Thalamo-frontal Psychosis

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A 43-year-old man presented with an 18-month history of acute-onset cyclical behavioural change affecting mood, appetite, sleep, and energy levels. This had followed an initial episode of transient drowsiness which lasted 24 hours. On examination, there was some evidence of visual memory and frontal lobe deficits. A brain CT scan showed bilateral thalamic infarcts and a brain SPECT scan showed bilateral hypoperfusion of the frontal lobes. To our knowledge, this is the first reported case of thalamic infarction associated with acute-onset cyclical affective psychosis with clinical and neurophysiological features of frontal lobe syndrome. The case also highlights the possible role of thalamo-frontal circuits in the pathogenesis of the Kleine-Levin syndrome.

British Journal of Psychiatry (1993), **163**, 113–115

Atypical psychiatric syndromes have been reported following thalamic infarction (Bogousslavsky *et al*, 1988). There are often no neurological disturbances of note, so that the infarcts, which are uncommon, may be overlooked. There is evidence that damage to the thalamus, or to a sufficient part of the thalamocortical projection, plays a key role in the occurrence of ipsilateral cortical hypometabolism, and this in turn is probably responsible for the psychiatric disturbances (Pappata *et al*, 1990). We report a case of bilateral thalamic infarction which we believe illustrates both the complexities of diagnosis and the possible underlying mechanisms in such cases.

Case report

A 43-year-old right-handed, married man who ran his own business was referred to us by a consultant neurologist for assessment of his mental state. He appeared to have undergone a complete change of personality and it was not clear whether this was a primary psychiatric disorder, or whether there was an organic or, alternatively, a purely behavioural, basis for it.

One and a half years previously, apparently quite well, he was watching television when he suddenly felt himself 'going' for a few seconds and then lost consciousness. His wife, noticing that he slumped, found him unrousable, with some mild drooping of the left side of the mouth. In hospital he was drowsy but resisted some parts of the examination. On review by a psychiatrist the next morning, he was alert but complained of having been depressed and lacking in energy over the previous year, since he had been compelled by the council to close one of his shops. His wife, however, described him as a happy man and commented that he had been cheerful and lucid until the collapse, whereas he now seemed apathetic, as well as fatuous, giggling, and treating questions as a joke. He had mild left-sided pyramidal signs and was referred to the neurologists. After four days he was discharged, as his disorder was thought to be 'non-organic'. There was a further brief readmission one month later because of drowsiness, apathy, and memory impairment. A computerised tomographic (CT) scan at this point showed a small infarct in the right thalamus.

Over the subsequent six months he was 'like a zombie', sleeping and eating excessively (especially his children's crisps and sweets), and behaving inappropriately (e.g. going out in his slippers to get fish and chips). On average, every three weeks, he would suddenly become alert and would play with the children, begin hatching plans, sleep little during the night, and the next day he would be excitable and elated. After about 36 hours he would suddenly relapse to his former apathetic condition. He was thought to be malingering. A consultant psychiatrist to whom he was eventually referred treated him with lofepramine, imipramine, and 12 sessions of electroconvulsive therapy (ECT) with little or no improvement.

There was a family history of cardiovascular disease and depression on the father's side. There was no personal, medical, or psychiatric history of note. He rarely drank alcohol and did not smoke.

On admission he was overweight and normotensive. His manner was histrionic and tearful, but he sometimes joked or smiled somewhat incongruously. He was subjectively depressed and had ideas of guilt about the effect that his condition had had on work and family life. He had poor self-esteem but no feelings of hopelessness. There was no diurnal mood variation; other biological symptoms have been described above. He stated that he was suffering from "psychological depression" and complained that he was like "an engine that won't tick over".

Routine investigations, including full blood count, erythrocyte sedimentation rate, full biochemical profile, thyroid function tests, serum B12, folate, and syphilis serology, were normal or negative. A pituitary endocrine screen was normal but fasting cholesterol was slightly raised, and he was placed on a low-cholesterol diet. Autoimmune screening revealed raised anti-nuclear factor and DNA-binding but when these were repeated, they were normal; cardiolipin levels were also normal. An echocardiogram showed a small pericardial effusion which was asymptomatic. Routine and activated electroencephalograms (EEGs) were normal, as were brain-stem evoked potentials. A CT scan of the head showed bilateral thalamic infarcts in the region of the midline nuclei

