AN UNUSUAL CASE OF CEREBRAL MALARIA

BY

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This case is reported because of the large number of parasites in the blood film and the severe clinical signs, in spite of which recovery followed.

Clinical History

The patient, a soldier aged 22, was admitted to a C.C.S. in North Africa on July 10, 1943. We subsequently learnt that while on local leave in North Africa he became ill, but attributed the illness to the heat and did not consult a medical officer. He had no clear memory of how he reached this C.C.S.; he last remembers travelling in a train with other soldiers, who finally took him to the central M.I. room of this area.

He was admitted late at night, about five or six days after the onset of the illness. On examination he complained of headache and vomiting. He was drowsy but not unconscious, and could answer questions reasonably well. The temperature was 102.4° F. The spleen was easily palpable. The urine was of normal colour. Blood slides showed a very heavy malarial infection. The thick film was crowded with parasites. Examination of the central parts and the edges of the thin film revealed that, on an average, 35% of the red cells contained parasites. Of the infected cells 82% had one ring, 17% had two rings, and 1% had three or four rings per cell. Several crescents of *Plasmodium falciparum* were also seen.

He was given 10 gr. of quinine dihydrochloride in 20 c.cm. of water intravenously and 12 gr. by mouth at 11.30 p.m., the latter dose being repeated in six hours. Next day his condition was only fairly satisfactory; he was still drowsy, but he took 10 gr. of quinine six-hourly by mouth without vomiting. The temperature remained normal all day. A blood film showed large numbers of parasites to be still present. He took fluids fairly well, but passed only very small amounts of urine.

Early on the morning of July 12 the patient was found to be quite unconscious, cold, and collapsed. The tongue was hard and dry. The temperature was 97° F., the blood pressure 80/60, and the pulse 90 per minute. Hiccup was present, and breathing was shallow. As the patient appeared to be dying he was given an immediate injection of nikethamide (coramine). No urine had been passed since the previous night and the bladder appeared to be empty, but when a catheter was passed an ounce of urine was obtained which contained albumin but no blood. Microscopically, granular and hyaline casts were seen. A glucose-saline drip was put up, and by this route he was given in the course of the day 30 gr. of quinine dihydrochloride and two blood transfusions, each of 500 c.cm., without a reaction of any kind. The patient was Group B, and each donor was of this group. The serum and red cells of the patient and of each donor were cross-matched and the results read microscopically at the end of one hour. A blood film of the patient showed large numbers of parasites to be still present. The haemoglobin before the transfusion was 70% (Sahli). By evening his condition had improved; the B.P. had risen to 105/80, and the temperature was 101° F. No urine was passed that day.

The following morning—July 13—the patient was semiconscious, and was able to take fluids by the mouth. The temperature was normal, the conjunctivae showed slight jaundice, and a specimen of urine voluntarily passed was typical of that seen in blackwater fever. Spectroscopic examination revealed the presence of oxyhaemoglobin. No red cells were seen in the centrifugized deposit, but granular and hyaline casts were present. While the compatibility of the transfused blood appears to have been established by indirect grouping and careful direct cross-matching, the possibility remains that the haemolysis observed was not due to quinine but to antibodies in the recipient's blood which could not be detected by the methods at our disposal. There was no history of any previous blood transfusion. The intravenous drip was continued; no further quinine was prescribed, and the patient was given by mouth one drachm of sodium bicarbonate hourly to alkalize the urine rapidly. In the course of the day he was given two intramuscular injections of mepacrine methanesulphonate (atebrin musonate), each of 0.1 g., and the urine gradually returned to a normal colour. At 6 p.m. the temperature was 103.6° F.; he was given mepacrine hydrochloride (atebrin) 0.1 g. by mouth, and this was repeated in 6 hours. At 9 p.m. the temperature, which had been taken hourly, had risen to 106° F., and the patient, after having remained semiconscious all day, became delirious and restless. Cold sponges were given half-hourly until 11 p.m., when the temperature had fallen to 102° F.

The intravenous drip was stopped, as oedema of the sacrum was found to be present; he was passing urine freely.

On July 14 the patient's general condition was much improved; for the first time he was quite conscious and rational. The morning temperature was 98° F. A blood film showed no parasites; the red cells exhibited a marked degree of macrocytosis, and megaloblasts were present. The urine still contained albumin and casts. Mepacrine hydrochloride was continued in a dosage of 0.1 g. t.d.s. That evening the temperature rose to 104.8° F.

On July 15 his general condition was better, but he was found to have thrombophlebitis of the left axillary vein (this arm was used for the drip) with oedema of the forearm and hand. The morning temperature, which so far had always been normal, was 100.4° F.

Temperature chart of the case.

