a bilateral extensor plantar response; no evidence of meningeal irritation. Urine, N.A.D.

In view of the fact that he had recently been in an endemic centre of malignant tertian malaria the diagnosis of cerebral malaria was entertained. Blood films were examined and revealed a heavy infection with *Plasmodium falciparum*, numerous ring-stage parasites being present. This finding was later confirmed by Dr. Houston of the Pathology Department, Sunderland Royal Infirmary.

Treatment.—Quinine sulphate 10 gr. (0.65 g.) was given orally at 2 p.m., and the patient was able to take sips of water by mouth. Acid quinine hydrochloride 10 gr. in 10 ml. of sterile distilled water was administered half an hour later by slow intravenous injection. Rectal glucose-salines were ordered four-hourly. At 11.30 p.m. the coma was somewhat deeper and the patient was still restless and incontinent of urine. Temperature 99.8° F. (37.7° C.), pulse 108, respirations 24. He was now unable to take anything by mouth. The intravenous quinine was repeated. On the morning of Sept. 9 his condition was unchanged: Temperature 99.8° F., pulse 104, respirations 24. Neck rigidity had now appeared. Lumbar puncture was performed under local analgesia and 10 ml. of clear fluid under slightly increased pressure withdrawn. As the patient was not now retaining fluids per rectum a glucose-saline intravenous drip was started. He was still incontinent and could take no fluids by mouth. On the morning of the 10th his condition was greatly improved; he was conscious and rational, and taking copious fluids by mouth. Temperature 101.4° F. (38.55° C.), pulse 92, respirations 28. His further convalescence was uneventful, and a standard quinine-mepacrine course was instituted. On the 12th a blood film revealed no parasites; his temperature was 97.4° F. (36.3° C.), pulse 72, and respirations 20, and he was discharged home.

Discussion

In arriving at a diagnosis in this case the following points were of importance: (a) A recent visit to a malarious area; (b) history of headache, vomiting, and rigors; (c) sudden descent into coma. The suspicion of cerebral malaria thus aroused, coupled with absence of the clinical picture of any of the more common causes of coma in this country, led to the examination of blood films with resulting confirmation of the diagnosis.

As the clear-cut history in this instance may not be paralleled in other cases of cerebral malaria occurring in Britain, several other conditions must be considered in the differential diagnosis. The most important of these are:

1. *Meningitis* (in particular the hyperacute and fulminating forms).—The frequent occurrence of signs of meningeal irritation in cerebral malaria may confuse the diagnosis, and a lumbar puncture may be essential to differentiate.

2. *Alcoholic Coma*.—It is stated that cerebral malaria often closely simulates alcoholism. This has resulted in fatalities from misdiagnosis, and emphasizes the importance of examining blood films in doubtful cases of coma.

3. *Cerebral Vascular Accident*.—(a) Subarachnoid haemorrhage: In this condition severe headache followed by rapid onset of stupor or coma is characteristic, and meningeal irritation is usually well marked. Lumbar puncture, however, readily establishes the diagnosis. (b) Cerebral haemorrhage, thrombosis, or embolism: The production of embolism by malaria parasites may lead to various peripheral manifestations, among which hemiplegia, monoplegia, and aphasia have been described.

4. *Uraemia*.—The most likely causes of this condition in young adults are malignant hypertension and the alkali treatment of peptic ulcer associated with renal insufficiency. The onset of coma may be rapid, and prodromata equivocal. Examination of the urine, blood urea, and alkali reserve will differentiate the condition from cerebral malaria.

The present case occurred in a man who returned from an endemic area within the accepted incubation period of the disease, and illustrates the importance of considering a diagnosis of cerebral malaria in cases of coma of uncertain origin, particularly in Service personnel returning from overseas. This is especially important, as early diagnosis and adequate treatment are so essential in a disease which carries a 40% mortality in treated cases (Sanford, Crawford, and Warr, 1940). Endemic cases are unlikely to occur, as tropical strains of the malignant tertian parasite fail to survive in the mosquito at temperatures below 75° F. (24° C.) (Shute, 1945).

