LITTLEDIKE, E.T., WITZEL, D.A. & WHIPP, S.C. (1968) Insulin: Evidence for inhibition of release in spontaneous hypocalcaemia. *Proceedings of the Society for Experimental Biology and Medicine*, **129**, 135.

MALAISSE, W.J., BRISSON, W.R. & MALIASSE-LAGAE, F. (1971) Cyclic AMP-induced translocation of calcium in isolated beta cells. *Diabetes*, **20**, 328.

MILNER, R.D.G. & HALES, C.N. (1967) The role of calcium and magnesium in insulin secretion from rabbit pancreas studied *in vitro*. *Diabetologia*, **3**, 47.

NORDIN, B.E.C. & FRASER, R. (1956) A calcium infusion test. I. Urinary excretion data for recognition of osteomalacia. *Lancet*, **i**, 823.

RASMUSSEN, H. (1964) Effects of calcium upon cellular metabolism. *Annals of Internal Medicine*, **60**, 526.

RAY SARKAR, B.C. & CHAUHAN, U.P.S. (1967) A new method for determining microquantities of calcium in biological materials. *Analytical Biochemistry*, **20**, 155.

SALVESEN, H.A. (1954) A note on the relation of the parathyroids to carbohydrate metabolism. *Acta endocrinologica*, **16**, 349.

WILSON, R.B., BLUM, J.W. & KRONFELD, D.S. (1971) Plasma calcium, glucose and insulin concentrations in hypocalcaemic parturient cows. *Diabetes*, **20**, 382.

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A brainstem syndrome associated with *Mycoplasma pneumoniae* infection—A report of two cases*

S. J. JACHUCK
B.Sc., M.B., B.S

C. GARDNER-THORPE†
M.B., B.S., M.R.C.P.

F. CLARK
M.B., B.S., F.R.C.P.

J. B. FOSTER
M.B., B.S., F.R.C.P.

The Departments of Medicine and Neurology, Newcastle University Hospital Group, Newcastle upon Tyne, NE4 6BE

Summary

Two patients with a serologically-proved infection with *Mycoplasma pneumoniae* (MP) developed cranial nerve pareses which cleared spontaneously within 1 month of the onset. The sixth and seventh cranial nerves were the most severely affected. It is suggested that the signs were due to a mild brainstem encephalitis associated with the MP infection. The benign course of the syndrome is emphasized. The neurological complications of MP infection may be commoner than has been generally supposed.

Introduction

Simultaneous multiple cranial nerve palsies in young adults are uncommon. In a significant proportion of cases a structural cause is not found. In some patients an episode of brainstem demyelination can be incriminated. Rare causes include sarcoidosis, post-infective radiculopathy, diabetes mellitus, encephalitis, diphtheria and spinal anaesthesia. The term 'rheumatic neuritis' has been used in some cases in which a definite diagnosis cannot be made (Brain and Walton, 1969).

Although pneumonitis is probably the commonest clinical presentation of infection with *M. Pneumoniae*, it is known that the nervous system may also be involved (Yeshnick, 1956; Taylor *et al.*, 1967; Hodges, Fass and Saslow, 1972; Endtz *et al.*, 1972), especially in men and in the young. Eighth cranial nerve involvement has been described in only two patients (Dishoeck, 1963). Four varieties of neurological complication, each with distinct cerebrospinal fluid changes, have been reported in the literature—

(1) Psychosis, usually in the elderly; (2) meningoencephalitis; (3) meningitis; (4) radiculopathy.

The purpose of this paper is to report the combination of unilateral sixth (abducent) and seventh (facial) cranial nerve palsies in two patients with seroligical evidence of *M. pneumoniae* infection.

Case reports

Case 1

A 30-year-old electrician, noticed double vision on looking to the left, together with weakness of the left side of the face, on 26 June 1973. He had previously been well and had not noticed any other neurological symptoms. He was admitted

*Reprints requests to Dr S. J. Jachuck, The Departments of Medicine and Neurology, Newcastle University Hospital Group, Newcastle upon Tyne NE4 6BF.

† Present address: Department of Neurology, Royal Devon and Exeter Hospital (Wonford), Barrack Road, Exeter, Devon, England.

to hospital on 6 August 1973. Examination revealed a complete left lateral rectus palsy and coarse phasic nystagmus on attempted gaze to the left. The right eye did not adduct fully. Moderate weakness of the left orbicularis oculi muscle was found together with minimal weakness of the left side of the face. Neurological examination did not reveal any other abnormality. The blood pressure was 120/80 mmHg.

Lumbar puncture was performed on 10 August 1973. The pressure of the cerebrospinal fluid (CSF) was normal. The CSF contained 19 white cells/mm^3 and the biochemical analysis was normal. At a subsequent lumbar puncture cells were not found in the CSF and the protein was 20 mg/100 ml. Neither bacteria nor viruses were cultured from the CSF. The blood count was normal and the ESR 19 mm/hr. The serum MP Complement Fixation Test (CFT) titre was 1 : 640. Audiometry revealed bilateral mild perceptive deafness. Caloric tests showed directional preponderance to the right. He was treated with corticotrophin for 10 days and was discharged from hospital. The CFT titre fell to 1 : 40 within 2 months of the onset of symptoms. When he was seen on 5 January 1974 the symptoms had resolved although first degree bilateral horizontal phasic nystagmus was present.

