

CASE REPORT

An MRI and neuropathological study of a case of fatal status epilepticus

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We report a case of fatal status epilepticus of unknown origin resulting in acute neuropathological changes in the hippocampus and claustrum.

The case history, brain magnetic resonance images, and results of neuropathological study of the whole brain were obtained.

The subject was a 35 year old male with no significant previous medical history who presented with generalized epileptic seizures progressing to status epilepticus. He died 6 days after developing status epilepticus. Magnetic resonance imaging (MRI) brain scans were performed before and four days after developing status epilepticus. The first scan was normal and the second showed high signal lesions on T2 weighted images in the medial aspects of both temporal lobes and in the right claustrum. Neuropathological studies showed severe neuronal loss in the Sommer section of both hippocampi with early glial reactive changes. Similar changes were seen in the claustrum on both sides. There was no evidence of other causes of brain injury such as infectious encephalitis or global hypoxic–ischaemic change.

The patient died of status epilepticus for which no underlying cause was found despite extensive investigation. In this case the radiological and pathological changes found bilaterally in the claustrum and hippocampus appear to be the direct result of the status epilepticus.

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Key words: status epilepticus; hippocampus; claustrum.

INTRODUCTION

There is a well-established association between status epilepticus and a constellation of neuropathological abnormalities. In adults dying during or shortly after status epilepticus the most constant finding is of acute neuronal ischaemic cell change and astrocytic reaction in the Sommer sector of the hippocampus. Similar changes are seen in the cerebellar cortex, the thalamus, the striatum, and the cerebral cortex. In some cases none of these acute changes are observed¹. Chronic changes of atrophy, neuronal loss, and gliosis (hippocampal sclerosis) are found in many patients with long-standing epilepsy of

temporal lobe origin². There has been debate as to whether the hippocampal changes are the cause or a consequence of status epilepticus³. In many previous case reports the interpretation of the neuropathological findings is complicated by the coexistence of conditions such as infectious encephalitis, and by complications of status epilepticus such as ischaemia or hypoglycaemia which might themselves contribute to the abnormalities subsequently found. We report the magnetic resonance imaging (MRI) and neuropathological findings in a case of status epilepticus with a fatal outcome after 6 days, where no such complications evolved and where no underlying cause was identified.

CASE REPORT

A 35 year old man developed seizures 4 days after the onset of a mild flu like illness. His first fit began as a motor seizure affecting both arms, followed by loss of consciousness and then confusion. He was admitted to hospital after this fit, and shortly after had a generalized tonic-clonic seizure. There was no significant previous medical history, and no history of contact with infectious illnesses, or of alcohol or drug abuse. There was no significant family history. Examination was unremarkable apart from a mild pyrexia and slight drowsiness with disorientation in time. There were no focal neurological signs. CT brain scan on the day of admission (day 4 of the illness) was normal. CSF analysed on day 4 was acellular with normal glucose and a slightly raised protein (0.7 g l^{-1}). Further CSF samples on days 5 and 7 were also acellular. Apart from a neutrophilia of 10.2, routine haematology and blood biochemistry were normal. Microbiological studies were negative, including CSF viral cultures and serology for a range of organisms. A positive polymerase chain reaction result for herpes simplex was obtained from CSF on the second sample but was negative on the first and third samples. There was no rise in herpes simplex titres between days 7 and 14 (1 : 48 both). The patient was treated with intravenous phenytoin and acyclovir, but had a further fit 12 hours after admission. The next day he had four generalized seizures. An MRI brain scan on day seven was normal, and an EEG showed generalized slow wave activity only. At 9 days the patient began to deteriorate with decreasing conscious level and increasing seizure frequency. He developed status epilepticus, phenobarbitone and thiopentone were added to his treatment, but the seizures were not controlled. The patient continued to have minor motor activity suggestive of ongoing epileptic activity. A repeat EEG at 12 days showed periodic complexes and frequent seizure discharges consistent with continuing status epilepticus. A repeat MRI scan was performed at 13 days (Figs 1 and 2). Treatment was withdrawn at 15 days and the patient died of cardiovascular and respiratory complications.

RESULTS

Radiology

The patient had MRI scans on days 7 and 13 of his illness, that is 2 days before and 4 days after developing status epilepticus. The first scan was normal (not shown). The second shows high signal change on T2 weighted images in the medial aspects

of both temporal lobes (Fig. 1). There is high signal change in the right claustrum and possibly also in the left claustrum (Fig. 2).



