The peripheral neuritis in each of these cases made its appearance before any general effects of D.N.O.C. poisoning were noted by the patient, and indeed before these would be expected as judged by the serum D.N.O.C. level. It is therefore tempting to speculate whether the symptoms were due to the action of D.N.O.C. locally following its absorption through the skin. D.N.O.C. stimulates the general metabolism of man by acting peripherally and directly on the cell, and it exerts its action independently of thyroxine. It is believed that the carbohydrate metabolism and breakdown is increased and that the resultant energy is converted to heat rather than muscular work. Where skin contamination is great, as in these two cases, the local concentration of D.N.O.C. at the site of absorption must be much greater than in the blood stream, and it is possible that under these circumstances a local effect might be exerted on the tissues before general symptoms would occur, and even without the necessity for their occurrence. The localized appearance of symptoms in these cases are suggestive. The hands, which were the most contaminated parts of both patients, were affected first and most severely, and in Case 2 the feet, which were unstained with D.N.O.C., were unaffected. The sweating which was noticed in Case 1, and which was strictly confined to those areas particularly exposed to D.N.O.C., certainly suggests a local action by the chemical.

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OCULAR NERVE PALSY ASSOCIATED WITH SEVERE HEADACHE

BY

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In 1955 Jackson described four cases of ocular nerve palsy associated with severe headache occurring in diabetic patients. He pointed out that such an association of pain and ocular nerve palsy in diabetics has been only rarely mentioned in the literature (Groenouw, 1920; Herson, 1948; Larson and Auchincloss, 1950; Goodman *et al.*, 1954). Hirson *et al.* (1953) have also described a similar case. I have recently seen two cases of this syndrome in diabetics and an entirely similar case in a non-diabetic.

Case Reports

Case 1.—A man aged 60 was first seen in April, 1954, complaining of thirst, polyuria, and loss of weight. He was found to have diabetes and was well controlled on a mixed dose of 20 units of soluble and 20 units of zinc-protamine insulin. In June he developed diplopia due to a right external rectus palsy. This recovered spontaneously in August. Towards the end of March, 1955, he developed pain localized in the first and second divisions of the right fifth nerve. This increased in intensity and was followed by complete third-nerve palsy on that side at the beginning of April. There were no other abnormal physical signs; the Wassermann reaction was negative and radiographs of the skull and a right carotid angiogram were normal. In May complete recovery of paresis took place, with relief of the pain.

Case 2.—An elderly obese woman aged 72 was first seen in 1951 with thirst and pruritus vulvae. She was found to be a diabetic and was treated with a 1,500-calorie diet. She did not attend the diabetic clinic, and was lost sight of until October, 1955. A fortnight previously she had wakened with complete ptosis of the right eyelid, and a week later severe pain started in the area of the first division of the fifth right nerve. On physical examination she was found to have a complete third-nerve palsy on the right side. Her diabetic condition was somewhat better than might have been expected, inasmuch as her urine was clear of sugar most of the day. There was, however, diabetic retinopathy, with loss of knee- and ankle-jerks. Her blood pressure was 180/110. The W.R. was negative. Her condition gradually resolved, relief of pain preceding recovery of the paralysis, which had disappeared by the early part of December, 1955. The patient refused admission to hospital, and other investigations were not possible.

Case 3.—A man aged 51 was first seen on November 10, 1955, when he gave a history that seven weeks previously he had started to have severe pain in the distribution of the first division of the left fifth nerve. This was accompanied by drooping of the lid of the left eye and double vision. The pain abated after two weeks, and by the time he was seen in the out-patient department his ptosis and double vision had disappeared. On examination there were no abnormal physical signs, no sensory loss in the area of the left fifth nerve, and no diminution of the left corneal reflex. His blood pressure was 140/80, and the urine was clear. X-ray examination of the skull, the W.R., glucose-tolerance test, full blood count, and E.S.R. were all normal.

Discussion

The first two of these cases support Jackson's observations that a syndrome of ocular nerve palsy associated with headache occurs in diabetics. The third case is clinically identical, except that the patient is not a diabetic.