Case 2

A 21-year-old insurance agent developed double vision on 16 June 1973. He was febrile. Within 4 days he was again well. Two weeks later he noticed a sensation of giddiness on turning the head quickly, tingling in the right upper lip and drooping of the right side of the mouth. He was admitted to hospital. The oral temperature was 38·4°C and it rose to 40°C within 24 hr. The abnormal physical signs consisted of a left lateral rectus palsy, a left lower motor neurone facial weakness and nystagmus on upward and bilateral gaze. Photophobia, neck stiffness, lymphadenopathy and respiratory signs were not found. The blood pressure was 120/70 mmHg and the pulse rate 120/min.

Lumbar puncture was performed and the CSF was at normal pressure. The CSF contained 1 white cell/mm^3, 37 mg protein/100 ml and 56 mg sugar/100 ml. Organisms were not cultured from the CSF. The serum MP CFT titre was 1 : 40 on 13 July 1973 and 17 August 1973, but it had fallen to nil on 31 October 1973. Electroencephalography, skull X-ray and brainscan were normal. The peripheral blood contained 2500 white cells/mm^3 (68% neutrophils, 27% lymphocytes, 4% monocytes and 1% eosinophils).

He was discharged from hospital without treatment. The symptoms and signs had disappeared 1 month after discharge.

Discussion

M. pneumoniae infection is usually diagnosed by CFT and isolation of the agent on artificial culture media. The CFT is positive in more than 90% of patients with proved *M. pneumoniae* infection (Stephens, 1973). A four-fold or greater rise in the CFT titre (seen here in Case 1) is generally accepted as diagnostic of *M. pneumoniae* infection. Occasionally the rise in the CFT titre is delayed 4–6 weeks after the acute infection. In three of the seven cases reported by Stephens, the CFT titre in the acute stage was 1 : 20 or less. In our second patient the first blood sample was taken 4 weeks and the second sample 8 weeks after the onset of the illness. A CFT titre of 1 : 40 on both occasions was attributed to early and late sampling. The diagnosis of *M. pneumoniae* infection was confirmed when the CFT titre fell to nil after 18 weeks.

The neurological deficit seen in these two patients was attributed to brainstem dysfunction rather than to peripheral involvement of the sixth and seventh cranial nerves. The presence of horizontal nystagmus and nystagmus on vertical gaze in both patients, together with the failure of full adduction of the right eye in Case 1, support this suggestion. The finding of directional preponderance on caloric testing further supports the central localization of the disturbance.

In neither patient was a previous history of similar illness obtained. The signs were clearly localized. Both patients recovered completely. CSF studies were normal in Case 2 but the cell count was raised in Case 1. The organism was not isolated from the CSF. These two patients probably suffered from a MP brainstem meningoencephalitis similar to that described by Hodges *et al.* (1972). However, the CSF protein content in both patients and the cell count in Case 2 were normal.

The previously reported neurological complications of *M. pneumoniae* infection have varied widely from mild headache to meningomyelitis, transverse myelitis, cerebellar ataxia, hemiplegia, ascending paralysis and cranial nerve palsies but it is encouraging to note the good prognosis. Antimicrobial therapy is not effective. Although the first patient described here was treated with corticotrophin, there does not appear to be any evidence in the literature to suggest that this is beneficial.

Conclusion

The pathology and the mechanism of *M. pneumoniae* infection of the nervous system is poorly understood. Central nervous system signs in *M. pneumoniae* infection may not be so rare as the literature suggests. Patients with a bizarre brainstem syndrome, especially those in the younger age groups,

should be screened for *M. pneumoniae* before a presumptive diagnosis of multiple sclerosis is made.

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References

BRAIN, LORD & WALTON, J.N. (1969) *Brain's Diseases of the Nervous System,* 7th edn. Oxford University Press, London.

DISHOECK, H.A.E. VAN (1963) Virus infection in two cases of sudden perceptive deafness. *Acta oto-laryngologica* (Suppl.) **183,** 30.

ENDTZ, L.J., JOELE, L.J., HOOGLAND, P. & HERS, J.F. Ph. (1972) Manifestations neurologiques de l'infection par le *Mycoplasma pneumoniae. Review of Neurology,* **127,** 487.

HODGES, G.R., FASS, R.-J. & SASLOW, S. (1972) Central nervous system diseases associated with *Mycoplasma pneumoniae* infection. *Archives of Internal Medicine,* **130,** 277.

STEPHENS, M.D.B. (1973) *Mycoplasma pneumoniae* infection in General Practice. *Practitioner,* **210,** 805.

TAYLOR, M.J., BURROW, G.N., STRANCH, B. & HORSTMANN, D.M. (1967) Meningoencephalitis associated with pneumonitis due to *Mycoplasma pneumoniae. Journal of the American Medical Association,* **199,** 813.

YESHNICK, L. (1956) Central nervous system complication of primary atypical pneumonia. *Archives of Internal Medicine,* **97,** 93.