DIABETES INSIPIDUS FOLLOWING CLOSED HEAD INJURY

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Diabetes insipidus is a rare disease and it is a very uncommon sequel of head injury. Fitz (1914) found that the incidence of the disease attributable to any cause was fourteen cases per hundred thousand admissions to a general hospital, and Rowntree (1924) found thirteen cases per hundred thousand admissions to the Mayo Clinic. Rabinowitch (1921) found one case of diabetes insipidus among fifty thousand admissions to a general hospital. In only two of fifty-six cases reported by Rowntree (1924) and two, or possibly three, of forty-two cases reported by Jones (1944) was the diabetes insipidus due to head injury. Rand and Patterson (1937) have stressed the rarity of post-traumatic diabetes insipidus by stating that no case occurred in one hundred and fifty thousand admissions to a neurosurgical unit.

Kahler (1886) reported twenty-six cases of diabetes insipidus following head injury, and Rand and Patterson (1937) recorded six cases; the majority of reports on the clinical features of the condition, however, have been based on one or two cases. Fink (1928), Turner (1928), and Warkany and Mitchell (1939) have reviewed the literature, and Riddoch (1938), Symonds (1943), and Rowbotham (1945) have recorded their impressions. It is the most common hypothalamic disorder following trauma. The injury has usually been severe and the skull fractured, the fracture generally involving the base. Thirst and polyuria begin a few days to several months after the injury. The severity of the symptoms varies from case to case, and may fluctuate in some patients. Fever sometimes improves the condition. The duration of the symptoms cannot be predicted, but most cases do recover. The response to pituitrin therapy is usually good, but sometimes symptoms are only partly relieved and in a few cases it has no effect. Other evidence of hypothalamic injury is sometimes present, a reduction in perspiration and obesity, and disturbance in sex functions. Cranial nerves are often involved, the optic and oculo-motor being those most commonly affected.

Of all non-fatal closed head injuries (gunshot wounds and those with dural penetrations excluded,) admitted to the Military Hospital for Head Injuries, Oxford, during the years 1940–45, which numbered about five thousand, thirteen suffered from diabetes insipidus. We have had the opportunity of studying three (Cases 5, 9, and 12) of these personally, the records of the other ten, and the records of five cases (Cases 14–18) treated in the Nuffield Department of Surgery, Oxford, under Professor Sir Hugh Cairns. This series of eighteen cases is reviewed in an attempt to add to our present rather inadequate knowledge of the clinical features and pathology of the condition.

The Table indicates the relevant features in each case.

Site of Trauma and Severity of Injury

The site of injury was judged by the position of cutaneous abrasions, bruises, or lacerations of the scalp or face, taking into consideration the position of fractures when present, and in all but three cases it was possible to determine with reasonable certainty the site at which the head was struck. In nine cases the blow was frontal, in six occipital. In twelve cases the skull was fractured—six in the frontal area, four in the occipital, and two in the middle fossa.

The severity of a closed head injury is difficult to assess and depends on several factors. The best single guide to severity, however, is the duration of the post-traumatic amnesia (P.T.A.) to which the degree of residual disability often bears a direct relationship, and Russell (1942) classifies cases with P.T.A. less than two hours as slight, two to forty-eight hours as moderate, and over two days as severe. It is seen that the majority of our cases

