BILATERAL INFARCTION OF THE ANTERIOR CINGULATE GYRI AND OF THE FORNICES

Report of a Case

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SUMMARY

A 70-year-old woman had complex behavioural changes of sudden onset. The symptoms consisted of indifference, docility and inappropriate urination, but predominantly in a lack of attention. She was unable to maintain the attention necessary to perform a goal-directed activity and she was distractable by any stimulus, such as a sound, an object, or a word, which might induce behaviour irrelevant to the preconceived activity. She also exhibited a confabulatory-amnestic syndrome.

Neuropathological examination of the brain revealed infarcts in the territories of both anterior cerebral arteries. The rostral part of the anterior cingulate gyrus (Acg), small areas of the adjacent medial prefrontal cortex, and the underlying white matter were destroyed bilaterally. Infarction involved the deep territory of the left anterior cerebral artery, with a bilateral lesion of the fornices.

This cingulate damage was more restricted than the Acg lesions reported in some cases of akinetic-mutism, which extended more caudally, but was presumably larger than the lesions created in psychosurgery. The impairment of attention was analyzed according to the possible roles of the cingulate and of the fornix lesions as causing a dysfunction between the frontal lobes and the hippocampal formations.

INTRODUCTION

Clinical-anatomical cases of bilateral infarction of anterior cingulate gyrus (Acg) have rarely been reported. The clinical consequences have been akinetic-

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mutisms (Nielsen and Jacobs 1951; Amyes and Nielsen 1953; Barris and Schuman 1953). We report a case in which the patient had no reduction of motor or speech activities, but showed complex behavioural changes, and principally a lack of attention. Infarction in both anterior cerebral arteries territories affected bilaterally the rostral part of Acg and the fornices.

CASE REPORT

Mrs D.F., 71 years old, was admitted to hospital because of sudden loss of consciousness, which had lasted 5 hours. One year before admission, she experienced brief loss of consciousness, without any sequelae. On examination she was wide awake. There was no motor or sensory impairment. A right Babinski's sign, a slight bilateral grasp reflex and a strong sucking reflex were noticed. Generally her motor activity was not decreased but it followed no organized plan. She handled objects which were in reach, walked aimlessly in her room entered other bedrooms and followed the medical staff during the visit. Mictions were uncontrolled, occuring anywhere the patient was, without bothering her or affecting her activity.

Standard neuropsychological examination could not be done, because of marked lack of attention. She was immediately distracted by a noise, an object, or a word. Orders or questions had to be incessantly repeated to obtain a correct response. Even during eating her attention had to be continually directed. For example, while eating correctly, the patient suddenly dipped her napkin into her glass and sucked at it, or cleaned her table with it. Every time she was shown an object silently, whatever her activity, she stopped, seized the object and used it properly, as if it was a normal thing to do. This compulsive use of things was such that, once having fallen on her knees accidentally, she started polishing the bars of her bed with her sheet.

She was absolutely indifferent. She expressed no emotion, wearing a kind half-smile on her face. If she was reproached with her misbehaviour, for instance urinating in front of everybody, or walking about naked, she would agree. If one insisted on her incoherent and contradictory attitude, she would apologise, or would give a playful or whimsical answer. Her serenity was not dampened when she was reminded of the painful events of her life. She would always agree with everyone. She was quite helpful and docile and never refused to give a hand to her neighbours. She expressed neither hunger nor satiation. For example, once she was left 24 hours without any food and she did not complain while her neighbours were being served. During this fast she answered that she had not eaten very much, or she invented an imaginary meal, but she never said that she was hungry. The first time she ate after the period of fasting, she showed neither eagerness, nor satisfaction and as usual she had to be urged to go on with her meal. A few days later she ate two normal meals served with only half an hour interval without looking surprised.

Nociceptive stimulation produced a reaction showing that they were actually painful. But when such stimulation was repeated, each seemed to surprise the patient as if it was the first one, and was followed by an immediate return to her usual behaviour. It was the same with visual or auditory stimulation. For instance, any clapping startled her even though it was regularly repeated for a long time.

It was difficult to test most of her higher functions, her performances varying exceedingly, according to her attention. Her speech, spontaneously reduced, could be normal and even fast. A hesitation upon the choice of a phoneme, however, resulted sometimes in a neologism. It was impossible to obtain a logical sequence. Here is an example of a dialogue, in which numerous admonitions by the examiner have been deleated for conciseness:

Where is Rome? and Moscow? Do you know New York? In which country is New York? Of course not! Where are those people? Who are those people? and these women (nurses)? Who am I? In Italy At Church Yes, I have been there Moscow Italy They are in factories They are X (untranslatable neologism) They work in a factory A cousin A dentist

Why are you here?
But where are you?