The dosage of quinine used in this case was somewhat higher than that advocated by Manson-Bahr (1942)—i.e., 5 to 7 gr. (0.32 to 0.45 g.)—but no untoward reactions were encountered. Intramuscular mepacrine is now being used in preference to intravenous quinine in these cases, as the likelihood of toxic

reactions is even less with the former drug, but it was not immediately available for use in this instance.

Summary

A case of cerebral malaria, with recovery, occurring in Great Britain is described.

The differential diagnosis is discussed.

The importance of early diagnosis and prompt adequate treatment is emphasized.

Our thanks are due to Dr. W. Campbell Lyons, M.O.H., South Shields, for permission to publish this case; to Dr. Houston, Pathology Department, Sunderland Royal Infirmary, for his report on the blood films; to Dr. N. Strang, deputy medical superintendent, who allowed us to treat the case in his ward; and to Dr. W. Downing, South Shields, who referred the case to us.

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KALA-AZAR WITH ONSET OF SYMPTOMS IN GREAT BRITAIN

BY

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In view of the return to Britain of many of our soldiers from the shores of the Mediterranean, where kala-azar is endemic, the following case may be of interest. It serves to illustrate the fact that symptoms of kala-azar may not appear for the first time until the patient reaches this country, when the disease may simulate a primary attack of malaria.

Case History

The patient, a man aged 29, served as a soldier in North Africa and Italy for 3½ years. During that time he had no symptoms of illness. He returned to England and was apparently well for four months. On April 18, 1946, he noticed small lumps in both groins, and the next day an attack of shivering and sweating began. He continued having one of these attacks each day, but in spite of them felt quite well. Apart from slight initial nausea his appetite remained good and there were no other symptoms. On April 27 he was sent into hospital as a case of primary malaria.

On admission his general condition was fair. He had a sallow complexion (this became dusky later in the disease), and his tongue was brown and furred. A soft swelling was palpable in the left hypochondrium, extending for three or four fingerbreadths below the costal margin. It was of an indefinite outline, and was first noted as " ? kidney; ? spleen." The liver edge was not palpable at this stage. The inguinal glands were felt to be slightly enlarged. The heart, lungs, and C.N.S. were normal clinically. Temperature, 101.2° F. (38.4° C.); pulse, 104; respirations, 22. During the first week after admission to hospital the patient had an intermittent high pyrexia reaching 102°–103.8° F. (38.9°–39.9° C.), with daily rigors and sweating. Occasionally there were two spikes of temperature during the 24 hours. He continued to "feel fine." By April 30 the mass in the left hypochondrium had increased in size and was obviously the spleen. The liver edge was also palpable for two fingerbreadths below the right costal margin. Skiagrams of the chest showed some congestion at the right costo-phrenic angle (presumably due to the enlargement of the liver); otherwise the chest was clear. A blood count showed: white cells, 2,140 per c.mm. (polymorphs 68%, lymphocytes 29%, monocytes 2.5%, eosinophils 0.5%); red cells 3,650,000 per c.mm.; Hb, 70%; C.I., 0.95. Repeated blood smears were negative for the malaria parasite. The urine showed no abnormality and the diazo reaction was negative.

As a diagnostic measure, starting on May 1, a course of two days' quinine 10 gr. (0.65 g.) t.d.s., followed by three days' mepacrine 0.1 g. t.d.s., was given, with no effect on the temperature. This was followed by penicillin injections (15,000 units three-hourly for 8 days), which proved equally ineffective. On May 2 agglutination tests on the serum were negative for typhoid, paratyphoid, dysentery, and *Brucella abortus* and *melitensis* organisms. Many dilutions were used with the *Br. abortus* to exclude the possibility of a zone reaction. A blood Wassermann reaction was also negative. On May 14 a formol-gel test was strongly positive. The next day a sternal puncture was performed and a few Leishman-Donovan bodies were found in the smear. An inguinal gland puncture, however, did not reveal any parasites in the stained film.