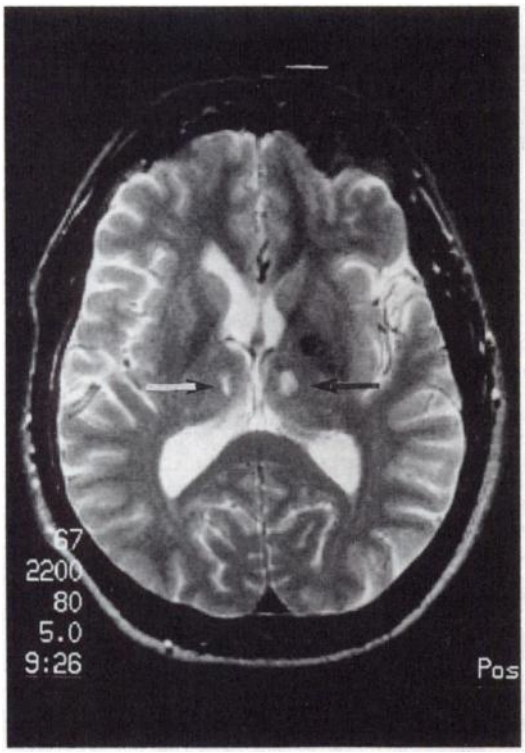

Fig. 1 Brain CT scan showing bilateral thalamic infarction.

(see Fig. 1). A single-photon emission computerised tomography (SPECT) scan (using labelled HMPAO) showed severe hypoperfusion of both frontal lobes (left more marked than right) and of both thalami. There was also a mild increase in tracer deposition in the upper mesial parietal cortex bilaterally. A cerebral digital subtraction angiogram was normal.

Neuropsychological assessment revealed a full-scale IQ of 107 and mixed performance on memory tests. The main deficit was in delayed recall of the Rey-Osterrieth figure (Osterrieth, 1944/45). There were no language or perceptual deficits. Frontal testing was within normal limits apart from a particularly poor performance in both parts of the Trail Making Test (Armitage, 1946), and the Cognitive Estimates Test (Shallice & Evans, 1978).

Despite an appearance of depression, his libido remained intact, and he was sexually disinhibited in his approaches to women on the ward. The most striking feature of his mood was profound apathy, and he became quite irritable when prompted to get out of bed. His self-care was poor, and he ate in excess. He was treated with imipramine and a strict behavioural programme. There were two episodes of elation: the first, lasting about two days, occurred six weeks after admission; and the second, which was more prolonged, at 12 weeks. This episode was frankly manic; he laughed, prayed and cried, and had a labile affect, marked pressure of speech and flight of ideas, lack of sleep, and increased appetite. Although his mental state was not accessible at the time, it has since transpired that during this episode he suffered delusions of self-reference and grandiosity and visual hallucinations. From this point his mood gradually settled, he became sociable and cooperative, his sleep and appetite reverted to normal, and on discharge he had been euthymic for five weeks. A month later, however, he had a final brief episode of increased activity. He was then started on lithium therapy and has for the last six months remained euthymic. He still feels, however, unable to return to work.

Discussion

It is probable that the infarct to the right (and less certainly the left) thalamus occurred at the time of the original episode. Aetiological factors for the infarcts could have been hypercholesterolaemia against the background of a family history of cardiovascular disease. The mild, transient left-sided pyramidal signs may represent an acute oedematous reaction affecting the adjacent posterior limb of the internal capsule. A similar picture was described by Boiten & Lodder in 1990.

The sudden onset of grossly altered mood and behaviour is not typical of a functional depressive disorder, and taken with evidence of periodic hypersomnia, hyperphagia, and possibly hypersexuality is suggestive of an organic cause.

Additional evidence for an organic basis is provided by the poor performance on some tests of fronto-subcortical function and by problems with visuo-spatial recall. The latter have been reported in association with non-dominant thalamic lesions (Speedie & Heilman, 1982).

Affective disturbance is highly characteristic of non-dominant thalamic infarction and usually takes the form of apathy, lack of initiative, and some irritability (Bogousslavsky *et al*, 1988). Our patient conformed to this pattern but, in addition, showed evidence of facetiousness and inappropriate behaviour which on occasion became frankly manic. Only one case with similar features has been reported (Bogousslavsky *et al*, 1988). The cyclical or periodic nature of the disorder in our patient was in many ways suggestive of the Kleine-Levin syndrome, although some authors would exclude obvious organic factors for this diagnosis. If this premise is rejected, however, this case would provide fresh evidence for the role of the thalamus rather than the hypothalamus in the pathogenesis of this disorder (Smolik & Roth, 1988).

The mechanism is likely to involve the concept of diaschisis, first described by von Mannikow in 1914 (Szelier *et al*, 1991). The term refers to a reduction

of metabolic activity in distant brain structures which is most often implicated in subcortical stroke (Pappata *et al*, 1990).

