FATAL MENINGITIS DUE TO A CAPSULATED NEISSERIA

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In this paper a fatal case of meningitis is reported in which a capsulated *Diplococcus* of the Neisserian group was isolated from the purulent cerebrospinal fluid. A capsulated Gram-negative *Diplococcus* growing readily on agar was isolated from the nasopharynx and the cerebrospinal fluid by von Lingelsheim (1906, 1908) and called by him *D. mucosus*. Similar organisms were also isolated from the nasopharynx by Elser & Huntoon (1909). Cowan (1938) reported two cases operated on for cerebral tumour in which *D. mucosus* was grown from the cerebrospinal fluid. These strains were regarded by him as contaminants setting up a low-grade infection in a brain which, exposed for operation, offered little resistance to infection. Two cases of meningitis due to a capsulated *Diplococcus* have been reported by McFarlan (1941) and Bray & Cruickshank (1943); both these patients responded well to sulphapyridine and recovered. Edwards (1944) described a fatal case of meningitis due to an atypical Neisseria which in many respects resembled *D. mucosus*, although it was not capsulated. The rarity with which capsulated Neisseriae are associated with pathogenicity is considered sufficient justification for reporting the following case.

CASE HISTORY

The patient was a woman aged 25. There was a 2 weeks' history of headache and pain in the back and slurring of speech and aphasia for 10 days before admission. Towards the end of this time there was increasing drowsiness and photophobia and 1.g. of M. and B. 760 was therefore given 4-hourly for 48 hr. As there was no improvement, the patient was admitted to King's College Hospital in a semi-comatose condition on 16 April 1945.

Her temperature was then 102°, the pulse rate 120 and the respirations 22; head retraction, photophobia and a positive Kernig's sign were present, and there was a pink macular rash on the chest and abdomen. No localizing signs were found on examining the central nervous system. Lumbar puncture was done with the following results: pressure 300 mm.; cells 292/cu.mm. with 70% lymphocytes; protein 200 mg./100 ml.; globulin test positive; chlorides 580 mg./100 ml.; sugar absent. On direct examination within 2 hr. of collection Gram-negative diplococci were seen in moderate numbers. They were both intra- and extracellular and showed some degree of pleomorphism. A capsulated Gram-negative *Diplococcus* was isolated on culture. Later the same day more fluid was withdrawn and 10,000 units of penicillin injected intrathecally. The next day, 17 April 1945, there was little change in the patient's condition. The cerebrospinal fluid was still under extreme pressure. The other findings were: cells 486/cu.mm., mainly lymphocytes; protein 160 mg./100 ml.; chlorides 660 mg./100 ml. No organisms were seen on direct examination and the culture was sterile. A further 10,000 units of penicillin were injected. A blood count done at this time showed 9·6 thousand leucocytes per cu.mm. On the following day both the patient's condition and the cerebrospinal fluid showed little change. An intrathecal injection of 10,000 units of penicillin was again given.

On 19 April 1945 the patient was still pyrexial, semi-comatose and irrational, although the neck rigidity and photophobia were perhaps less marked. Signs of consolidation at the base of the left lung were now beginning to appear and this was confirmed by X-ray. The pressure of the cerebrospinal fluid was still more than 300 mm. and the culture remained sterile. Its penicillin content was such that the Oxford *Staphylococcus* was inhibited by the undiluted fluid only. A further 10,000 units of penicillin were given intrathecally, and in view of the patient's lack of improvement a course of sulphadiazine, 2 g. 4-hourly, was started. The next day the patient was worse and examination of cerebrospinal fluid showed the following: pressure 300 mm.; cells 182/cu.mm., chiefly lymphocytes; protein 180 mg./100 ml.; chlorides 600 mg./100 ml. No organisms were seen and cultures were sterile. 10,000 units of penicillin were again injected.

By the following day, 21 April 1945, the condition of the patient had markedly deteriorated. Localizing neurological signs were still absent, but the coma had deepened, the signs in the chest had spread and the respirations had risen to 140/min. Death occurred the same day. A purulent nasal discharge developed

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a day or two before death from which a few colonies of *Str. viridans* and *Str. pneumoniae* were grown. It was unfortunately not possible to carry out a post-mortem examination.

BACTERIOLOGICAL FINDINGS

On further investigation the organism isolated from the cerebrospinal fluid was found to possess the following characteristics:

Morphology: Gram-negative cocci mainly arranged in pairs and groups with their opposing surfaces flattened. Capsules were demonstrated both by Muir's stain and by nigrosine.

Agar and blood agar after 24 hr. incubation aerobically: Good growth of low, convex, slightly yellowish colonies, 1–2 mm. in diameter, with a regular edge and easily emulsified. Confluent and mucoid growth at line of inoculation. There was no haemolysis. Growth was rather better at 37° C. than at room temperature.

MacConkey's agar aerobically: No growth after 24 hr., but there was a scanty growth after 48 hr. The colonies were about 1 mm. diameter, low domed, regular edge and slight yellowish tinge.

Loeffler serum slope aerobically: Confluent and mucoid growth at line of inoculation after 24 hr. Colonial appearances were similar to those on agar.

Heart broth aerobically after 24 hr.: Some turbidity with a slight granular deposit easily shaken up.

Biochemical reactions: There was no fermentation of glucose, mannite, maltose, lactose, sucrose or salicin after 4 weeks' incubation. Litmus milk was unchanged and the Indole, Voges-Proskauer and methyl-red reactions were all negative.

There was no agglutination of a formalized suspension of the organism in the 56° C. bath by meningococcal sera types I and II or by the patient's own serum. The organism was found to be four times as resistant to penicillin as the Oxford *Staphylococcus*. Animal inoculation was not carried out.

DISCUSSION

The changeability shown by the Gram-negative nasopharyngeal diplococci in their colonial appearances, pigment formation and biochemical reactions is emphasized by Wilson (1928) and Wilson & Smith (1928). They regard these organisms as a single group, the members of which are liable to undergo considerable variation. Seventy-eight strains were examined on different media by Wilson & Smith who found that practically no two agreed in their colonial appearances and biochemical findings. They concluded that no satisfactory basis for classification of the nasopharyngeal Neisseriae could be found and considered *Diplococcus mucosus* to be a mucoid and capsulated variant of the group.

This variability is also seen in a comparison of the characters shown by the capsulated strains isolated by Cowan, McFarlan, Bray and Cruickshank and by the one here reported. Smooth and rough colonies of varying colour and exhibiting different fermentation reactions are described. A feature common to three of these strains is their power of growing on MacConkey's agar. This ability was shared by a non-capsulated strain isolated from the cerebrospinal fluid by Edwards.

As the organism reported here does not conform in every respect with any of the capsulated strains previously described, it is probably best regarded as a capsulated variant of the Neisserian group rather than a distinct species. The evidence strongly suggests that this organism was the cause of the meningitis although it was only observed and isolated on one occasion. Its disappearance from the cerebrospinal fluid following penicillin therapy and its relative sensitivity to that drug suggest that recovery from the meningeal infection might have occurred if pulmonary complications had not supervened.

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