TABLE

DETAILS OF CASES

Case No.	Age	Nature of injury and date	Site of injury	P.T.A. in days	Diabetes insipidus				Associated hypothalamic or pituitary disorder	Associated injury to			Radiograph of skull
					Day of onset after injury	Duration (months)	Maximum recorded 24-hour output of urine (oz.)	Response to pituitrin		Olfactory nerves	Optic nerve	Optic chiasm	
1	27	Motor cycle accident 16.3.40	Occipital	19	9	1	150+	Yes	—	+	—	—	Nothing abnormal
2	21	Motor car accident 6.11.42	Frontal	24	16	5/30	150+	Yes	—	—	—	—	Nothing abnormal
3	20	Lorry accident 20.10.42	Occipital	7	31	1	180	Yes	—	+	+	—	Nothing abnormal
4	19	Road accident 20.10.41	Occipital	17	12	1	200+	Unknown	Pathological laughter	—	—	—	Vertical fissured fracture occipital
5	27	Motor car accident 15.6.45	Frontal	21	18	4	362	Yes	—	+	—	+	Fracture roof of right orbit running into frontal sinus; fracture nasal bones
6	19	Fall 30 ft. 25.2.41	Frontal	21	15	5	280	Yes	—	+	—	+	Fissured fracture frontal involving sinus
7	20	Aeroplane crash 10.4.43	Unknown	5 *T*	10	2	?	Yes	—	—	—	—	Nothing abnormal
8	26	Lorry accident 28.7.42	Frontal	2/24	14	6½	250	Yes	—	+	—	—	Fractured right frontal involving sinus
9	39	Bomb blast: thrown forward 8.4.41	Frontal	13	13	9	?	Unknown	Adiposo-genital syndrome	+	—	—	Nothing abnormal
10	38	Fell backward striking head on stone floor	Occipital	10	10	7	150+	Yes	—	+	—	—	Fissured fracture left occipital
11	37	Road accident 28.10.44	Occipital	>21	17	>22	200	Yes	Outbursts of rage	—	—	—	Fissured fracture left occipito-parietal
12	34	Car accident 12.10.45	Frontal	7	30	>13	350	Yes	Anterior pituitary deficiency	—	—	+	Nothing abnormal
13	36	Car accident 19.11.40	Frontal	2	11	>38	465	Yes	—	+	—	—	Fissured fracture left frontal; both maxillæ and right zygoma
14	27	Road accident 6.7.44	Occipital	3	?	>15	?	Unknown	—	+	—	—	Vertical fissured fracture occipital into foramen magnum
15	20	Bomb blast 15.7.44	Frontal	5	7 to 14	>12	500	Yes	—	—	—	—	Fissured fracture frontal
16	22	Fall from bus 2.5.44	Unknown	10	14 to 28	>30	600	Yes	—	—	—	—	Fissured fracture temporal running into middle fossa
17	30	Car accident 1935	Frontal	21	?	>96	400	Yes	—	+	—	+	Fissured frontal fracture maxilla and mandible
18	19	Car accident 22.9.38	Unknown	21	?	2	320	Unknown	—	+	—	+	Bridged bella ? interruption in continuity of petro-clinoid ligaments

suffered very severe injuries. In five only was the P.T.A. less than one week, and in only one of these was it less than two days.

Onset, Course, and Treatment of Diabetes Insipidus

Accuracy in determining the time of onset of diabetes insipidus is difficult, since so often the patients are confused and incontinent in the early stages after the injury. Moreover, limitation of fluid intake, which occurs if the patient is unable to demand extra drink, masks the condition. The symptoms were first noticed by the staff, or complained of by the patients, from nine to thirty-one days after the injury. In six cases the diagnosis was made with the aid of fluid intake and output charts before the period of post-traumatic amnesia was judged to have ended, and in two cases it was diagnosed on the day it ended. It might be argued that in these cases it had been present since the injury, but unnoticed. In the remaining five cases it was possible to estimate the time of onset more accurately, because there was a clear interval of from five to twenty-two days during which the patients were fully orientated and rational, before they complained of symptoms. There was, therefore, in these cases, a definite delay in the onset of the disease.

The degree of polyuria and polydipsia may at first be mild, and may reach the maximum days or even weeks later. Precise information is not available in most of our cases regarding fluctuations in the severity of the condition, because the natural course of the disease was usually altered by therapy. In three cases, however, we have information concerning the development of the disease. The symptoms were first noticed in one (Case 5) eighteen days after the injury, when the urinary output was 160 oz.; it gradually increased, and reached the maximum recorded output of 362 oz. four days later, when treatment with pituitrin was started. In Case 12 the measured urinary output showed a steady increase to a maximum of 400 oz. eight days after the onset of symptoms. The third (Case 8) was noticed to have excessive thirst and increased urinary output, 160 oz. fourteen days after the injury, but it was not till five and a half weeks later that he complained of symptoms, by which time the output of urine had shown a steady increase to 250 oz. and treatment was started.

