boplastin generation, and serum fibrinogen were normal. Clot retraction was slightly defective. No drug history other than occasional A.P.C. tablets was obtained. She was given ascorbic acid 400 mg/day. On follow-up she showed a mild intermittent thrombocytopenia. The lowest value was 62,000/mm.^{3} She still bruised occasionally and the gums continued to bleed easily.

Her history was given with reluctance and two points emerged later. Firstly, she had taken two double whiskies (or more) at midday for some years and additional alcohol later in the day. She was advised to discontinue alcohol. Bruising and gum bleeding subsequently ceased, and the platelet count has remained in the normal range. Secondly, her mother was said to have a chronic anaemia and to bruise easily. The mother was also investigated (see below) and found to have Gaucher's disease. Sternal marrow puncture was therefore carried out on the daughter and a very occasional Gaucher cell found. Megakaryocytes appeared normal in number.

A widow aged 72, mother of the above patient, was seen in November 1968 with a 10-year history of bruising and bleeding gums. She had undergone hysterectomy for menorrhagia 20 years previously. For the past three years bilateral arthritis of the hips impaired her mobility. On examination she had obvious pingueculae on both eyes and yellowish-brown skin pigmentation. A firm spleen was palpable three fingerbreadths below the costal margin. Haemoglobin concentration was 10·1 g/100 ml; W.B.C. 3,200/mm^3; platelets 42,000/mm^3; serum vitamin B_{12}, folate, and iron were in the normal range. Sternal marrow puncture showed numerous clusters of Gaucher cells. Erythropoiesis was normoblastic; haemoglobinization was defective. There was a considerable increase in haemosiderin, mainly in Gaucher cells, some of which showed pronounced erythrophagocytosis. Many "ring" sideroblasts were seen. She was treated with pyridoxine, 100 mg twice daily, without response.

Nine months later she was admitted to hospital with increasingly severe pain in both hips and progressive disability. She was then unable to walk more than 100 yards (90 m) with the aid of sticks. Haemoglobin was 9·4 g/100 ml, W.B.C. 6,100/mm^3 with normal differential, and platelets 33,000/mm^3. The prothrombin, bleeding, and cephalin times were normal. Radiographs of both hips showed severe arthritic changes.

A left McKee arthroplasty was performed three days after admission (Mr. Nigel Harris). Management included fresh blood and platelet concentrate transfusion. She developed mild jaundice, serum bilirubin 4·1 mg/100 ml, which persisted for 10 days. Platelets fluctuated from 30,000 to 153,000/mm.^{3} Histology of the left femoral head showed foci of Gaucher cells but no osteolytic destruction. The articular surface and underlying bone showed extensive changes of osteoarthritis.

A right McKee arthroplasty was performed a month later. She had an uneventful postoperative course.

Comment

Adult Gaucher's disease can be relatively benign. The elder of the two patients was aged 72 and had well-established disease, yet underwent bilateral McKee arthroplasty with good functional results. She was found to have sideroblastic anaemia with many typical "ring" sideroblasts in the marrow, unresponsive to pyridoxine. Gaucher's disease joins the growing list of disorders which may give rise to a failure of haem synthesis whose visible expression is the "ring" sideroblast in the marrow and a dimorphic anaemia (Mollin, 1965). She had persistent thrombocytopenia, and operative management included transfusion of platelet concentrates. She had well-marked skin pigmentation. Haemosiderosis in Gaucher's disease is well documented (Brill and Mandelbaum, 1913). Its cause is not discussed in previous case descriptions. The observation, in this case, of erythrophagocytosis with excess haemosiderin in Gaucher cells, combined with the features of sideroblastic anaemia, links this form of pigmentation with that well recognized in other sideroblastic anaemias.

The daughter was shown to have an early or a mild form of the disease when Gaucher cells were specifically looked for, after diagnosis in the mother. Her complaint had been easy bruising and gum bleeding associated with intermittent thrombocytopenia. In her case, however, the presence of Gaucher cells did not seem to be related to the thrombocytopenia. She had been accustomed to taking significant amounts of alcohol every day. Ethanol is now recognized as a potent depressor of marrow function: megaloblastic anaemia with folate deficiency may occur; spontaneous reticulocytosis after discontinuing alcohol has been known for some time (Sullivan and Herbert, 1964).

There is recent evidence that alcohol may cause thrombocytopenia without affecting other blood elements and without folate deficiency (*Journal of the American Medical Association*, 1970). The effect on platelet production is reversible, as it was in the present case.

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Primary Clostridium welchii Meningitis

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British Medical Journal, 1971, **1**, 591–592

A case of *Clostridium welchii* meningitis unassociated with head injury or brain abscess is reported. The illness began with a perforated duodenal ulcer.

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Case Report

A 38-year-old Chinese waiter, resident in Britain for 12 years, was well until May 1969, when he was admitted elsewhere with a perforated duodenal ulcer. The perforation was oversewn and covered with omentum. Postoperatively he had a low fever, which responded initially to antibiotics. After two weeks, however, he developed a small sterile right-sided pleural effusion and his fever had returned. At laparotomy no pus or other abnormality was found, apart from a possibly oedematous liver. The fever continued, and nine days later jaundice appeared. Biochemically this was of the hepatocellular-damage type and was attributed, on the basis of time intervals, to toxicity to halothane, which had been used at both operations. The jaundice became severe and hepatic coma supervened. Supportive therapy was given and he gradually became less jaundiced, though fever up to 100°F (37·8°C) persisted. He had by now lost a great deal of weight. A white cell count showed a neutrophil leucocytosis (18,500/mm^3). Three months after the first operation a further laparotomy was performed, but no pus or other abnormality was found, though an operative liver biopsy was subsequently reported to show changes compatible with halothane toxicity.

