

Analysis of abnormalities in pituitary gland in non-missile head injury: study of 100 consecutive cases

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SUMMARY Pituitary glands, obtained at necropsy from a consecutive series of 100 patients who had died as a result of non-missile head injuries, were examined to define the incidence and pathogenesis of abnormality.

It is widely recognised that the hypothalamo-hypophysial axis may be damaged as a result of a non-missile head injury¹⁻⁵ and that massive infarction may occur in the anterior lobe of the pituitary gland if the pituitary stalk is torn.⁶⁻⁸ Necrosis of the anterior lobe of the pituitary gland may also occur as a consequence of raised intracranial pressure and distortion of the brain.⁹

This analysis was undertaken in an attempt to define the incidence and pathogenesis of abnormalities in the pituitary gland in patients dying as a result of a non-missile head injury.

Material and methods

The pituitary glands were obtained at necropsy from a consecutive series of 100 patients who had died as a result of non-missile head injuries in the Institute of Neurological Sciences, Glasgow.¹⁰ There was no selection of cases on our part, but as the division of neurosurgery only admits patients with head injuries referred from other hospitals, there was inevitably some clinical selection. There were 81 men and 19 women; the age ranging from 8 months to 85 years; and the duration of survival ranged from nine hours to seven months. Most injuries were attributable to road traffic accidents (44%) or falls (44%).

In every case the hypothalamus and the pituitary stalk were carefully examined as the brain was being removed from the skull. The pituitary gland was then dissected out of the pituitary fossa and fixed for between 24 and 48 hours in 10% formol saline. It was then bisected in the horizontal plane just below the

site at which the pituitary stalk enters the pituitary gland, so as to allow as comprehensive an assessment of the anterior and posterior lobes as possible. In some cases the upper part of the pituitary gland was cut in the sagittal plane so that the lower end of the stalk could be examined microscopically. The pituitaries were embedded in paraffin wax and 7 µm sections—sometimes at several levels—were stained by haematoxylin and eosin. If some abnormality was observed sections were stained by numerous other techniques including haematoxylin and van Gieson, Masson's trichrome, periodic acid Schiff and orange G, and the Palmgren technique. All histological abnormalities seen were plotted on a series of line diagrams of the pituitary gland, and these formed the basis of the present analysis.

Particular attention was paid to the occurrence of infarction in the anterior lobe of the pituitary gland. The precise size of such infarcts can only be determined by volumetric analysis,¹¹ but this was not undertaken in the present analysis. If an infarct

Table 1 *Abnormalities identified in 100 pituitary glands studied*

<i>Pathology</i>	<i>No of patients</i>
<i>Infarction:</i>	
Anterior lobe: Large	13
Medium	5
Small	20
Total	38
Posterior	2
Anterior and posterior lobes	2
<i>Haemorrhages:</i>	
Anterior lobe	3*
Posterior lobe	12**
<i>Microadenomas:</i>	11

*Two had anterior lobe infarction.

**Four had anterior lobe infarction.

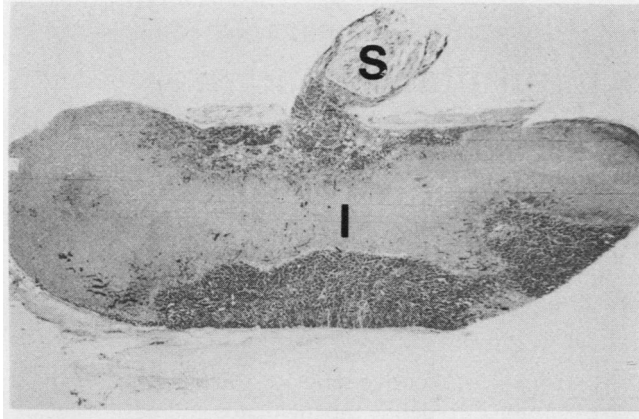


Fig. 1 Sagittal section of pituitary gland through pituitary stalk (S) shows large pale staining infarct (I) affecting most of anterior lobe. Darker areas in subcapsular region are viable anterior pituitary tissue. (Haematoxylin and eosin.) $\times 6.5$.

affected 80% or more of the cross sectional area of the anterior lobe in a horizontal equatorial section it was classified as large; between 30% and 80% as medium; and less than 30% as small.

The brain of each case had already been subjected to a detailed neuropathological analysis.^{10,12-17} Information was therefore available concerning distortion and herniation of the brain, and all brains were assessed for histological evidence of a high intracranial pressure using the criteria suggested by Adams and Graham.¹⁸

The clinical records were analysed to ascertain if the patient had had a cardiorespiratory arrest, systemic hypotension, artificial ventilation, or had displayed any evidence of pituitary dysfunction.

Results

Table 1 summarises the pathological findings of the 100 pituitaries examined.

ABNORMALITIES IN THE ANTERIOR LOBE

Infarcts were observed in 38 cases (38%); they were

large in 13 (Fig. 1), medium in five, and small in 20 cases (Fig. 2). The earliest visible sign of necrosis was pallor of staining of the cytoplasm of the parenchymal cells and some pyknosis of their nuclei—that is, appearances rather similar to those produced by autolysis. It was, however, usually easy to distinguish early infarction from autolysis by the coexistence of normal parenchymal cells around the infarct (Fig. 3). The next stage was the appearance of coagulative necrosis, when the dead cells are absorbed, and the infarct ultimately replaced by a shrunken fibrous scar.

Every one of the large infarcts had a similar distribution, residual parenchyma being restricted to a narrow subcapsular band (Fig. 3) and a broader wedge adjacent to the posterior lobe. Infarcts of medium size tended to be located in the central region of anterior lobe, and if they extended close to the capsule they were typically separated from it by a narrow band of surviving parenchymal cells. Small infarcts occurred in any part of the lobe and were occasionally multiple (Fig. 2). In those cases in which the stalk was examined histologically there was no evidence of thrombosis in the portal vessels.

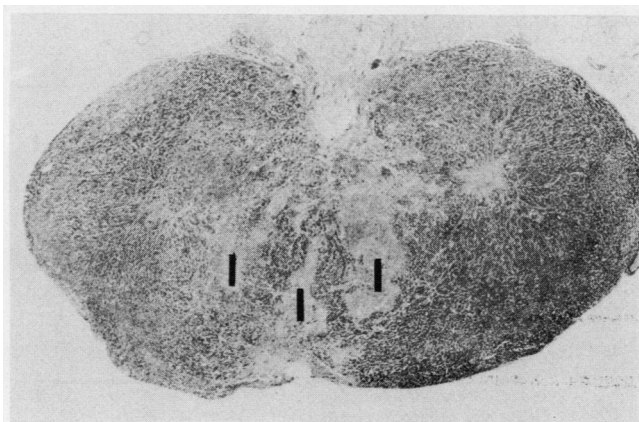


Fig. 2 Horizontal section of pituitary gland shows three small infarcts (I) in centre of anterior lobe. (Haematoxylin and eosin.) $\times 6.5$.

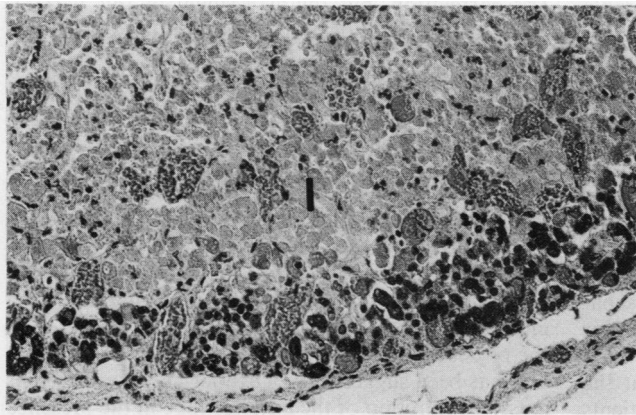


Fig. 3 In most large infarcts (I) of anterior lobe of pituitary gland thin subcapsular rim of viable parenchymal cells can be seen. (Haematoxylin and eosin.) $\times 180$.

Table 2 summarises the incidence of several variables including raised intracranial pressure, lateral and downward shift of the hypothalamus, fractures of the skull, assisted ventilation, and survival time in patients with infarctions of the anterior lobe of the pituitary.

Haemorrhage

This was seen within the anterior lobe in only three cases. There were associated anterior lobe infarcts in two of these cases.

Adenomas

Small chromophobe adenomas were incidental findings in 11 pituitaries.

ABNORMALITIES IN THE POSTERIOR LOBE

Infarction

Infarcts were observed in the posterior lobe in two cases, both being associated with large infarcts in the anterior lobe.

Haemorrhage

This was noted in 12 cases. The haematomas were usually circumscribed lesions in the centre of the lobe. There were associated anterior lobe infarcts in four of these cases, although in only two instances was there clinically important structural damage.

The pituitary stalk was normal macroscopically in all but one of the 100 cases. In this case the stalk was completely transected and there was a large infarct in the anterior lobe of the pituitary.

Discussion

From this analysis of the pituitary glands from 100 unselected non-missile head injuries it seems that the most common important abnormality in the pituitary gland is infarction in the anterior lobe. Of the 38 cases with anterior lobe infarcts, 13 were large, five were of medium size, and 20 were small. Small infarcts are often found in routine necropsies of patients dying from a wide range of disorders,^{9 19-21} and they seem to be of little clinical importance. The clinical importance of large and medium sized infarcts is difficult to assess as it is widely accepted that a considerable proportion of the anterior lobe of the pituitary must be destroyed before hypopituitarism becomes evident clinically.²² Nevertheless, before the period covered by the present analysis, we observed at least one case in which death seemed to be attributable to massive pituitary necrosis, while in another in the present series, who had had a large infarct and who survived for more than one week after a head injury, the administration of steroids a day or so after injury

Table 2 Correlation of infarcts in pituitary gland with other clinical and pathological features

	Infarcts in anterior pituitary	Neuropathological evidence of raised intracranial pressure	Lateral shift of hypothalamus (3 mm)	Downward displacement of hypothalamus	Ventilation (> 24 hours)	Fractured base of skull (through pituitary fossa)	Survival (> six days)
Large	13	13	11	7	11	12 (3)	1
Medium	5	5	4	3	1	4 (1)	0
Small	20	16	7	5	10	17 (0)	11
No infarct (62 cases)		46	18	13	8	38 (1)	25

to combat "cerebral oedema" produced considerable clinical improvement.

In the acute stage of head injury electrolyte imbalance such as hypernatraemia²³ and hyperchloraemia²⁴ have been well documented. Treip⁵ suggested that these changes could be due to disturbed adenohypophysial function, although in the 14 cases described by Higgins *et al*²⁴ nine of the pituitaries were examined and six showed merely haemorrhage and thrombosis. Of the patients in our series with large and medium sized infarct, hyperchloraemia or hyperkalaemia were noted in five separate cases. Two of these patients also had posterior lobe infarcts.

Diabetes insipidus after trauma is rare,²⁵ but the measurement of urinary output in comatose patients is difficult. In one of the cases studied (a large infarct of the anterior lobe of the pituitary) urinary outputs of 4 and 4.51 were recorded on consecutive days immediately preceding death, while in four other cases the daily urinary output was greater than 31. The cases with anterior and posterior lobe infarcts did not have increased urinary outputs. The interpretation of these findings is difficult, but they emphasise the importance of clinical awareness of fluid and electrolyte problems in patients with head injuries.

The mechanism of anterior lobe necrosis is presumably that of interference with the flow of blood through the long hypothalamo-hypophysial portal vessels in the pituitary stalk. If the stalk is completely transected in man and in various experimental animals massive infarction of the anterior pituitary results.^{6,7} In contrast, the posterior lobe is spared due to its independent arterial supply.²⁶ Daniel and Pritchard⁸ showed that by cauterising individual portal vessels in the pituitary stalks of rats they were able to produce small infarcts in the anterior lobe. In this series, however, the pituitary stalks were macroscopically normal in all but one of the cases with infarcts. This suggests that the blood flow through the hypophysial portal vessels may be interrupted without actual transection of the stalk.

The results show that every patient with a large or medium sized infarct had had, at some stage, raised intracranial pressure (Table 2). Wolman⁹ reported 12 cases of infarction in the anterior lobe in 270 patients in whom there was evidence of a tentorial pressure cone. He suggested that mechanical factors such as lateral displacement of the hypothalamus could have a role in the pathogenesis of anterior lobe infarction. This is substantiated by our findings: 83% of cases with large and medium sized infarct had significant mid line shift, whereas only 29% of those with normal pituitaries had mid line shift. Downward displacement of the hypothalamic structures seems to show

less correlation, but the assessment of this variable was necessarily more subjective than that of mid line shift.

There was a high incidence of fracture of the base of the skull in the cases with infarction in the anterior lobe, but only occasionally did the fracture affect the pituitary fossa. Daniel and Treip³ maintained that a fracture of the base of the skull is one of the two consistent clinical findings in relation to massive infarction of the pars distalis, the other being prolonged coma disproportionate to the severity of the head injury. By contrast, Ceballos¹ found that the incidence of anterior lobe infarction was unrelated to the presence of a fractured skull.

It has been suggested by Orthner and Meyer²⁷ that massive infarction of the anterior lobe in the presence of an intact stalk is the result of shock following trauma combined with anoxia. It is, therefore, of interest to note that 11 of the 13 cases with massive infarction had suffered a cardiorespiratory arrest and had required artificial ventilation for more than 12 hours before their death. A possibility raised by this finding is that the microscopic appearance of infarction may, in fact, be an associated feature of the "respirator brain" picture.²⁸ In only four of these cases, however, did the brain strongly show features of "respirator brain" change, and of these, two were well established infarcts that had clearly occurred before the establishment of artificial ventilation. In 25 other patients in the series who were ventilated for more than 12 hours the pituitary glands were normal. Daniel *et al*²⁹ have drawn attention to the high incidence of massive pituitary infarction in patients maintained on mechanical ventilation, but from our observations it seems that artificial ventilation, if a causative factor, is not the sole contributor to infarction in the anterior lobe.

Although the incidence of head injuries was far higher for men than for woman (4:1), there was a disproportionately high incidence of infarction of the anterior lobe of the pituitary in men, the ratio being 9:1. Ceballos¹ also noted a higher incidence in men.

Infarction in the anterior lobe of the pituitary is common in patients with head injuries, and such infarcts were large in 13% of the present series of cases. Clearly, factors other than traumatic transection of the stalk contribute to massive infarction in the anterior lobe, and it may well be that most patients with large pituitary infarcts will almost certainly succumb as a result of raised intracranial pressure, distortion of the brain, and cardiorespiratory arrest. Nevertheless, the analysis reported here suggests that clinicians should have a better awareness of the possibility of massive pituitary necrosis in the management of head injuries.

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