The course of the disease varied in severity and duration. The majority, eleven, recovered spontaneously within nine months of the onset. Of the remaining seven cases, one (Case 14) was improving and had only mild symptoms fifteen months after the onset, and the other six showed no sign of recovery. Three of the unchanged cases (Cases 11, 12, and 15) were observed for thirteen to twenty-two months. In the other three cases (Cases 13, 16, and 17) with persistent diabetes, the disease was considered to be permanent as it had been present for longer than two and a half, three, and eight years respectively.

Fourteen cases were treated with posterior pituitary extract, either hypodermically or as snuff, and complete relief of symptoms resulted in all of them, provided adequate dosage was used. The response to pituitary therapy is not known in four cases, either because recovery had occurred (Cases 9 and 18) before the patients came under observation, or because treatment was considered unnecessary as improvement was already taking place and symptoms were not troublesome (Cases 4 and 14). No cases resistant to pituitrin were encountered.

Associated Intracranial Damage

Injuries to the olfactory nerves and optic chiasm or nerves were striking in their frequency. More than half (eleven cases) suffered from bilateral anosmia, five had visual field defects characteristic of a chiasmal lesion, and one had damage to the right optic nerve. No other signs of focal intracranial damage were common, and evidence of hypothalamic disorder, other than diabetes insipidus, was uncommon. One patient only (Case 9) presented other undoubted evidence of hypothalamic dysfunction, an adiposo-genital syndrome, which gradually developed during the first fifteen months following the injury. Two cases (Cases 4 and 11) showed emotional abnormality of a type which suggested a hypothalamic lesion, and in one case (Case 12) there was evidence of anterior pituitary dysfunction.

The infrequency of other hypothalamic syndromes following head injury is remarkable. When the material for this study was being collected, the records of all surviving cases of closed head injury at the Hospital for Head Injuries that had been indexed as having evidence of hypothalamic damage were examined, and all thirteen were found to have diabetes insipidus. Minor or transitory manifestations of hypothalamic disorder may have been missed, but it is highly improbable that such conditions as narcolepsy, impotence, or adiposo-genital syndrome would have been overlooked, even if they occurred as late symptoms, since the majority of cases have been followed up for more than two years and many for four years.

Comment

Riddoch (1938) and Symonds (1943) have stated that diabetes insipidus is the most common disorder

of hypothalamic function following closed head injury, and the evidence in this series strongly supports this view. It usually follows severe trauma to the front or back of the head, the same type of injury which has previously been shown to result most commonly in damage to the olfactory nerves, optic chiasm and nerves (Russell, 1943 ; Leigh, 1943 ; Traquair and others, 1935 ; Turner, 1943).

There appears to be no relationship between the severity of the injury and the delay in onset of the diabetes insipidus or its duration.

Although the precise mode of action of the posterior pituitary anti-diuretic hormone is not understood, there is general agreement that the gland is stimulated to secrete by nerve impulses passing to it from the supra-optic and paraventricular nuclei in the anterior hypothalamus via the supra-optic hypophyseal tract in the pituitary stalk. Experimentally, it has been shown that a bilateral lesion of these neurones is necessary for the production of diabetes insipidus (Fisher and others, 1938 ; Heinbecker and White, 1941 ; Magoun and Ranson, 1939). In these cases the polyuria is controlled by pituitrin, and Dandy (1940) has shown that section of the pituitary stalk in man can result in permanent diabetes insipidus which responds to pitruitin. There are rare cases of diabetes insipidus unresponsive to pituitrin which Dreyfus (1931) suggested occurred only when the tubero-mamillary nuclei are damaged.