There were rales over the lower lobes of both lungs but no dullness. It was decided that he had a hypostatic pneumonia, and was put on sulphadiazine 1 g. four-hourly. The temperature reached 102° and 101° F. on the next two nights, and thereafter settled, remaining normal all day on July 21. By this time the lung signs had disappeared.

Summary

A case of cerebral malaria is reported in which 35% of the red cells were infected by one or more parasites of *Plasmodium falciparum*.

The most-pronounced cerebral symptoms came on after the patient had been on large doses of quinine for 36 hours.

Transient haemoglobinuria followed 30 gr. of intravenous quinine and two blood transfusions.

Hyperpyrexia was found to be developing after three days of intensive quinine treatment.

Hypostatic pneumonia complicated recovery.

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EFFECTS ON RATS OF PROLONGED FEEDING
WITH THE STAPLE AFRICAN DIET

BY

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It is known from numerous surveys and observations that pulmonary tuberculosis and other diseases of the respiratory tract are especially prevalent among the Africans (South African negroes). It is also common knowledge that cirrhosis of the liver and especially primary cancer of the liver are very often encountered in this people. In an extensive investigation into the incidence of cancer in South Africa, Berman (1940, 1941) has shown that in a series of 253 cases of cancer of all organs in adult male Africans working in the Witwatersrand gold mines no fewer than 222, or 90%, were primary in the liver. This remarkable state of affairs is even more strongly emphasized when it is remembered that liver cancer is the rarest neoplasm in Europeans.

Several factors are regarded as contributory to this high incidence of cancer, one of which is cirrhosis, which is almost invariably associated with liver cancer. There is a considerable body of opinion which regards this susceptibility to liver cancer

in the pigmented peoples as due to some racial factor. Des Ligneris (1940) has shown that extracts from the cancerous and non-cancerous livers of Africans are capable of producing neoplasms of the skin when painted on the backs of mice. The extracts from normal Europeans are said to be less potent in this respect. A similar experience has been reported by Hieger (1940).

Effect of African Diet on Rats

Malnutrition among the Africans is widespread in South Africa. The overwhelming majority feed on a diet consisting largely of maize meal (mealie pap) and sour milk. This forms the staple from the time of weaning throughout life. Before invoking a racial or a genetic factor in modifying the incidence of disease it seemed highly desirable to ascertain the effect of the African diet on normal animals. Accordingly 125 rats weighing from 40 to 50 g. were fed exclusively on mealie-meal porridge and sour milk. The mealie-meal porridge was concentrated to form a solid mass, while the sour milk was prepared from fresh milk allowed to ferment in a warm room. The animals received liberal amounts of this food. Apart from thinning of the hair over the abdomen and hind legs and roughening of the tail, no obvious signs of acute avitaminosis were recognized.

After 14 months 12 rats were killed and a full post-mortem examination was performed. The others are being studied biochemically. In all of those killed some degree of liver pathology was evident macroscopically. This varied from diffuse enlargement of the whole liver with obvious fatty change to a widespread nodular cirrhosis, the latter usually involving the left side of the liver. In one case there was complete atrophy of the left lobe, with enormous compensatory hypertrophy of the right lobe—so much so that the enlarged lobe extended almost into the pelvis. In this instance the remains of the left lobe could be seen as two small appendages of cirrhotic tissue.

In this series of rats it seemed that the liver first enlarged and underwent fatty changes and later cirrhosis supervened, or else complete atrophy of the affected lobes occurred, with corresponding enlargement of the right side. The heart was grossly enlarged, and in 9 cases one or both lungs showed recent or old-standing inflammatory lesions with areas of bronchiectasis or abscess formation. The fat in the mesentery, retroperitoneal, or subcutaneous regions was abundant. The skull was very much thickened, especially in the occipital region. The suture lines could be readily identified by the zones of great vascularity. The upper incisor teeth were particularly affected; many of them were broken, some fused, and others loose. The pituitary was enlarged, the thyroids were atrophied, and the suprarenals were small and of greyish colour. In four cases the lymph glands of the peri-oesophageal region and above the lesser curvature of the stomach or above the abdominal aorta were of dark-brown colour, due to the presence of haemosiderin. The jejunum in those cases of advanced cirrhosis contained a dark viscid material which gave the reaction of blood. It is noteworthy that although many thousands of rats were examined post mortem over a number of years no lesions in the liver of the kind described above were ever observed.

Comment

The significant features of this feeding experiment in rats are the gross pathology in the liver, the frequency of lung lesions, the enlarged heart, the abundance of adipose tissue, the thickened skull, and the dental affections, all of which occurred without any recognizable manifestations of acute vitamin deficiency.

