manifestations of marrow depression occur weeks or months after the drug has been stopped. In the former, the current evidence is that the reversible bone marrow suppression following chloramphenicol results from inhibition of mitochondrial protein synthesis. In the other, there is a strong suggestion of a stem cell lesion. The rare occurrence of this complication is suggestive of individual predisposition.

It is tempting to use some of these signs to explain the findings in the three patients following the use of chloroquine. It would appear that patients 1 and 2 belong to the dose-related categories. In patient 1, the primary effect of the drug was anaemia, it was only after the further use of the drug months later that the condition was aggravated. In patient 3, there is no relationship to dose and he had severe aplasia which occurred three weeks after the drug had been administered.

Acknowledgments

The authors wish to thank Dr Jega Pasupathi, Physician, General Hospital, Batticaloa, for referring patients 2 and 3; Dr Doris Pieris, Consultant Pathologist, General Hospital, Colombo, for her help with the haematological investigations, and the Director of Health Services for permission to publish this paper.

References

- BRAUER, M.J. & DAMASHEK, W. (1969) Hypoplastic anemia and myeloblastic leukemia following chloramphenicol therapy. *New England Medical Journal*, **287**, 1003.
- DOUGAN, S. & WOODLIFF, H.J. (1965) Acute leukaemia associated with phenylbutazone treatment - review of literature of a further case. *Medical Journal of Australia*, **1**, 217.
- McDUFFIE, F.C. (1965) Bone marrow depression after drug therapy in patients with SLE and rheumatoid diseases. *Annals of Rheumatic Diseases*, **24**, 289.
- MUKHERJI, P.A. (1957) Acute myeloblastic leukaemia following chloramphenicol treatment. *British Medical Journal*, **1**, 1286.
- NAGARATNAM, N. (1976) Unusual manifestations of leukaemias and allied disorders. *Cooray Memorial Oration, Sri Lanka Cancer Society*.
- NEVA, F.A. (1967) Malaria - recent progress and problems. *New England Medical Journal*, **277**, 1241.
- POLANA, M.K., CATS, A. & VAN OLDEN, G.A.J. (1965) Agranulocytosis following treatment with hydroxychloroquin sulphate. *Lancet*, **i**, 1275.
- PROPP, R.T. & STILLMAN, J.S. (1967) Agranulocytosis and hydroxychloroquin (correspondence). *New England Medical Journal*, **277**, 492.
- SAARINI, M.I. & LINMANN, J.W. (1973) Pre-leukemia: the hematological syndrome preceding acute leukemia. *American Journal of Medicine*, **55**, 38.
- VINCENT, P.C. & DE GRUCHY, C. (1967) Complications and treatment of acquired aplastic anaemia. *British Journal of Haematology*, **13**, 977.
- YUNIS, A.A. (1975) Pathogenetic mechanisms in drug induced bone marrow injury. *Third Meeting of the International Society of Haematology, Asian-Pacific Division, June 1975, Jakarta, Indonesia*.
- YUNIS, A.A. & BLOOMBERG, G.R. (1964) Chloramphenicol toxicity, clinical features and pathogenesis. *Progress in Haematology*, **4**, 138.

Postgraduate Medical Journal (February 1978) **54**, 112-114.

Cytomegalovirus infection and the Guillain-Barré syndrome

A. G. ARNOLD*
M.B., Ch.B., M.R.C.P.

D. S. LAWRENCE
M.B., B.S., M.R.C.P.

G. CORBITT
Ph.D., Dip.Bact.

The Departments of Medicine and Virology, North Manchester Hospital Group

Summary

A fatal case is described of the Guillain-Barré syndrome due to cytomegalovirus infection, which was associated with hepatitis, myocarditis and viral pneumonia.

Previous cases, which have usually run a benign course, are reviewed. Attention is drawn to the possible adverse effect of steroid therapy.

* Present address: Chest Clinic, The Churchill Hospital, Headington, Oxford OX3 7LJ.

Case report

A 22-year-old cabinet maker was admitted to hospital with a three weeks' history of sore throat, cough, headache and generalized myalgia. Two weeks before admission he developed progressive weakness and paraesthesiae of the arms and legs.

On examination he was afebrile, but he was sweating profusely. There was marked generalized lymphadenopathy and the fauces were mildly injected. He had a persistent tachycardia of 120-140/min.

Mild, transient hypertension was noted initially (BP 150/100 mmHg), but subsequently he remained normotensive. All other abnormalities were confined to the central nervous system. He was fully conscious and well orientated, and there was no evidence of meningism. The optic fundi were normal. He had dysphagia and a weak cough, but the palate and tongue moved normally. There was moderate, bilateral lower motor neurone facial weakness. The remaining cranial nerves were intact. In the limbs there was a profound, flaccid quadriplegia with absent tendon reflexes and a severe glove and stocking sensory loss to all modalities.

A lumbar puncture was performed and cerebrospinal fluid was obtained at normal pressure, containing $0.003 \times 10^9/l$ lymphocytes and 1.4 g/l of protein. The haemoglobin was 15.8 g/dl and the white cell count was $11.2 \times 10^9/l$, with a normal differential. No atypical mononuclear cells were seen in two blood films and the Paul Bunnell test was negative on two occasions. Liver function tests were abnormal on admission and deteriorated during his second week in hospital. Peak values were: bilirubin 65 mmol/l; alkaline phosphatase 1250 i.u./l (normal up to 100 i.u./l); alanine aminotransferase 338 i.u./l (normal up to 40 i.u./l). Hepatitis B associated antigen was negative. An ECG showed sinus tachycardia and borderline left ventricular hypertrophy. The chest radiograph was normal on admission.

He was treated with tetracosactrin 1 mg daily, but muscular weakness and sensory loss progressed. Tracheostomy and artificial ventilation became necessary. He developed a chest infection and bronchoscopy was required on several occasions to clear bronchial secretions. His condition gradually deteriorated and he died following a cardiac arrest seven weeks after the onset of his illness.

During the fourth week of his illness, complement fixation tests showed an antibody titre of 1 in 160 to cytomegalovirus (CMV). IgM and IgG antibodies specific to CMV were present, indicating that the infection was recent. Although CMV was not isolated during life from throat swab, CSF or urine, it was cultured in human fibroblasts after four weeks' incubation from a post-mortem specimen of liver.

At post-mortem the heart showed acute inflammation of the posterior wall simulating a recent myocardial infarction, but histology revealed a non-specific myocarditis. The lungs showed features of a virus pneumonia and the liver showed acute venous congestion. The peripheral nerves showed myelin degeneration with oedema and mild lymphocytic infiltration. Central chromatolysis was seen in the dorsal root ganglia and anterior horn cells. