ANTERIOR AND POSTERIOR PITUITARY FAILURE AFTER HEAD INJURY

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Head injury has been reported as a cause of diabetes insipidus (Porter and Miller, 1948), and less commonly of anterior pituitary failure (Witter and Tascher, 1957). The case presented here is that of a girl in whom diabetes insipidus developed after a minor head injury. She died in hypopituitary coma six years later, and a post-mortem examination revealed unusual pathological features.

Case Report

The patient, born in 1936, had had no serious illnesses in childhood and was quite healthy until the age of 15, when she was knocked down by a car in a road accident. There was only momentary loss of consciousness, but she was admitted to hospital, where x-ray examination of the skull revealed no fracture. She was kept in hospital for 10 days and then discharged perfectly well, two scalp wounds having healed.

The patient was next seen two years later complaining of polyuria, polydipsia, and loss of over a stone (6.4 kg.) in weight, and, although a poor witness, she said the symptoms dated from shortly after the time of the accident. There was no family history of any similar trouble. On examination she was seen to be a thin girl with a blood-pressure of 140/90 mm. Hg; no abnormal physical signs were detected. She was a dull, immature type of person, and at first it was thought her thirst might be due to hysteria. However, the diagnosis of diabetes insipidus was made when it was found that her urinary output measured up to 6.5 litres daily, while the specific gravity of the urine remained at 1004 after 24 hours' deprivation of water. Nicotine and intravenous hypertonic saline had no antidiuretic effect, but after an injection of "pitressin" the concentration of urine rose and the volume sharply diminished. The Wassermann reaction and Kahn test were negative and x-ray films of the skull and chest were normal. No other abnormalities were found. While in hospital the patient was uncooperative and refused to take pitressin by injection. She was discharged, taking two ampoules of pituitary snuff daily, which was sufficient to control her symptoms.

She was next seen nine months later, aged 18, complaining of vomiting and amenorrhoea. Menstruation had previously been normal since it started at the age of 10. She was found to be pregnant, and in June, 1955, after a normal pregnancy and labour an infant girl was born; there was no post-partum haemorrhage. She was discharged home breast-feeding the baby and taking 3 ml. of pitressin tannate by daily injection.

The patient failed to keep subsequent out-patient appointments and was not seen again for three years, until October, 1958, when she was referred by her own doctor. After the pregnancy menstruation had continued normally for about two years, but there had been amenorrhoea for the previous 12 months. Although she had stopped taking pitressin she no longer complained of thirst or nocturia. On examination she was lethargic and rather plump, the cheeks were flushed and the eyebrows scanty, and the dry skin and facies were strongly suggestive of myxoedema. Her voice was slurred and there seemed to have been a mental slowing since her last examination. The blood-pressure was 90/60 mm. Hg. Breast development was moderate and the pubic and axillary

hair were normal. There was no visual field defect and on x-ray examination the pituitary fossa appeared normal. Further investigation gave the following results:

		After 120 units A.C.T.H. gel	
24-hour urinary sodium		146 mEq	.. 28 mEq
" " " potassium		55 mEq	.. 75.5 mEq
" " " 17-ketosteroids		10.7 mg.	.. 8.8 mg.
" " " 17-ketogenic steroids		Nil	.. 17.4 mg.
Serum sodium		157 mEq/l.	
Serum potassium		5.5 mEq/l.	
Serum cholesterol		375 mg./100 ml.	
Basal metabolic rate		31% below standard	

Anterior pituitary failure was diagnosed, with secondary hypofunction of the thyroid gland, adrenal cortex, and ovaries. Meanwhile the diabetes insipidus had become less severe and the daily urinary volume varied between 2 and 5 litres. Treatment was started with cortisone 25 mg. twice daily, but before any further progress could be made the patient discharged herself from hospital, despite repeated warnings of the possible dangers of her illness.

