and later obtunded. Oxycodone was discontinued. She became more alert and was able to communicate with gestures. Neurological examination, however, showed anarthria and inability to swallow, chew, or move her lips and tongue on command. Comprehension was retained during the whole episode, a fact that was proved after recovery, as the patient remembered specific details and events that had occurred during the entire incident. No focal signs were observed. Corneal, gag and jaw reflexes were preserved. Reflexive buccofacial movements such as yawning or coughing were present. Limb praxis was normal and eye movements were intact. Deep tendon reflexes were weak and no pyramidal signs were elicited. Routine blood tests disclosed mild normocytic anaemia and chronic renal failure, with no change in her haemodynamic status. Infective and inflammatory screens were negative. Computed tomography of the brain showed moderate to severe brain atrophy and bilateral subcortical lacunar lesions. These findings were similar to those observed 1 year earlier. No evidence of a new subcortical infarction was seen. The electroencephalograph (EEG) showed continuous rhythmic delta activity mixed with sharp waves and long periods of spike and wave ictal discharges (fig 1, left panel), consistent with NCSE. Intravenous valproic acid was initiated. Regular haemodialysis was continued. During the next few days she was able to initiate speech, move her tongue and buccoral muscles. She progressively regained her ability to swallow. On EEG performed 24 h after initiation of treatment, the spiky activity seen earlier had disappeared. Diffuse slowing of the background with gradual improvement was observed over a few days. An EEG performed 9 days later was normal (fig 1, right panel).

Two weeks after admission, owing to complete recovery, the treatment for epilepsy was gradually discontinued. Since then, the patient's neurological status and repeated EEGs have been normal.

Discussion

The clinical signs in this patient were consistent with FCMS. This condition, which may be congenital or acquired, persistent or intermittent, includes severe anarthria, loss of voluntary muscular functions of the face and tongue, and impaired mastication and swallowing, with preservation of reflex and autonomic functions.¹ The aetiology of FCMS is heterogeneous: vascular insults in adulthood, such as bilateral subsequent strokes; infections of the CNS, such as herpes simplex encephalitis or acute disseminated encephalomyelitis. FCMS can be congenital, owing to bilateral dysgenesis of the perisylvian region. FCMS as a manifestation of epilepsy has been described nearly exclusively in childhood.^{2,3}

The clinical picture of our patient was initially attributed to an overdose of oxycodone. Only consciousness and not the facial, pharyngeal and lingual and mastication movements, however, improved with discontinuation of the treatment. Uraemic aetiology could not be implicated, as there was no change in the renal status during the whole episode because the patient was regularly haemodialysed.

NCSE was diagnosed only by EEG, which showed an electroencephalographic pattern compatible with the diagnosis. NCSE seems to be associated with a high mortality and morbidity, justifying aggressive treatment.

Oxycodone hydrochloride is an opiate derivative. Oxycodone and its metabolites are excreted primarily through the kidneys. In cases of renal failure, precautions should

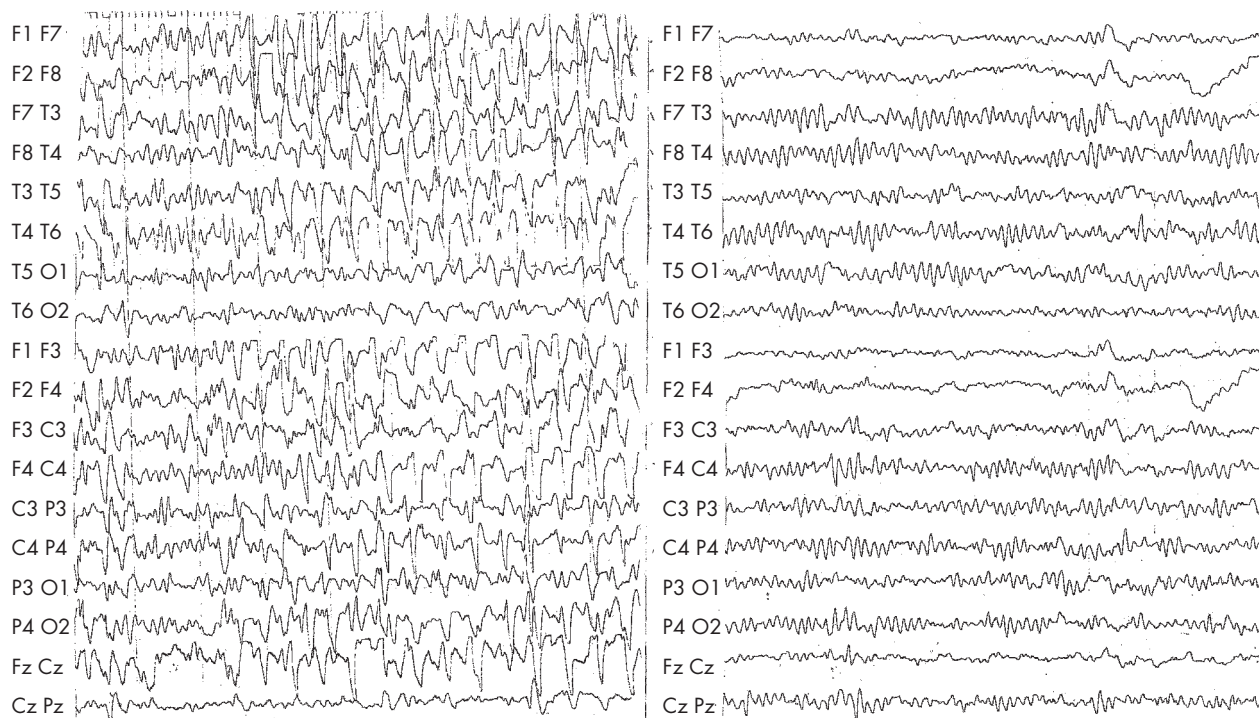


Figure 1 Left panel: electroencephalograph (EEG), recorded during the florid phase of the opercular syndrome, shows diffuse slow-wave activity and generalised repetitive synchronous sharp-wave complexes. Right panel: 9 days later, the EEG shows a 9–10 Hz background rhythm and disappearance of the sharp-wave complexes.