Medical Memoranda

Torula Meningitis in Malaya

Cerebrospinal blastomycosis has been recognized for over 50 years, but is still a rare occurrence. Only one case has previously been reported in Malaya (Institute of Medical Research, 1953). The following case shows several well-known features of the disease, but is unusual in that it ran a rapid course, death occurring within four weeks of the onset. In addition the presenting symptoms—sudden and complete blindness and deafness—are impressive.

CASE REPORT

A 44-year-old Chinese newspaper-seller was admitted to Taiping Hospital on December 27, 1955, complaining of headache, deafness, and blindness. He had been perfectly fit until three weeks previously, when he began to suffer from severe early-morning headaches associated with vomiting and accompanied by numbness and weakness in all limbs. These gradually became more disabling, and after seven days he was too weak to leave his bed. Loss of vision came on suddenly at this time and progressed to complete blindness in 48 hours. Shortly afterwards he was noticed to become increasingly deaf, and by the day of admission he was semi-conscious. There was no vertigo or tinnitus and he had taken no quinine or other drug. His past health had been good and his family history had nothing of note. He had never suffered a severe head or spinal injury.

Examination revealed an emaciated semiconscious patient, completely deaf and blind, who responded in an agitated fashion to tactile stimuli. He complained continually of severe frontal headache. His speech was normal. Investigation of the nervous system showed definite neck rigidity, with a positive Kernig sign; fundi normal, apart from a small white area near the left disk resembling a choroidal tubercle; pupils dilated, equal, and unreactive to light, but ocular movements apparently normal; and complete nerve deafness. The remaining cranial nerves were normal. The limbs were flaccid, with gross reduction in power and some wasting. Tendon reflexes were absent and plantar responses extensor. There were no skin lesions, and other systems showed nothing of note; the blood pressure was 140/90; the urine was normal; no malarial parasites were found on routine blood film, haemoglobin was 60%, and the blood Kahn reaction was negative.

On lumbar puncture the C.S.F. pressure was 250 mm. of water. The fluid was clear; cells, 10 per c.mm.; protein, 35 mg. per 100 ml. Chloride and sugar contents were normal, and culture on blood agar was sterile. A few yeast cells were seen, but were thought to be contaminants.

During the first 48 hours in hospital his condition remained unchanged, he had no fever, and his headache was relieved by the lumbar puncture. Although drowsy he was easily rousable and able to feed himself. He retained sphincter control and issued loud commands at intervals to the nursing staff for the urine bottle. On the third day in hospital he became more drowsy, and was found to have a complete internal and external ophthalmoplegia.

Lumbar puncture was repeated, showing 10 lymphocytes per c.mm. and 90 mg. protein per 100 ml. Large numbers of budding yeast organisms were seen on direct film. Culture and mouse-inoculation tests showed these organisms to be identical with those of *Cryptococcus neoformans* (see below).

The patient became more and more deeply unconscious, with paralysis of all limbs and incontinence of urine, and he eventually died of respiratory failure after one week in hospital.

Treatment.—Streptomycin sulphate, 1 g. intramuscularly and 100 mg. intrathecally, was given for the last four days of life, but appeared to have no effect.

PATHOLOGICAL RECORD

At necropsy the main features were found in the central nervous and respiratory systems. Both lungs were haemorrhagic and sodden with oedema affecting both lower lobes and the right middle lobe.

The meninges appeared normal, but were exceptionally dry and tough, and were tightly bound down to the cortical tissue over the vault. The underlying white matter in this region presented a "sandy" appearance and imparted a gritty sensation to the touch. The ventricular system was normal and there was no apparent obstruction to the flow of C.S.F., which had a slightly opalescent appearance. Serial sectioning of the brain showed no abnormality apart from a general hyperaemia and congestion.

On microscopical examination cryptococci were found in large numbers in the meninges over the vault and around the base of the brain. There was relatively little inflammatory reaction and no evidence of suppuration or granulomatous change. Sections of the brain in the region of the frontal cortex showed organisms in the Virchow-Robin spaces. Unfortunately the cranial nerves were not examined microscopically. Scanty organisms were also seen in the liver and spleen.

Initial wet nigrosine preparations of centrifuged cerebrospinal fluid deposit and macerated brain showed the presence of the organism in large numbers. These took the form of round yeast cells varying considerably in size from 3 to 8 μ . Many budding forms were present, and a large number were surrounded by thick, clear, highly refractile capsules. A striking characteristic was the complete absence of mycelia.

The organism was cultured on blood agar and Sabouraud's dextrose-agar medium at 37° C. and 28° C., and a free pure growth on both media occurred after 72 hours' incubation at 37° C. and rather longer at 28° C. This consisted of small dome-shaped semi-transparent mucoid colonies, prepared films of which showed the original capsulated Gram-positive yeast form, proliferating by blastospores only, with no mycelia.

Fermentation tests showed that the organism grew readily in glucose, lactose, mannitol, dulcitol, and maltose peptone waters, slowly forming acid in glucose and maltose only, and without producing gas in any.

Antibiotic-sensitivity tests, using a blood-agar plate and impregnated paper disk technique, proved the strain to be completely resistant to 10 μ g. of penicillin, chlortetracycline, chloromycetin, and oxytetracycline per ml., and to 20 μ g. of streptomycin per ml.

Three adult male white mice were subsequently inoculated intraperitoneally as follows: (A) 0.1 ml. of the original C.S.F.; (B) 0.1 ml. of a suspension in sterile normal saline; and (C) 0.1 ml. of a preparation from the colonies of the blood-agar culture. B died on the 11th day, C on the 17th, and A on the 43rd. Necropsy and wet nigrosine preparations from all three animals showed the yeast cells to be widely disseminated in the peritoneum, spleen, lungs, and brain, whilst the original organism was recoverable from the brain on culture.

Thus it was conclusively shown that an organism resembling *Cryptococcus neoformans* was recovered from the brain and C.S.F., subsequently cultured, and proved to be highly pathogenic to mice.

We are indebted to the S.M.&H.O., Perak, Malaya, for permission to publish this case.

R. W. ROSS RUSSELL, M.B., B.Chir.,
Captain, R.A.M.C.

D. DEAN, M.B., Ch.B.,
Captain, R.A.M.C.
British Military Hospital, Kamunting, Taiping, Malaya.

REFERENCE

Institute of Medical Research, Kuala Lumpur (1953). Annual Report.