Fig. 1: A T2 weighted axial MRI brain scan performed four days after developing status epilepticus showing high signal lesions in the medial temporal lobes bilaterally.

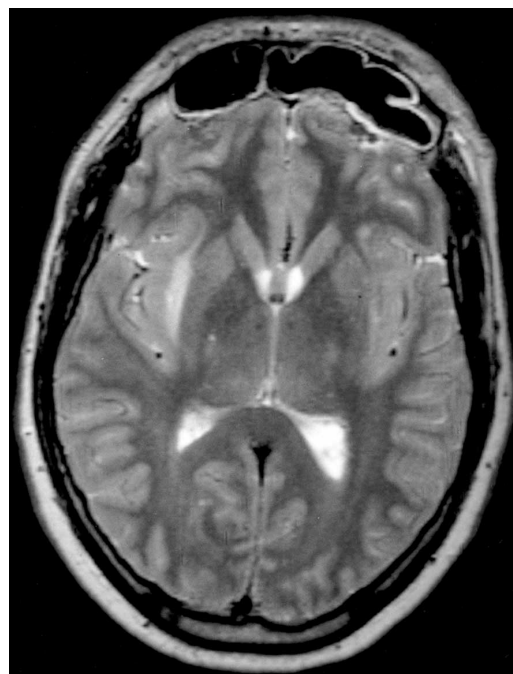


Fig. 2: A T2 weighted axial MRI brain scan performed four days after developing status epilepticus showing high signal change in the right claustrum and possible early signal change in the left claustrum.

Neuropathology

Macroscopically the brain was slightly swollen with no other visible abnormality. There was marked neuronal ischaemic cell change and acute astrocytic reaction in the Sommer sector and end folium of both hippocampi (Fig. 3). Similar changes were seen in the claustrum bilaterally. There was no evidence of encephalitis. Immunocytochemical staining for abnormal prion protein was negative. Examination of the arterial watershed regions showed no evidence of established global hypoxic ischaemic change.

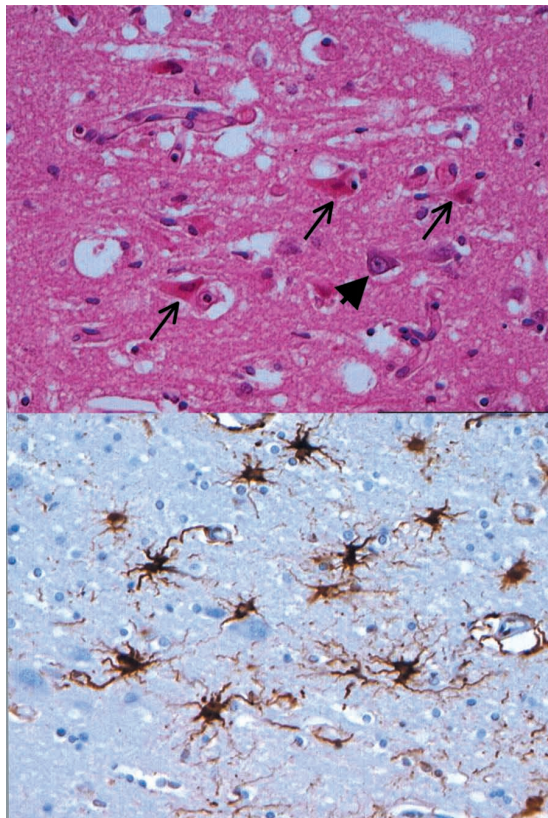


Fig. 3: (Upper panel) Pyramidal layer of the hippocampal Sommer sector, showing acutely ischaemic neurones (arrows) and one more normally preserved neurone (arrow head). Haematoxylin-Eosin, $\times 300$. (Lower panel) Claustrum, showing acutely reactive astrocytes. Immunocytochemistry for glial fibrillary acidic protein, $\times 300$.

DISCUSSION

We have presented a case of status epilepticus of unknown cause with a fatal outcome. The patient had no history of epilepsy. There was no history or evidence of drug or alcohol abuse and his clinical course did not suggest these as causes of his epilepsy. He had a brief non-specific prodromal illness with mild fever, but there was no evidence of viral encephalitis. The cause of his epilepsy remains unclear.

There are previous reports of status epilepticus arising *de novo* in infectious disorders (for example in legionnaires disease) without evidence of direct CNS infection⁴. It is possible that the patient reported here likewise developed status epilepticus as a para-infectious phenomenon, but extensive microbiological investigation did not identify an organism.

