FIVE CASES OF NEISSERIAL MENINGITIS

Including one caused by *Neisseria flava*

Major W. J. C. PARKER, M.B., B.S., D.Obst.R.C.O.G., R.A.M.C.

Lieutenant-Colonel H. A. J. REAY, M.B., M.R.C.P., M.R.C.P.(Edin.), R.A.M.C.

British Military Hospital, Iserlohn, B.A.O.R.

MENINGITIS caused by *Neisseria meningitidis* has been extensively documented, but there have been few reports in the English literature of meningitis due to "minor *Neisseria*". *Neisseria* are gram negative diplococci and are grouped as follows (adapted from Wilson and Miles, 1964):—

N. meningitidis, 2 main antigenic types; *N. gonorrhoea*: *N. catarrhalis*: *N. pharyngis sicca*: *N. pharyngis flava*, subdivided by variations in fermentation, referred to by some authors as *N. subflava*, and in this paper as *N. flava*; *Diplococcus mucosus*: *N. ovis*. *N. flavescens*, grows on semi-solid plain agar and does not ferment sugars.

N. flava differs from *N. meningitidis* in that the otherwise similar colonies are yellowish in the former and blueish in the latter, but these pigments take several days to develop and are therefore of less value diagnostically. However, *N. flava* will grow at room temperature (about 22° C) in air, whereas *N. meningitidis* requires a carbon dioxide-enriched atmosphere and a temperature of 37° C. *Neisseria flava* does not agglutinate with *N. meningitidis* antisera.

Case reports

Five children with neisserial meningitis were admitted to this hospital during the year 1st July, 1966 to 30th June, 1967 from the Canadian military community in this area, which includes some 5,400 Canadian dependent relatives under the age of twenty-one years. The first two cases to be described were caused by *N. meningitidis*.

Case 1

E.C., male, aged seven years, a previously fit child, was admitted on 30th November, 1966. He developed joint pains on the morning of admission, became feverish, and during the afternoon developed a purpuric rash. On admission in the early evening of the same day he was febrile (105° F = 40.6° C), semi-conscious, and had a rapidly extending purpuric rash especially of the face and limbs.

During examination he became moribund and the blood pressure was unrecordable. Immediate therapy with intravenous hydrocortisone, ampicillin, and sulphadiazine was given. He remained unconscious and very ill for three days, after which he made slow and steady progress. There was marked muscle wasting and the areas of purpura had sloughed, leaving many large eschars, which took three months to heal fully. By then he had made a complete mental and physical recovery.

Cerebrospinal fluid (C.S.F.) on day of admission—protein 25 mg, 15 white cells, no organisms on gram staining. 2 days later—protein 90 mg, white cells 760/cmm, 15 per cent being lymphocytes. Gram negative diplococci were grown from initial blood culture and CSF, on chocolate agar in 10 per cent carbon dioxide at 37° C. The growth was sent to the Royal Army Medical College, Millbank, and was reported as "typical *Neisseria meningitidis* agglutinating with Type 1 antiserum to titre".

This was a meningococcal septicaemia with meningitis and probably Waterhouse-Friderichsen syndrome, with full recovery of the patient after intensive therapy.

Case 2

W.W., male, aged three years, a previously well child, was admitted on 28th March, 1967. His illness started on the same day, when he was noticed to be sleepy and feverish. That evening he developed a purpuric rash on trunk and limbs. On admission the child was comatose and hypotensive with a rapidly extending purpuric rash. There was minimal neck stiffness.

C.S.F. was normal, and the white cell count in the peripheral blood was 2,300/cmm.

A diagnosis of fulminating meningococcal septicaemia was made, and immediate intravenous therapy with ampicillin, sulphadiazine and corticosteroids was started. Despite this the child's condition continued to deteriorate and he died in twenty-four hours.

Post mortem findings—A well-nourished child showing a profuse haemorrhagic rash over the trunk, limbs and face. There was massive bilateral adreno-cortical haemorrhage and histologically there was no remaining organized cortical tissue. A gram negative diplococcus was cultured from the blood only, and identified biochemically and serologically as *N. meningitidis*. The cause of death was massive bilateral adrenal haemorrhage due to an overwhelming meningococcal septicaemia.

Case 3

B.L., male, aged eighteen months. Admitted 5th December, 1966 with a four-day history of fever, vomiting and increasing neck stiffness. Examination revealed neck stiffness and a positive Kernig's sign. There was no rash and he was not shocked.

C.S.F. appeared milky and there were increased cells and protein. Intracellular gram negative diplococci were seen on staining.

Treatment with ampicillin, sulphadiazine and corticosteroids ensued, with an uneventful course to full recovery.

A neisserial organism grew well from the C.S.F. on agar at room temperature, and was sent to the Royal Army Medical College. The organism was identified as of the *N. flava* group, growing at room temperature in air and producing acid in glucose and maltose only. It was shown to be auto-agglutinable in saline, and for this reason specific antisera were not tested.

Case 4

B.C., male, aged three years. Admitted 10th May, 1967 with a twenty-hour history of fever, muscle twitching and delirium. Examination revealed an irritable febrile child with marked neck stiffness, but without rash or hypotension.