The advent of functional imaging has made this phenomenon easier to study. Scans of patients with thalamo-capsular or pure thalamic stroke reveal ipsilateral cortical hypometabolism and this is associated with neuropsychological deficit (Baron *et al*, 1989). As neither phenomenon occurs in pure capsular infarction, both appear to be dependent on thalamic involvement (Pappata *et al*, 1990). Baron noted that thalamo-cortical pathways include non-specific systems which project diffusely in the ipsilateral cortex. One of the functions of these pathways is to relay the ascending reticular activating system which modulates hemisphere arousal: disruption might lead to dysfunction and hence hypometabolism in cortical neurones.

A more recent study suggests that infarcts in the medial thalamic nuclei may lead to particularly marked hypoperfusion of the frontal lobes and basal ganglia (Szelier *et al*, 1991). Both the clinical picture and the SPECT phenomena in our patient accord with this finding. Disruption of specific basal ganglia-thalamo-frontal circuits, which have been extensively reviewed elsewhere (Alexander *et al*, 1990), probably mediates this more specific effect on the frontal lobes.

Although neuroimaging in affective disorders have yielded only tentative conclusions, frontal involvement has been a consistent finding, and hypometabolism in the frontal region, especially in the left dorsal antero-lateral prefrontal cortex, has been shown in patients with depression (Baxter *et al*, 1989).

A further unusual feature of this case is the length of time over which the clinical picture extended, as most patients show almost full recovery at one year (Cambon *et al*, 1987).

Conclusion

There has been one previous case report of thalamic infarction associated with an acute-onset frontal lobe syndrome. Like ours, this began with transient impairment of consciousness and eventually resolved. Other cases have been associated with apathy. However, to our knowledge, this is the first reported case of a cyclical psychosis with distinct manic and depressive features. Taken with other reports of affective disturbance in thalamic infarcts, it suggests the concept of a 'thalamo-frontal psychosis' which may be mistaken for a functional affective disorder. In addition, these psychiatric disturbances, in the context of periodic hypersomnia and hyperphagia, point to the role of the thalamofrontal axis in the pathogenesis of the Kleine-Levin syndrome.

References

ALEXANDER, G. E., CRUTCHER, M. D. & DELONG, M. R. (1990) Basal ganglia-thalamo-cortical circuits: parallel substrates for motor, oculomotor, 'prefrontal' and 'limbic' functions. In *Progress in Brain Research* (eds H. B. M. Uylings, C. G. van Eden, J. P. C. de Bruin, *et al*). Elsevier.

ARMITAGE, S. G. (1946) An analysis of certain psychological tests used for the evaluation of brain injury. *Psychological Monographs*, **60** (no. 277).

BARON, J. C., LEVASSEUR, M., MAZOYER, B., *et al* (1989) The link between cortical hypometabolism and neuropsychological deficit after thalamic lesions: a PET study. *Journal of Cerebral Blood Flow and Metabolism*, **9** (suppl. 1), S740.

BAXTER, L. R., SCHWARTZ, J. M., PHELPS, M. E., *et al* (1989) Reduction of prefrontal cortex glucose metabolism common to three types of depression. *Archives of General Psychiatry*, **46**, 243–250.

BOGOUSSLAVSKY, J., FERRAZZINI, M., REGLI, F., *et al* (1988) Manic delirium and frontal-like syndrome with paramedian infarction of the right thalamus. *Journal of Neurology, Neurosurgery and Psychiatry*, **51**, 116–119.

BOITEN, J. & LODDER, J. (1990) Ataxic hemiparesis following thalamic infarction. *Stroke*, **21**, 339–340.

CAMBON, H., BARON, J. C., PAPPATA, S., *et al* (1987) Recovery of metabolism after thalamic lesions in humans: a manifestation of plasticity? *Journal of Cerebral Blood Flow and Metabolism*, **7** (suppl. 1), S194.

OSTERREITH, P. A. (1944/45) Le test de copie d'une figure complexe: contribution a l'etude de la perception et de la memoire. *Archives de Psychologie*, **30**, 205–353.

PAPPATA, S., MAZOYER, B., TRAN. DINH, S., *et al* (1990) Effects of capsular or thalamic stroke on metabolism in the cortex and cerebellum: a positron tomography study. *Stroke*, **21**, 519–524.

SHALLICE, T. & EVANS, M. E. (1978) The involvement of the frontal lobes in cognitive estimation. *Cortex*, **14**, 294–303.

SPEEDIE, L. J. & HEILMAN, K. M. (1982) Amnesic disturbance following infarction of the left dorsomedial nucleus of the thalamus. *Neuropsychologia*, **20**, 597–604.

SMOLIK, P. & ROTH, B. (1988) Kleine-Levin syndrome. Ethiopathogenesis and treatment. *Acta Universitatis Carolinae*, monograph **128**, 1–94.

SZELIER, B., HERHOLZ, K., PAWLIK, G., *et al* (1991) Widespread functional effects of discrete thalamic infarction. *Archives of Neurology*, **48**, 178–182.

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