In experimentally produced diabetes insipidus there is a delay in onset of the permanent polyuria, usually six to twenty-two days (Biggart and Alexander, 1939 ; Fisher and others, 1938 ; Heinbecker and White, 1941), but it may be as long as six or ten weeks (Fisher and others, 1938). Heinbecker and White (1941) have shown in dogs that this delay can be abolished by removing all the pitressin-secreting tissue at operation, this suggesting that the latent period represents the time during which the denervated neuro-hypophysis produces pitressin. They also showed that the severity of the polyuria depended on the extent of damage to the supra-optic hypophyseal connexions, maximum and permanent polyuria following complete section ; but, provided 15 per cent. of the fibres remained intact, the dogs recovered from their diabetes insipidus.

Holbourn (1943), in his studies on the mechanism of head injury, stresses the importance of changes in rotational velocity of the head, drawing the analogy of a full flask of water suddenly rotated, when it can easily be seen that the water tends to stay behind and only the flask rotates. Russell (1932) has suggested that movement of the brain relative to the skull at the time of injury may account for the frequency of anosmia in occipital injuries from tearing of olfactory filaments as they pass through the cribiform plate of the ethmoid. Traquair and others (1935) consider that the same mechanism may account for chiasmal lesions through the tearing of the small pial blood vessels supplying the chiasma. They also suggest that hypothalamic lesions may be produced in this way. It would seem likely, however, that in such an antero-posterior displacement or rotation of the brain within the skull the supra-optic hypophyseal connexions lying superficially in the anterior hypothalamus and in the pituitary stalk might be injured by being stretched, since the pituitary is held rigidly in the sella turcica.

There is no doubt that in the present series of cases the onset of diabetes insipidus was delayed, and this might suggest that the neurones are not damaged at the time of injury but are interfered with by a delayed pathological process, for example, organizing blood clot round the pituitary stalk on pressure from an arachnoid cyst (Kourilsky and others, 1942). However, the delay in onset is consistent with experimental observation and does not rule out neuronal damage at the time of injury. It is interesting to notice in this connexion that the period of delay in our cases corresponds fairly closely to that found in experimental animals.

The pathology probably varies in different cases. Laceration of the hypothalamus or pituitary by a displaced fragment of bone, or tearing by separation of a fracture of the sphenoid, are very improbable in our cases, for in none was there radiological evidence of a fracture involving the sphenoid or of a displaced bone fragment at the base of the brain. Interference with the blood supply to the hypothalamus from tearing of the fine pial vessels might account for some cases, but if this were a usual mechanism it would be strange that other hypothalamic syndromes are not encountered more frequently. An arachnoid cyst in the chiasmal region has been found at operation to be the cause of diabetes insipidus (Kourilsky and others, 1942), and the symptoms have been relieved immediately by incision of the cyst. However, one would expect pressure from a cyst or constriction of the pituitary stalk from organized blood clot to result in a permanent diabetes insipidus unless the pressure were relieved surgically, and it is seen that the majority of cases undergo spontaneous recovery within nine months. We think it probable, therefore, that the lesion is most commonly in the pituitary stalk, due to stretching from displacement of the brain at the time of injury, and that the duration of symptoms and severity of the diabetes

insipidus may depend on the extent of neuronal damage in the supra-optic-hypophyseal tract. The rarity of other hypothalamic syndromes and of permanent refractory diabetes insipidus is probably due to the high mortality rate from more extensive injury to this part of the brain.

Summary

1. Eighteen cases of diabetes insipidus following closed head injury have been studied and the relevant features tabulated.

2. In fifteen in which the site of injury could be determined it was frontal or occipital.

3. The symptoms were usually first noticed during the second or third week after injury.

4. All cases treated responded to pituitrin.

5. Spontaneous recovery took place in the majority, in eleven within nine months.

6. Associated injury to the olfactory nerves and optic chiasm is common; other hypothalamic syndromes are rare.

7. The mechanism of the injury is discussed, and it is suggested that a traction lesion of the pituitary stalk would best explain most cases.

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