C.S.F.—white cells 4,500/cmm, polymorphs 99 per cent, protein 75 mg per cent.

Initial therapy was given intravenously consisting of ampicillin and sulphadimidine and corticosteroids. Recovery was uneventful.

A gram negative diplococcus was grown from the C.S.F. on chocolate agar at 37° C. Unfortunately, it did not survive transit to a reference laboratory.

Because of these reports, the records of a previous case were looked at retrospectively.

Case 5

P.S., female, aged two years. This child was admitted on 2nd July, 1966 having had high fever for twenty-four hours. She was observed to have occasional twitching of the limbs and would not respond to approach although she was not in stupor. There was no rash. Minimal neck stiffness was present.

C.S.F.—white cells 9,500/cmm, polymorphs 90 per cent, protein 250 mg per cent; a few gram negative cocci were seen.

She was treated with intravenous ampicillin, sulphadiazine and corticosteroids. However, by next morning she was sufficiently well to get up and take oral feeds. Her subsequent course was uneventful and she made a complete recovery.

Culture of the C.S.F. produced an organism reported at the time as *Neisseria flavescens*. Details on which this opinion was based cannot now be traced.

Discussion

Benson et al (1928) reported a seven months old infant who presented with a two months' history of tremor and vomiting following a discharging ear and eye. There were 3,000 cells in the C.S.F., mostly polymorphs, and a gram negative diplococcus, cultured on dextrose agar, was classified as *N. sub-flava* from its yellowish-green pigment and negative agglutination tests with specific antisera for *N. gonorrhoea* and *N. catarrhalis*. This infant died on the twenty-seventh day after diagnosis, three months after the onset. These authors referred to four cases of non-fulminant meningitis ascribed to *N. catarrhalis* by other workers, but could find no previous cases of *N. flava* (or *sub-flava*) meningitis. Savini (1957) described two cases of meningitis due to an organism identified as *N. pharyngis* var. *flava* by cultural, morphological and biochemical characteristics, and two other cases due to *N. catarrhalis*. All four recovered on what would now be considered very small doses of penicillin alone.

Lewin and Hughes (1966), who comment that *Neisseria sub-flava* is a common inhabitant of the upper respiratory tract but rarely pathogenic, reported three cases of meningitis and two of septicaemia from which they cultured and identified this organism. Their experience differed from the above reports, and from our own, in that four of their five cases had a petechial rash, and two died early in the course of the disease. With regard to *N. flavescens* meningitis there is little published information. Branham (1930) found a new meningococcus-like organism, *N. flavescens*, in an epidemic of cerebro-spinal fever, in which most of the cases were treated with polyvalent anti-sera. Prentice (1957) described a case of a mild meningitis in a ten year old boy. Treatment was with oral penicillin.

In our small series we were struck by the contrast between the fulminating course of the two cases in which the neisseria was clearly identified as *N. meningitidis* compared with the other three; in two there is doubt as to the type and in one *N. flava* was identified. These last three cases were slower in presentation and later in diagnosis and treatment, but despite this ran a relatively benign course. While this series is too small and our bacteriological information too limited to draw any firm conclusion, we suggest that a prospective bacteriological study of a larger series of neisserial meningitis should be carried out to confirm or refute the impression that types other than *N. meningitidis* are not rare among the non-fulminant cases.

Summary

Of five successive cases of neisserial meningitis admitted to the children's ward of this hospital in one year, the two fulminant, one fatal, were due to *N. meningitidis*, and of the three milder, one was due to *N. flava* and two to neisseria of uncertain type. An apparent relationship between clinical severity and the type of neisseria responsible, warrants further study.

Acknowledgements

We are indebted to Lieutenant-Colonel E. E. Vella, M.D., M.C.Path, of British Military Hospital, Iserlohn and to the Department of Pathology, Royal Army Medical College, for their assistance.

REFERENCES

- BRANHAM, S. E. (1930). *Publ. Hlth*, **45**, 845.
 BENSON, H., BRENNWASSER, R. and D'ANDREA, D. (1928). *J. infect. Dis.*, **43**, 516.
 LEWIN, R. A. and HUGHES, W. T. (1966). *J. Amer. med. Ass.*, **195**, 821.
 PRENTICE, A. W. (1957). *Lancet*, **i**, 613.
 SAVINI, R. (1957). *Nuovi Ann. Ig.*, **8**, 665.
 WILSON, G. S. and MILES, A. A. (1964). *Principles of Bacteriology and Immunity*, 5th Ed. Arnold, London.

Honorary Consultant to the Army

Professor B. G. Maegraith, M.A., D. Phil., D.Sc., F.R.C.P., has been appointed Honorary Consultant in Malariology to the Army, in succession to the late Professor G. Macdonald.

Order of St. John of Jerusalem

Those recently appointed to, or promoted in, the Most Venerable Order of the Hospital of St. John of Jerusalem include the following:—

As Commanders (Brothers): Major-General M. H. P. Sayers.

As Officers (Brothers): Colonels A. B. Dick, W. Lees, M. M. Lewis, D. G. Levis, J. J. Voller.

As Serving Brother: Major (NM) W. R. Ingoe.