In our case the radiological and neuropathological studies combined suggest evolving lesions in the hippocampal regions and claustrum bilaterally. The radiological findings in the medial temporal lobes are similar to those previously reported in MRI studies of status epilepticus^{5,6}. The neuropathological changes are consistent temporally with death 6 days after onset of status epilepticus. The association of hippocampal abnormalities with chronic epilepsy² and status epilepticus¹ is well established. The nature of the neuropathological changes found depends on how long standing they are. In early cases there are ischaemic changes in neurones in vulnerable areas (the Sommer sector and end folium of the hippocampus, the cerebellar and cerebral cortex, thalamus, and striatum) with acute astrocytic reaction. In later cases there is neuronal loss and gliosis in these areas. It is generally accepted that status epilepticus directly results in hippocampal sclerosis, but many of the reports are of cases with encephalitis, with severe complications of status epilepticus such as hypoxia or hypoglycaemia, or with other major systemic illness. It is possible that these other factors may contribute to the hippocampal abnormalities seen in these cases. In our case, no underlying cause was found despite extensive investigation. The CSF and serological studies showed no evidence of encephalitis, and herpes simplex encephalitis was excluded by neuropathology. The patient did not develop major systemic disturbances such as hypoxia, and the neuropathological studies excluded significant global cerebral hypoxia. These factors suggest that in this case, the abnormalities detected on MRI and on neuropathology are a direct result of the patient's status epilepticus. An alternative explanation would be that the hippocampal changes caused the status epilepticus, rather than the other way round. We believe that the clinical picture, the appearance of new changes on MRI after onset of status epilepticus, and the neuropathological changes found, make this explanation unlikely.

There have been few reports of abnormalities in the claustrum in association with epilepsy. Neuropathological changes in the claustrum have been reported in mature rats after kainic acid induced limbic seizures⁷, and in epileptic beagles⁸. Paediatric cases have been reported in which MRI demonstrated reversible lesions in the claustrum in association with status epilepticus⁹ and herpes simplex encephalitis¹⁰.

It is possible to speculate that there might be non-reversible but asymptomatic neuropathological changes in these cases. Margerison and Corsellis² performed an extensive survey of neuropathological changes in chronic epilepsy and status epilepticus and reported no abnormalities in the claustrum. The findings in our case therefore appear to be unusual but are likely to be due to the patient's status epilepticus.

REFERENCES

1. Corsellis, J. A. N. and Bruton, C. J. Neuropathology of status epilepticus in humans. In: *Advances in Neurology, Vol 34, Status Epilepticus*. (Eds A. V. Delgado-Escueta, C. G. Wasterlain, D. M. Treiman and R. J. Porter). New York, Raven Press, 1983: pp. 129–139.
2. Margerison, J. H. and Corsellis, J. A. N. Epilepsy and the temporal lobes. A clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. *Brain* 1966; **84**: 499–530.
3. Wasterlain, C. G., Fulikawa, D. G., Penix, L. and Sankar, R. Pathophysiological mechanisms of brain damage from status epilepticus. *Epilepsia* 1993; **34** (Suppl.): S37–S53.
4. Peliowski, A. and Finer, A. A. Intractable seizures in legionnaires disease. *Journal of Pediatrics* 1986; **109**: 657–658.
5. Meierkord, W., Wiesmann, U., Niehaus, L. and Lehmann, R. Structural consequences of status epilepticus demonstrated with serial magnetic resonance imaging. *Acta Neurologica Scandinavica* 1997; **96**: 127–132.
6. Tien, R. D. and Felsberg, G. J. The hippocampus in status epilepticus: demonstration of signal intensity and morphologic changes with sequential fast spin-echo MR imaging. *Radiology* 1995; **194**: 249–256.
7. Nitecka, L., Tremblay, E., Charton, G., Bouillot, J. P., Berger, M. L. and Ben-Ari, Y. Maturation of kainic acid seizure—brain damage syndrome in the rat II. Histopathological sequelae. *Neuroscience* 1984; **13**: 1073–1094.
8. Montgomery, D. L. and Lee, A. C. Brain damage in the epileptic Beagle dog. *Veterinary Pathology* 1983; **20**: 160–169.
9. Sperner, J., Sander, B., Lau, S., Krude, H. and Scheffner, D. Severe transitory encephalopathy with reversible lesions of the claustrum. *Pediatric Radiology* 1996; **26**: 769–771.
10. Kimura, S., Nezu, A., Osaka, H. and Saito, K. Symmetrical external capsule lesions in a patient with herpes simplex encephalitis. *Neuropediatrics* 1994; **25**: 162–164.