This syndrome of ocular nerve palsy associated with headache, presumably due to involvement of branches of the fifth nerve, has been recognized for a long time, and has been attributed to orbital periostitis affecting the sphenoidal fissure. Brain (1947) has pointed out that the prognosis of this disorder is good and recovery takes place within a few months.

In Jackson's cases, and in those reported here and in the literature referred to, such spontaneous recovery within three months was invariable. In my cases recovery took place independently of treatment. This property of complete recovery within a relatively short space of time is in my opinion the most noteworthy feature of this syndrome, and must always be borne in mind when speculating upon its aetiology. It suggests that the proximate aetiology of diabetic and non-diabetic cases is the same, and that therefore the syndrome is not specific to diabetes, although it may well be relatively common in that condition.

In recent years cases such as these have usually been ascribed to pressure upon nerves exerted by supraclinoid aneurysms of the internal carotid artery. There are reasons for believing, however, that such aneurysms may not be responsible for all of these cases. Firstly, the natural history of this disorder with its short course and spontaneous recovery does not accord well with that of aneurysm (Jefferson, 1938). Secondly, if these cases are due to aneurysm it is difficult to understand why recovery is not followed more often by occlusion of the internal carotid artery with the production of central signs. Finally, there is the evidence against aneurysm provided by those occasions when angiography has failed to demonstrate an aneurysm.

It seems, therefore, that this syndrome of ocular nerve palsy associated with headache is perhaps relatively common in diabetes but not specific to that disease, that recovery usually takes place within three months, and that some cases at least are not due to supraclinoid aneurysm of the internal carotid artery.

Summary

Three cases are reported of nerve palsy associated with headache; two of the cases were in diabetic patients. The aetiology of the condition and its relationship to diabetes are discussed.

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Medical Memoranda

Primary Carcinoma of Liver Presenting as Hypoglycaemia

Primary carcinoma of the liver is a comparatively common form of malignant disease amongst the Chinese population of Malaya and usually presents clinically with abdominal symptoms, loss of weight, and a hard enlarged liver. A case associated with hypoglycaemia has not previously been reported in Malaya, and, so far as I know, only four cases have been published. Beers and Morton (1935) described one case and in a review of the literature found two other cases previously reported, one by Nadler and Wolfer (1920) and Elliot (1929), and the other by Crawford (1931). A fourth case was reported by Thompson and Hilferty (1952).

CASE REPORT

A male Chinese mining labourer aged 42 was admitted to the General Hospital, Kuala Lumpur, on July 2, 1953, in a state of coma of approximately twelve hours' duration. No previous history was available at the time of admission.

Clinical examination showed: temperature, 99° F. (37.2° C.); pulse 80; respiration 30; B.P. 140/90. No jaundice. Abdomen: liver palpable two fingerbreadths below the costal margin—consistency hard but not nodular. Central vascular system, N.A.D. Respiratory system: signs of right pleural effusion (confirmed later by aspiration). Central nervous system: deeply comatose; no response to painful stimuli and patient could not be aroused; no neck rigidity; pupils equal and reacting to light; reflexes equal and normal except for absent lower abdominal and bilateral extensor plantar responses. Other systems: N.A.D.

Lumbar puncture was performed and the cerebrospinal fluid was found to be clear and under normal pressure. Laboratory examination showed: proteins, 45 mg. per 100 ml.; globulin, a trace; chloride (as NaCl), 720 mg. per 100 ml.; sugar, nil. A routine blood film showed no malaria parasites. Urine examination: no sugar, no acetone, no albumin, no bile.

In view of coma and absence of glucose in the C.S.F., a clinical diagnosis of hypoglycaemia was made; 40 ml. of 30% glucose was given intravenously and the patient became conscious immediately. Intravenous glucose therapy was repeated and he was encouraged to take glucose drinks frequently. On July 3 he was feeling well, and said he had had a slight cough and right hypochondrial pain about a month before admission which responded to treatment by his doctor. Apart from these symptoms he had no complaint. This had been the first occasion on which he had lost consciousness. There was no previous history of giddiness or weakness.