Another time

Why are you here?

I have been asked about the turnover At my aunt's

Because I liked it. This morning I was to go shopping but I stayed. This afternoon I am going to the photographer's because I have got skin growing on my nose, to send photographs to my daughter.

Are you happy or sad?

I am free, which is not so bad.

Subject to necessary encouragement and with occasional fancies, designation, denomination of objects and execution of simple gestures were quite correct. It was impossible to obtain a sentence constructed from a given word, often used however one minute later in spontaneous speech. Defining words, or explaining proverbs led to incoherencies. Reading was sometimes correct and sometimes the patient read hesitatingly, with paralexies, and then stopped. Writing her surname, Christian name and even a dictated sentence was sometimes possible. Usually the patient would spontaneously scrible circles. She could make an easy calculation, as long as her attention was directed. Problems were not solved, the facts giving rise to word associations. The first part of a multiplication could be done correctly, but, instead of adding in the last stage, the patient kept on multiplying. There was no real apraxia, but a previously executed instruction could disturb the new programm. A spontaneous or copied drawing must be correctly performed. She did not question unreasonable sentences. She could make easy comparisons (daisy and rose, milk and water, etc....).

Orientation in time and space was impaired, but she could find her own bed and go to the toilet. Formal memory testing was impossible to achieve, because of her lack of attention and distractibility. Repeated attempts at testing showed her inability to answer most questions exploring memory. Remote events were very difficult to recall. The number and names of her children were given at random but she remembered that one of them had died from meningitis. She knew that Maurice Chevalier was a singer and that Edith Piaf was dead. She had a marked anterograde amnesia. She could not recall what she has been eating a few minutes before. The subject of conversation was not retained, and if she was immediately questioned about it, she answered sometimes that she did not remember or that she did not know, but confabulations were also numerous. The digit span was usually of four, but once, seven digits were reproduced, in a rare moment of sustained attention. Besides verbal memory evaluation, her memory-based behaviour was also impaired. She met every person as if for the first time and she did not make any distinction apparently, between familiar people — roommates, nurses and doctors — and occasional visitors.

Other investigations were essentially normal. Blood pressure was 140/80 mmHg. Cardiac examination and ECG were normal. There was no vascular bruit. The EEG showed an alpha rythm of 6-8/s and irregular delta waves, mainly in the left frontal region. The ^{99m}Te brain scan was normal.

Her state essentially did not change throughout the entire 20 months of follow up, until she died suddenly.

NEUROPATHOLOGICAL FINDINGS

Post-mortem examination revealed an old myocardial infarction, with fresher lesions that were interpreted as the cause of death. Gross examination of the fixed brain (1165 g) showed an old, tan-coloured infarction, in the territories of both anterior cerebral arteries (ACA). Microscopic examination was performed on serial coronal sections after celloidin embedding. From the genu of corpus callosum to the mammillary bodies, sections were examined every 750 μ m. Sections were stained with hematoxylin and eosin, Loyez and Nissl stains.

The old cystic lesions with hemosiderin deposits destroyed both Acgs (area 24 of Brodmann) from the corpus callosum to the cingulate sulcus (Fig. 1). In the sagittal



Fig. 1. Coronal sections of brain demonstrating (A) infarct lesions of the rostral Acgs and adjacent medial frontal cortex, (B) softening of the Acg and of the underlying white matter, secondary demyelinisation, and infarct in the deep territory of the left anterior cerebral artery, (C) destruction of the anterior pillars of the fornix, and (D) atrophy in the left thalamus and absence of infarct lesion in posterior parts of the brain. (Loyez stain).





Fig. 2. Sagittal and coronal illustrations summarizing the infarct lesions (hatched areas).

direction, only the portion of Acg located around the genu of corpus callosum was affected, leaving undamaged the caudal part of Acg (Fig. 2). Lesions extended slightly more caudally on the right side. They overlapped slightly on the neighbouring cortical areas of the medial aspect of the frontal lobe (area 32 rostrally and area 9 dorsally) and a small encroachment was present at the top of the interhemispheric fissure on the left side. The underlying white matter, arcuate fibers and cingulum bundle were also damaged on both sides. Secondary demyelinisation was present in the anterior part of corpus callosum which was thinned and in the medial parts of the frontal lobes. The caudal part of Acgs, the posterior cingulate gyri, medial part of areas 6 and paracentral lobules were free of lesions, as was the remainding of cortex. Similar old infarcted cystic lesions were also present in the deep left ACA territory. They destroyed the more rostral parts of the head of the caudate and lenticular nuclei, but only on their medial and ventral aspects. The neighbouring portion of anterior internal capsule, the left fibers of anterior commissure and the anterior part of the temporal stem were also involved. In addition, at the level of the anterior commissure, the pillars of the fornix were severed, completely on the left, sub-totally on the right side.