A course of 21 injections of "anthiomaline" (a 6% lithium antimony thiomalate solution containing 16% of antimony) was given

from May 18 onwards, starting with 2 ml. I.M. on alternate days, the dose later being increased to 4 ml. Iron was given for the anaemia. The temperature swing gradually diminished in height, and became normal and remained so after the nineteenth injection (June 22). Clinically there was marked improvement, with cessation of sweats and diminution in the size of the spleen, and the white blood cells showed a steady increase. Blood counts were as follows. June 3: white cells, 1,460 per c.mm. (polymorphs 44%, lymphocytes 48%, monocytes 8%). June 13: white cells, 2,180 per c.mm. (polymorphs 29%, lymphocytes 62%, monocytes 9%). July 2: white cells, 4,660 per c.mm. (polymorphs 45%, lymphocytes 52%, monocytes 3%); red cells, 3,750,000 per c.mm.; Hb, 78%; C.I., 1.04.

Discussion

The diagnosis was that of a febrile disease with splenomegaly and leucopenia occurring in a patient returning from the Mediterranean area. Malaria was excluded by blood smears and the therapeutic test of quinine and mepacrine administration, enteric and undulant fever by the agglutination tests, and pulmonary tuberculosis by the chest skiagrams. Kala-azar was suggested strongly by the formol-gel test of Napier and confirmed by finding Leishman-Donovan bodies on sternal puncture. This was preferred to splenic puncture, which entails a risk of haemorrhage.

The long incubation period should be noted. It is stated variously to be from 1 to 6 months, but cases may occur 1½ years after exposure. As modern treatment with antimony has altered the mortality from 80% to a much lower figure the importance of early diagnosis is obvious. In 1944 the *Bulletin of War Medicine* remarked that a few proved cases of kala-azar had already been seen in this country among returning soldiers, and Thompson (1944) quoted a case occurring in an English seaman. Armstrong (1945) also described two examples of asymptomatic kala-azar in soldiers.

I am indebted to Dr. E. James, medical superintendent, for permission to publish this note, and to Mr. D. Butler for help with the laboratory investigations.

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Medical Memoranda

"Purpura Provocata" in Pellagra

During the time we acted as medical officers in prisoner-of-war camps in the Netherlands East Indies a great number of cases of pellagra in all its variations were observed. The purpose of this article is to draw attention to the occurrence of purpura as a specific symptom in these cases.

One of the best-known symptoms of pellagra is erythema, which shows a predilection for parts of the body exposed to the sun. The erythema may be pronounced, but usually does not lead to purpura. On the contrary, purpura may precede it, and has been known to occur on the site of subsequent erythema. What we wish to emphasize is that the purpura should not be considered a severe form of erythema.

Purpura is a specific symptom *sui generis*. It occurred not only along the whole course of the alimentary tract but also in the skin. Only in a minority of cases was hyperaemia with dilated capillaries of the lip mucosae and gums observed. It should be mentioned that bleeding of the gums hardly ever occurred, and in these rare cases it was often doubtful if it was due to vitamin C deficiency or to pyorrhoea, etc. Purpura, often responding to administration of vitamin C, was particularly common in the early days of imprisonment. To attribute the whole illness to vitamin C deficiency because of the coincident occurrence of purpura is obviously incorrect. In our opinion the purpura we observed belongs to the pellagra group of symptoms; but this will be discussed later.

The first case occurred in an officer, thin, pale, without internal symptoms, suffering from petechiae of the lower legs. He had been "punished" the previous day by the Japanese and had to stand to attention for seven hours. We made a diagnosis of "orthostatic thrombocytopenic purpura," fully aware that this was an unsatisfactory designation. Very soon it became clear that the petechiae, particularly on the lower legs and lower arms, should be regarded as one of the initial symptoms of pellagra. The linear distribution was striking. Haemorrhagic stripes even to a length of 10 in. (25 cm.) occurred, particularly if the patient was exposed to the sun,

the linear form being due to scratching because of lice or scabies. Indeed, in all cases purpura could be produced artificially by scratching the skin with the finger or a pencil, similar to Nikolsky's bullous phenomenon in pemphigus or Köbner's phenomenon in psoriasis and lichen ruber; purpura followed, however, the same day. Exposure to the sun accelerated the phenomenon.