On July 6 he became comatose despite frequent glucose drinks. He responded to glucose intravenously. After this

he very often lapsed into coma and did not respond to 5% glucose saline infusions, though he responded to 30% glucose intravenously for a shorter or longer interval, depending on the amount of glucose injected. Each day larger amounts of glucose had to be injected to obtain the same response. He developed a remittent fever which continued till death.

Laboratory Investigations.—Blood sugar on July 4, when conscious, was 113 mg. per 100 ml. Fasting blood sugar on July 9, 22 mg. per 100 ml., and on July 10, 15 mg. per 100 ml. Urea nitrogen, 10.67 mg. per 100 ml. (22.83 mg. urea per 100 ml.); N.P.N. 37 mg. per 100 ml. Faecal fat: Total, 6.7% of dried faeces. Neutral fat, nil. Total fatty acids, 5.5% of dried faeces. Fatty acids, 4.4% of dried faeces. Liver-function tests: icteric index, 13; thymol turbidity, 2 units (normal 0–5); alkaline phosphatase, 28.7 K.A. units (normal 10 to 13 units); serum proteins, 4.3 g.% (albumin 2.15 g., globulin 1.9 g.). Blood: W.B.C., 11,800 (polymorphs 88%, lymphocytes 12%); E.S.R. (Westergren), 15 mm. in one hour; serum potassium, 16 mg. per 100 ml.; serum sodium, 327 mg. per 100 ml. Urinary diastase, 10 units (Wohlgemuth): Kunkel's test, 8.5 units. Sputum: no acid-fast bacilli detected.

X-ray examination of the chest showed old tuberculous lesions at the left apex and a moderate-sized pleural effusion on the right side.

The possibility of an islet-cell tumour was considered, and the more or less normal liver-function tests seemed to exclude any gross hepatic involvement. Surgical opinion was sought, but owing to the patient's poor general condition an exploratory laparotomy was not performed. Deterioration in the general condition was rapid and he died on July 27.

Necropsy Report.—Body grossly emaciated. Abdomen: no free fluid present. Liver: right lobe enlarged and nodules of tumour visible below the surface; on cut section it was found to consist almost entirely of tumour with a thin layer of surrounding liver tissue of normal appearance; the left lobe was very small and had the typical appearance of portal cirrhosis; cut section showed the cirrhotic changes throughout the lobe without any evidence of tumour. Pancreas, duodenum, stomach, kidneys, adrenals, spleen, and heart were all found to be normal. The lungs showed scattered tuberculous foci in the left upper lobe and free fluid in the right pleural cavity; there was no evidence of metastases.

Histopathology.—Section from the right lobe of the liver showed multiple deposits of carcinoma, probably adenocarcinoma. Section from the left lobe showed multilobular cirrhosis. Lungs: old tuberculous lesions. Kidneys: N.A.D. Pancreas: N.A.D.

DISCUSSION

This case seems to be unique in that there was no previous history of symptoms suggestive of hypoglycaemic episodes prior to the sudden onset of coma which was the cause of admission to the hospital. In all the other reported cases previous symptoms were recorded, though one case (Beers and Morton, 1935) was initially admitted to hospital in coma. An interesting finding at necropsy in my case was the practical replacement of the right lobe with tumour, whereas the left lobe showed cirrhotic changes without any evidence of tumour. The other reported cases had tumour tissue in both lobes.

Diagnosis in the present case was difficult because hepatomegaly was negligible. The presence of a pleural effusion along with clinical as well as radiological evidence of pulmonary tuberculosis caused further difficulties in establishing the diagnosis during life. The liver-function tests were normal apart from an increased serum alkaline phosphatase (28.7 King-Armstrong units). This case shows once again that little reliance can sometimes be placed on these tests.

Mann (1927) showed experimentally in animals that removal of about 80% of the liver tissue produced a state of hypoglycaemia which required progressively increased