Three months later, in January, 1959, she was readmitted, having taken no cortisone during the intervening period. She was drowsy, pale, cold, and dehydrated; temperature 93° F. (33.9° C.); blood-pressure 80/50 mm. Hg. Investigations showed: serum sodium, 161 mEq/l.; serum chloride, 135 mEq/l.; blood sugar, 45 mg./100 ml.; blood urea, 51 mg./100 ml.; there was a normochromic, normocytic anaemia; Hb, 8.8 g./100 ml.

It was thought that she was suffering from the effects of panhypopituitarism, the dehydration being the result of diabetes insipidus. Within a few hours of admission her temperature fell to 90° F. (32.2° C.) and she passed into coma.

Treatment was started with 100 ml. of hydrocortisone, 40 g. of triiodothyronine, and 5 I.U. of thyrotrophic hormone in the first 12 hours, and when it became evident that large volumes of urine were being passed 5 units of pitressin tannate in oil was added. Subsequently maintenance doses of these drugs were prescribed as well as deoxycortone acetate and prophylactic penicillin. The patient was slowly warmed to 97° F. (36.1° C.), and the fluid and electrolyte balance maintained via an intravenous "polythene" catheter.

The coma persisted, and when, on the fourth day, there were signs of respiratory obstruction, a tracheostomy was performed. Shortly afterwards the blood-pressure fell to below 80/50 mm. Hg, and was raised with intravenous noradrenaline, which had to be continued for a further three days. By the end of the first week the patient was maintaining a normal temperature without extra external heating and the triiodothyronine was replaced by thyroxine. The persistent anaemia was treated by blood transfusion. Her condition remained unchanged during the second week, but towards the end of the third week she regained consciousness and spoke a few words. However, shortly afterwards a staphylococcal pneumonia developed and despite antibiotics and increased doses of cortisone she relapsed into coma.

Thereafter she gradually lost weight and her general condition deteriorated. During the fifth week head retraction, attacks of trismus, and teeth-grinding developed, and all four limbs became spastic in flexion with bilateral extensor plantar responses. She remained in this state for a further two weeks, punctuated by periods of hyperpyrexia rising to 105° F. (40.6° C.), and finally died six weeks after the onset of coma.

Post-mortem Findings

The body was that of a pale young woman with a tracheostomy opening on the front of the neck. Body build, fat distribution, and breast development were normal. Pubic and axillary hair growth was normal. The cardiovascular system showed no abnormality; the respiratory system a severe degree of congestion, especially of the lower lobes; and the alimentary system a moderate degree of ascites, but no other abnormality. In the genito-urinary tract there was a slight degree of hydronephrosis on the right side; the ureters and bladder and the uterus and tubes

were normal. Both ovaries were atrophic. The lymphatics were normal.

Endocrine System.—The pituitary gland *in situ* appeared normal. The stalk was intact and showed no sign of adhesions or of inflammation. The meninges in this area were also normal. On section of the gland the posterior lobe was found to be occupied by hard fibrous tissue. The thyroid gland was smaller than normal, weighing 14 g. The adrenal glands appeared normal and weighed 14 g. together.

Cranium and Contents.—There was no evidence of past head injury or any other abnormality of the skull. The brain was normal except for a feeling of toughness on cutting through the hypothalamus.

Histology

Pituitary Gland (Fig. 1).—There was a slight degree of post-mortem change affecting the anterior lobe, but no other abnormality was present. The posterior lobe and nearly all the stalk had been replaced by fibrous tissue. In the main body of the lobe it was dense and almost acellular, but along the border with the anterior lobe and in the stalk there were chronic inflammatory cells, mainly plasma cells, which in places formed denser foci. The cellular areas also

FIG. 1.—Pituitary gland and stalk. (Haematoxylin-Van Gieson. $\times 8$.)

contained fibroblasts—especially numerous in the stalk, where sclerotic changes were not prominent—and macrophages with coarse granules of haemosiderin in their cytoplasm. The only normal structures remaining in the stalk were a thin zone of pars tuberalis with the hypophyseal portal vessels anteriorly.