The mammillary bodies were shrunken with neuronal loss and gliosis, predominantly on the left side. Similar changes were found in the anterior and mediodorsal nuclei of the thalamus. Hypothalamus and septal nuclei were unaffected by the infarct. The brain stem was normal.

The circle of Willis showed slight atheroma without stenosis. The initial portion of the left ACA was narrow but patent. On the right it was wide. An anterior communicating artery was present. No occlusion was found anywhere.

DISCUSSION

Bilateral infarctions of the Acgs have been previously reported (Nielsen and Jacobs 1951; Amyes and Nielsen 1953; Barris and Schuman 1953). In these cases the patients showed a state of akinetic-mutism and death occurred rapidly, sometimes in a context of autonomic nervous disorders. Neuropathological examinations revealed cortico-subcortical infarctions, extending along the whole Acgs from the genu to the middle of the corpus callosum, thus involving much more caudal regions of Acg than in the present case. Moreover, lesions in these cases overlapped to some degree onto the medial parts of the frontal lobes, involving, at least on one side, the supplementary motor area. These facts could be determinant in the genesis of akinetic-mutism as suggested by 3 other case reports (Buge et al. 1975) and by the constatation of a dramatic, but transient, reduction of motor activity and speech following unilateral lesions of the caudal Acg and the contiguous supplementary motor area (Laplane et al. 1977; Madseu et al. 1978). In the present case, the Acg lesion concerned only the rostral part of the Acgs, just around the genu of the corpus callosum, leaving undamaged the caudal part of Acg that has been described as transitional between a limbic cortex and a motor type of cortex (Sanides 1972; Braak 1976). The medial premotor cortex was unaffected. These facts could account for the absence of reduction in motor activity.

Bilateral lesions of Acgs have been performed for the surgical management of psychiatric illness or intractable pain. Operative procedures differed greatly in the various studies. Some of the operations consisted of cutting the cingulum bundle, which created only small cortical lesions (Brown and Lighthill 1968; Ballantine et al. 1977; Long et al. 1978). Others consisted in cingulectomies, in which the rostral part of the Acg were excised, bilaterally, under direct visual control (Whitty et al. 1952; Le Beau 1954). After such cingulectomies, some degree of docility, indifference, and a slight loss of depth in general interests and pursuits were mentioned (Tow and Whitty 1953). These changes might be transient. A short

period of confusional state (Whitty and Lewin 1957) and of memory impairment (Whitty and Lewin 1960) were also described. The more constant result, after such operations, in man and in monkeys (Ward 1948; Glees et al. 1950; Showers 1959), can be termed a lowering of emotional reactions. Our patient showed the same emotional changes, but no intense disturbance of attention, as in our patient, has been described after cingulectomy or cingulotomy. There is a considerable discrepancy between the clinical picture of our patient and the post-operative states of the cingulectomized patients. This discrepancy can be explained by two main facts. First, in the absence of anatomical verification in cingulectomies, the brain removal is imprecise and, possibly, often less extensive than our patient's cingulate lesion. Moreover, evaluation of eventual behavioural changes is difficult, because of the usually severe psychiatric illness. However, it can be presumed that bilateral rostral Acg lesions do not produce a massive impairment of attention. The second fact which may account for the intense behavioural changes of our patient is the presence of associated lesions. The presumed clinical consequences of each of these associated lesions, i.e. damage to the fornices and to the frontal cortex adjacent to Acgs, will be now consecutively analysed.

A review of case reports of bilateral fornix lesions in man, subsequent to surgical section (Dott 1938; Cairns and Mosberg 1951), tumours (Woolsey and Nelson 1975) or following infarction (Brion et al. 1969) did not provide examples of behavioural changes similar to those of our patient. Brion et al. (1969) reported a clinical-anatomical observation of occlusion of the left anterior cerebral artery. In the superficial territory there was only a small partial softening of the left Acg adjacent to the corpus callosum. Infarction in the deep territory was a little more extensive than in our case. This patient had a typical Korsakoff psychosis, but the clinical state could not be considered as a severe dementia, with major attention impairment. From this comparison it seems that the bilateral fornix lesions and the left partial involvement of caudate, putamen, and anterior limb of internal capsule, alone, were not responsible for our patient's clinical syndrome.