After the third operation the fever continued but the jaundice cleared. Numerous courses of chemotherapy virtually throughout his illness included penicillin, streptomycin, kanamycin, ampicillin, tetracycline, carbenicillin, cephaloridine, and cloxacillin. Four

blood cultures taken during this period were sterile. He was now very emaciated, febrile, and complaining of continuous slight headache.

Four months after the first operation he was found to have persistent neck stiffness. The C.S.F. contained 700 white cells/mm³ and 90 mg of protein per 100 ml C.S.F. cultures were sterile. Treatment with parenteral chloramphenicol and penicillin brought no response, subsequent lumbar punctures showing a rising C.S.F. white cell count and protein content. He was transferred to the neurosurgical unit at this hospital seven weeks after the first lumbar puncture.

On admission he was very wasted, with meningism and a temperature of 99-101°F (37·2-38·3°C). He continued to complain of headaches. There were no localizing neurological signs. An E.E.G. was normal, as were cisternal myelography and bilateral carotid angiograms. Examination of cisternal C.S.F. showed it to be turbid, with a white cell count of 70/mm³ (90% neutrophils), protein 250 mg/100 ml, and sugar 18 mg/100 ml. A smear of the C.S.F. deposit showed numerous large Gram-positive bacilli. Cultures yielded a heavy growth of type A *Cl. welchii*.

Treatment was begun with benzylpenicillin 4 megaunits six-hourly intramuscularly and 20,000 units intrathecally on alternate days. This combined treatment was continued for four weeks, after which penicillin was given intramuscularly alone for a further 10 days.

The findings on examination of lumbar C.S.F. specimens are given in the Table; they show a slow but progressive response to

Changes in Temperature and C.S.F. Findings in a Man with Cl. welchii *Meningitis in Response to Treatment*

Date	Temperature		C.S.F.		
	°F	°C	W.C.C./mm³	Protein (mg/100 ml)	Sugar (mg/100 ml)
7/11/69*† ..	99·0	37·2	70	250	18
10/11/69‡	101·0	38·3	540	470	0
12/11/69	100·0	37·8	300	330	6
14/11/69	99·5	37·5	300	340	10
18/11/69	98·4	36·9	160	420	22
24/11/69	98·4	36·9	210	310	30
28/11/69	98·4	36·9	100	295	33
2/12/69	99·0	37·2	130	239	35
5/12/69	100·0	37·8	20	165	40
8/12/69	99·0	37·2	10	83	53

* Cisternal C.S.F. † Large Gram-positive bacilli were seen in the spun deposit of the first three specimens, and *Cl. welchii* was cultured from the first. ‡Two days after starting penicillin treatment. Intramuscular penicillin discontinued on 16 December, intrathecal penicillin discontinued on 5 December.

treatment, with a steady fall in white cell count and protein content and a rise in sugar concentration. The patient's condition improved steadily. The headache stopped, the fever settled, the neck stiffness disappeared, and he began to gain weight. He left hospital five days after finishing the course of penicillin, having been afebrile for two weeks; he was now restored to good health. Six weeks later he was still well, and examination of the C.S.F. showed no abnormality.

Comment

Reports of meningitis caused by *Cl. welchii* are few. All the recorded cases unassociated with brain abscess (Henderson *et al.*, 1954; Møller, 1955; Colwell *et al.*, 1960; Willis and Jacobs, 1964) and most clostridial brain abscesses have followed penetrating injury to the skull (Cairns *et al.*, 1947; Russell and Taylor, 1963). The present case occurred after duodenal perforation. Though there was a period of coma in the fourth week of the illness the clinical evidence attributes this to hepatic failure rather than to a metastatic brain abscess. Despite the administration of antibiotics it seems unlikely that an abscess could have resolved completely, leaving a persistent meningeal infection. It is more likely that the meningitis resulted from bacteraemia or septicaemia and failed to respond completely to chemotherapy until intrathecal administration was begun.

The low-grade fever, weight loss, and headache were features of this patient's illness from the time of the first operation. Signs of meningism were not observed, and lumbar puncture was not performed until four months after this. It is probable that attempts to isolate an organism failed because of the masking effect of chemotherapy. There was little clinical deterioration during the seven-week interval between the first lumbar puncture and his transfer to this hospital, by which time all chemotherapy had been stopped. The very gradual return of the C.S.F. to normal during successful treatment also suggests that this was a chronic infection. There was no evidence of gas formation by the organism. Willis (1969), who reviewed the subject of intracranial infections with *Cl. welchii*, noted that brain abscess caused by this organism is relatively benign.

We are grateful to our colleagues at other hospitals for information regarding the early course of this patient's illness. We would also like to thank Professor Sheila Sherlock, who kindly referred the patient to one of us (P.K.T.) at the Royal Free Hospital, London, when neurological complications became apparent.

Requests for reprints should be addressed to R.N.G.

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