It should be pointed out that purpura provocata in pellagra is not identical with Rumpel-Leede's phenomenon, in which haemorrhages occur *distal* to the tourniquet. In fact, both phenomena indicate the permeability of the blood vessels and the "haemorrhagic constitution." They may even be combined—e.g., in those cases of Rumpel-Leede's phenomenon in which haemorrhages also occur *under* the tourniquet. We regard this symptom as a severe form of Rumpel-Leede's phenomenon. If doubt is expressed with regard to the diagnosis of pellagrous purpura, that of vitamin-C-deficiency purpura being preferred, we would emphasize that all patients were proved to be suffering from pellagra or (as we prefer to call it) a polydeficiency. We agree with those who consider that the use of the term "pellagra" has been too restricted in the past, and that in its widest concept it embraces a poly- (or even an omni-) deficiency, in which lack of sometimes one and sometimes another vitamin dominates the syndrome.

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Adenoma of Islets of Langerhans

The following case seems to be interesting enough to merit publication.

CASE REPORT

The patient, a woman aged 59, was admitted to hospital late in the afternoon of Feb. 2, 1946. The only history was that she had sat down on the floor in the middle of a shop and refused to move.

On examination she was found to be conscious, but to all questions her only reply was: "I feel damn rotten." In the ward she was somewhat difficult to control. She was very obese, and her blood pressure was 245/140. No other abnormal signs were present. Morphine was given. By the early hours of the next morning she had quite recovered, but she could recall nothing save that she had gone out shopping that afternoon. She had had many similar attacks before and had found that they could be prevented by a cup of tea and some white bread. The attacks began in July, 1943. At that time they occurred at intervals of many months. Just before and after admission they averaged three or four a week.

During an attack her skin became cold and clammy. Her pupils were slightly dilated. Often the first warning was that she began to wink at everyone. Normally a very talkative person, she would become very quiet. Occasionally she became restless, and on one occasion threw bread crusts at some visitors. During one of these attacks her blood pressure was taken and it was found to be lower than her normal. The attacks were controlled in the early stages by giving 25–50 g. of glucose by mouth. This resulted in her recovery within five to twenty minutes. The patient was always unaware of what had happened.

Examination of the blood showed: red cells, 5,850,000; white cells, 4,200; Hb (Sahli), 105%; urea, 32 mg. per 100 ml.; Wassermann reaction, negative; B.S.R. and blood slide, N.A.D.; x-ray examination of skull, N.A.D.; urine, N.A.D.

Blood Sugar Estimations.—Feb. 7. 175 mg./100 ml. (four hours after a meal). Urine was negative, as it was throughout the glucose-tolerance curves. Feb. 12. Fasting level, 36 mg./100 ml. Feb. 13. Sugar-tolerance curve: fasting level, 32 mg./100 ml. 50 g. of glucose given; blood sugar after 1/2 hour, 96 mg./100 ml.; 1 hour, 117; 1½ hours, 108; 2 hours, 32; 2½ hours, 24. During an attack the reading was 19 mg./100 ml. Feb. 15. Fasting level, 75 mg./100 ml. Feb. 28. Sugar-tolerance curve: fasting level, 31 mg./100 ml. 50 g. of glucose given; blood sugar after 1/2 hour, 56 mg./100 ml.; 1 hour, 127; 1½ hours, 125; 2 hours, 80; 2½ hours, 44. The patient was quite unaware of the first blood being taken, but the 50 g. of glucose soon pulled her round.

A diagnosis of adenoma of the islets of Langerhans was made and a laparotomy was decided upon. This was done by Mr. W. J. Liddle, assisted by Dr. G. H. Moore, on March 28. A small round tumour was removed from the head of the pancreas. It was situated partly behind the duodenum, and it shelled out quite easily. A careful search was made for a possible second or third tumour but none was found. A continuous intravenous glucose-saline drip was begun before the operation. Blood was given in the theatre. An hour after her return to the ward the blood sugar was 219 mg./100 ml. The urine contained sugar the next day. The patient died on the evening of March 29. It may be added that she was conscious until shortly before death, but her breath smelt of acetone.

The tumour was 5/8 in. (1.6 cm.) in diameter; it was almost round, and firm in consistency. Section showed the presence of an adenoma of the islets of Langerhans.

I am indebted to Dr. J. R. Turner and Dr. Ison for permission to publish this report.

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