Hypothalamus.—The cellular fibrous tissue seen in the pituitary stalk extended upwards to the median eminence and the floor of the third ventricle and along part of its lateral walls. Dense strands of collagen were present between which the plasma-cell infiltrate tended to form perivascular foci. Haemosiderin-containing macrophages could be found throughout this abnormal tissue, which also contained numerous fibroblasts. Mrs. E. Beck examined sections of the hypothalamus and indicated the probable extent of the lesion (Fig. 2). It involved the suprachiasmatic region and the walls of the optic recess. The mamillary bodies, the ventro-medial hypothalamic nuclei, part of the dorso-medial nuclei and the medial part of the lateral hypothalamic nuclei had been destroyed. The optic chiasma, pre-optic nuclei, and diagonal band nuclei were normal, and the subthalamic and red nuclei were unaffected. The supra-optic and paraventricular nuclei were devoid of nerve cells. No trace of neurosecretory material was found either in the hypothalamus or in the neurohypophysis.

In the *thyroid gland* the acini were well filled with colloid, the lining cells were flattened and appeared to be inactive, and there was no fibrosis or lymphocytic infiltration. The *adrenal glands* were normal except for some post-mortem

change. Both *ovaries* were completely atrophic; serial sections showed no evidence of follicle formation, and the sclerotic remains of corpora lutea seen appeared to be very old. The endometrium of the *uterus* was thin and inactive; there was an increase in stromal collagen. The *liver* showed marked centrilobular fatty infiltration. The *lungs* were severely congested but there was no other abnormality. The *kidneys* showed a mild degree of acute pyelonephritis.

Discussion

Traumatic Diabetes Insipidus

The true incidence of diabetes insipidus due to head injury is not known. Blotner (1951) believes it to be greatly overestimated and cites cases with a history of concussion in which the lesion was later found to be a brain tumour. There was a history of trauma in 6 of his 50 "idiopathic" cases, but he did not regard this as significant. Pickles (1947) found four cases of diabetes insipidus in 2,500 patients with head injuries,

FIG. 2.—Diagram of pituitary gland and hypothalamus. Hypothalamic nuclei are represented by stippled areas and the extent of the histological lesion by hatching. AC=Anterior commissure. DM=Dorso-medial nucleus. MB=Mamillary body. NL=Neural lobe. OC=Optic chiasma. PD=Pars distalis. PH=Posterior hypothalamic nucleus. PR=Pre-optic nucleus. PV=Paraventricular nucleus. SO=Supra-optic nucleus. VM=Vento-medial nucleus.

three of which cleared up within four months. Porter and Miller (1948) found 13 cases of diabetes insipidus in 5,000 cases of closed head injury and collected five additional cases. The condition was not associated with minor injury. Of 18 cases, 13 had post-traumatic amnesia for over a week and 12 had a fracture of the skull, while there was olfactory damage in 11 cases, and optic nerve and tract damage in 6. In one case there was anterior pituitary dysfunction and another developed Fröhlich's syndrome. Porter and Miller considered the lesion causing diabetes insipidus to be in the pituitary stalk, attributable to stretching at the time of injury, and they suggest that the rarity of permanent traumatic diabetes insipidus is due to the high mortality of injuries in this area.

Very little is known of the pathology of post-traumatic lesions of the hypothalamus and pituitary. Henzi (1952)

reported a case of diabetes insipidus arising in a girl aged 11 after a severe head injury. Polyuria remained continuous until the patient's death at the age of 60, during which time she had seven pregnancies. At necropsy the pituitary gland was found embedded in scar tissue and there was no sign of a stalk. Microscopically there was scarring involving the posterior lobe and the tuber cinereum, and extending around the supraoptic nuclei, in which the number of cells was reduced. There was also some reduction in the cells of the paraventricular nuclei. The anterior lobe appeared normal.