The production of liver damage by means of a diet which forms the staple of the overwhelming number of Africans in South Africa is not without its sociological implications. It may also have repercussions in other parts of the world where economically impoverished individuals are forced to live on a diet similar to that of the African in the Union of South Africa.

This investigation was carried out in the Department of Anatomy, and all facilities were generously provided by the University of the Witwatersrand, Johannesburg. This and subsequent aspects of the problem represent, and will represent, the collaborative efforts

especially of Dr. Leon Golberg of the South African Institute for Medical Research, and of Christine Gilbert, Dr. Theodore Gillman, Joyce de Bruijne, Marianne Cassirer, and Joel Mandelstam of the Department of Anatomy. The work is proceeding actively to discover the factors responsible for the lesions produced experimentally in the rat.

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Medical Memoranda

Periarteritis Nodosa diagnosed Clinically

Following on the annotation on periarteritis nodosa published in the *British Medical Journal* of May 15, 1943 (p. 608), this case record may be of interest.

CASE HISTORY

A woman aged 34 was admitted to the Meath Hospital under my care in June, 1942, complaining of "asthma" for the past week. Previous to this attack she had never suffered from asthma or bronchitis or from any other serious illness. On admission her temperature was normal and her pulse rate 118. There was evidence of acute bronchitis, but otherwise physical examination revealed nothing abnormal. A chest radiograph was negative. The urine contained some albumin on admission, but no casts at any time. Investigation for protein sensitivity to foods, flowers, and animal emanations was negative. During her stay in hospital her temperature was occasionally slightly elevated, and her pulse rate after the first week settled down to 80. After a period of five weeks in hospital, during which time she was treated on general lines, the patient went home feeling fairly well.

In Sept., 1942, she began to have further attacks of asthma, for which she was treated with a stock vaccine by her general practitioner, who stated, however, that even a small dose of the vaccine often gave her quite a severe general reaction; and finally the treatment had to be abandoned. Shortly after this she got a thrombosis of the right long saphenous vein, which gave rise to fever at night-time. She recovered completely from the thrombosis, but in Nov., 1942, started to complain of extreme general weakness and malaise and a raised evening temperature. A blood culture done at this time was reported to contain *B. proteus*, but this was considered to be a skin infection. Owing to the presence of petechial haemorrhages on the chest and back, a blood examination was also carried out, with the following results: R.B.C., 4,100,000 per c.mm.; W.B.C., 26,000 per c.mm.; Hb, 65%; colour index, 0.8; platelets, 110,000 per c.mm. Differential count: polymorphonuclear leucocytes 85%, lymphocytes 12%, large mononuclears 3%. Prothrombin clotting time, 35 seconds.

The patient was readmitted to hospital with a temperature of 99° and a pulse rate of 96. On examination this time, in addition to her chest condition she had a very loud grating to-and-fro pericardial friction rub, heard all over the praecordium, but the heart sounds underneath did not appear to be altered. There was abundant albumin in her urine, and a catheter specimen revealed pus, red cells, and granular and hyaline casts. Her blood urea was 36 mg. per 100 c.cm. She was put on a nephritic diet. During the first week her temperature rose until it touched 103°, and her pulse rate became elevated to 120. At this stage she was treated with sulphathiazole (0.5 g. q.q.h.), but this gave rise to severe vomiting within the first 24 hours, and was discontinued. A second blood culture done a week after admission grew a staphylococcus—possibly also a skin infection—but the patient was started immediately on large doses of sulphadiazine, and during the next three weeks she received two courses each consisting of 25 g. Repeated white cell counts were done to check sulphonamide treatment; in the course of these a leucocytosis of 42,000 per c.mm. was recorded, with an eosinophilia of 9%. A fortnight or so after admission all signs of pericarditis had gradually disappeared. During her second period in hospital the patient had several attacks of asthma. At times also transitory painful lumps of about the size of a grain of rice appeared on her scalp and eyelids, and remained for about three days. In the middle of December she developed an angioneurotic oedema of the right arm. A little later there was a definite ulnar neuritis of this arm. Throughout her stay her urine was loaded with albumin, and casts were always present—granular, hyaline, and fatty. Her blood urea at all times remained within normal limits. She was discharged at the end of February at her own request.

Shortly after her return home she developed oedema of the legs, which gradually became a generalized oedema associated with ascites. During this time her urine on boiling became almost solid with albumin. In April, 1943, she had painful subcuticular lumps of about the size of a rice grain on the anterior surface of her forearms. Bullae then developed around each lump, and after from four to five days these burst, leaving punched-out crater-like ulcers with bluish-purple margins. At the same time the fingers, especially those corresponding to the ulnar distribution of the right hand, became blue, and dry gangrene ensued. The toes also became blue, but to a less degree. The patient's condition thereafter deteriorated rapidly until, about three weeks before death, the ulcers had coalesced to