Memory functions were difficult to analyze in the present case because of the major disturbances of attention. A specific deficit in memory processing on the one hand, and the inability to concentrate on the other hand, may be both responsible for the apparent memory defects. However, the patient's performance seemed to be better preserved in other cognitive functions than in memory. Moreover, the fact that very simple and familiar items, such as her birthdate, husband's name, number and names of her children, could not be reproduced, may be considered as an argument for specific memory impairment. Thus a confabulatory-amnestic syndrome with anterograde and retrograde amnesia was probably present in our patient. Any form of learning was impossible. The phenomenon of habituation to repeated external stimuli, which is considered to be the most elementary form of learning, was also abolished.

Some clinical disorders of our patient, such as docility, indifference, urination and grasping reflex are common features of a frontal lobe syndrome. The distractibility by irrelevant stimuli and the inability to sustain goal-directed

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behaviour, have been studied in frontal lobes lesions (Luria 1967). These disorders, termed also a "disturbance of the selectivity of mental processes" by Luria (1973), were more specially described in patients with bilateral lesions close to the medial areas of the frontal lobes (Luria et al. 1967). As in other descriptions (Elliott 1969), the lesions were the consequence of a large tumour, and the extent of the cerebral damage was imprecisely known. Thus it is impossible to determine the respective role of frontal lobe dysfunction (with special regard to the medial cortex) and of Acg dysfunction. In the present case, the frontal cortical lesions surrounding the Acgs lesions were probably not large enough to explain the symptomatology. It may be suggested that a cingulate lesion, when added to a frontal lesion, could produce more pronounced symptoms than those of a frontal lesion alone. This was supported by experiments in monkeys (Kennard 1955; Showers 1959; Watson et al. 1973), in which cingulectomy clearly enhanced the effects of a frontal lobe lesion. Such relationships between Acg and medial frontal cortex are supported too by studies of Acg stimulation (Smith 1945; Ward 1948; Bancaud et al. 1976). In man, such stimulation may produce attention disorders, and sometimes complex behavioural activities, such as compulsive use of objects placed in the visual field strongly resembling some of our patient's behaviour. These effects were thought to be the result of bilateral dysfunction, due to the spreading of stimulation, in both Acgs and medial frontal lobes (Bancaud 1976).

Lesions observed in the present case were located in 3 anatomical connections between frontal lobes and limbic cortex. (a) The fornix contains the rostral projections of the hippocampal formations (Swansson and Cowan 1977; Krayniak et al. 1979) destinated to septum nuclei and to the cortex through the hippocampo-mammillothalamo-cortical circuit. (b) Acg can be considered as a cortical bridge between hippocampus and neocortex (Powell 1978). It is closely related with prefrontal areas (Pandya and Kuypers 1969; Jacobson and Trojanowski 1977). (c) The cingulum bundle, contains projections from all parts of frontal lobe towards entorhinal areas and hippocampal formations (Adey and Meyer 1952). So, a quite complete disconnection was established between frontal lobes and the cortical components of the limbic system, chiefly hippocampus. The functional signification of these reciprocal fronto-limbic relationships have been emphasized especially in behavioural programming (Nauta 1971; Numan 1979).

Other arguments can be obtained from the case reports of extensive limbic lobe destruction in man following encephalitis. Some patients had, besides an amnestic syndrome, profound behavioural changes with docility, indifference, distractibility and inability to sustain a directed activity (Friedman and Allen 1969; Gascon and Gilles 1973). Lesions were very widespread, destroying not only the cortical and sub-cortical limbic formations, including Acgs, but also, to a variable degree, the temporal neocortex and parts of the frontal lobes. The patient reported by Barbizet et al. (1978), had the amnestic syndrome, but unlike the others, he was able to perform some complex tasks such as playing scrabble. Pathological examination (J. Poirier, personal communication) showed no involvement of frontal cortex. The comparison between these cases suggests that simultaneous frontal and limbic impairment is necessary to induce an intense impairment of attention. In the present case, lesions were comparatively restricted, but selectively located on the anatomical connections between frontal and limbic cortices.

In animals frontal lobes and limbic structures are known to receive a dense dopaminergic innervation (Lindvall et al. 1974; Berger et al. 1976), which takes its origins in the ventral tegmental area of the mesencephalon. Lesions of this ventral tegmental area (Le Moal et al. 1969, 1975; Stinus et al. 1978) in rats induced a permanent behavioural syndrome characterized by locomotor hyperactivity, hyperreactivity to external stimuli, hypoemotivity and perturbations of goal-directed behaviours such as hoarding. Furthermore, recent experiments produced evidence that some features of the rat syndrome, as aimless hyperactivity, were correlated with dopamine deprivation in the frontocingular areas (Tassin et al. 1978; Carter and Pycock 1979). Interspecies comparisons must be done cautiously. However, the comparison of these experimental symptoms to those observed in our patient is attractive, since in both situations there is impairment of frontal and limbic structures.

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