Beck and Daniel (1959) reported nine cases that had undergone hypophysectomy or pituitary stalk section for the relief of cancer, in all of which a barrier had been placed between the hypothalamus and the pituitary fossa. In those cases surviving only a few weeks a venous infarct was found in the proximal stump of the stalk at necropsy. Cases examined 2 to 26 months after operation were found to have regenerated nerve fibres in the stump, and some of these contained neurosecretory substance. Although signs of the old infarct, such as haemosiderin-containing macrophages, were present, the impression was of a regenerating posterior lobe in the proximal stump.

Hypothalamus and Anterior Pituitary

There is much experimental evidence that the hypothalamus controls the activity of the anterior lobe of the pituitary, and thereby the gonads, thyroid, and adrenal cortex, through the hypophysial portal vessels of the pituitary stalk (Harris, 1955a). It is probable that the nerve fibres from the hypothalamus liberate a humoral substance which is carried by the portal vessels to the anterior lobe. Thus trauma to the pituitary stalk interferes with anterior-lobe function by damaging the portal vessels. Daniel *et al.* (1959) have shown that such damage can result in infarction of the anterior lobe. This might possibly be followed by regeneration (Daniel and Prichard, 1958).

The results of electrical stimulation of different areas of the hypothalamus suggest localization of control of secretion of the different pituitary hormones (Harris, 1955b). Damage to these areas may result in a selective disorder of function in the anterior lobe. Thus inflammatory and neoplastic lesions of the posterior part of the hypothalamus are known to produce effects such as sexual precocity and hypogonadism (in Fröhlich's syndrome), which must be mediated through the anterior pituitary, although the gland itself is not involved by the lesion and appears histologically normal.

Conclusion

The findings in the present case are not easily interpreted in the light of previous observations. The initial head injury was not severe, but its time relation to the onset of the disease suggests that it was the cause. No alternative aetiological factor was discovered. It is likely that traumatic interruption of the supraoptico-hypophysial tracts produced diabetes insipidus soon after the injury and that retrograde degeneration resulted in the disappearance of nerve cells in the supraoptic and paraventricular nuclei. Anterior pituitary function remained apparently normal after the accident and throughout the subsequent pregnancy and lactation. This makes it unlikely that the anterior lobe could have been damaged at the same time as the neurohypophysis. Hypothalamic control of the anterior lobe must also

have been normal at this time. The presence of haemosiderin throughout the hypothalamic lesion, as well as in the posterior lobe, suggests the occurrence of either haemorrhage or infarction after the injury, but the subsequent evolution of the lesion is difficult to determine. Fibrosis in the central nervous system is unusual, and it may be that with the gradual spread of scarring in the hypothalamus control of anterior pituitary activity progressively weakened until, despite the presence of an apparently normal gland with an intact blood supply, hormone secretion diminished and the clinical picture of anterior pituitary failure resulted.

Summary

An account is given of the case of a girl of 15 in whom diabetes insipidus occurred after a head injury. She later developed anterior pituitary failure and died six years after the accident in pituitary coma. Post-mortem examination revealed widespread sclerosis throughout the neurohypophysis and the hypothalamus, but the anterior lobe of the pituitary appeared normal. Traumatic pituitary failure is discussed and an attempt is made to interpret the features of this case.

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SEPTICAEMIA CAUSED BY AN ORGANISM RESEMBLING PASTEURELLA SEPTICA AFTER A DOG-BITE

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Pasteurella septica is a Gram-negative coccobacillus commonly found in the throats of animals. Schipper (1947) isolated the organism from 14 of 102 trapped wild Norway rats; Smith (1955) found that 61 of 111 healthy dogs were carriers; and the pig, the cat, and the ox are also known to harbour the organism. Apart from its commensal habits, it is also an important pathogen of animals and birds, the cause of haemorrhagic septicaemia, which is highly contagious and usually fatal. Guinea-pigs, rabbits, and other animals inoculated by Schipper succumbed within a day, and he stressed that the possibility of a rat-bite should always be considered when domestic animals die suddenly.

Whereas human infection has curiously never been attributed to rat-bite, there are on record many cases which followed the bites and scratches of other animals,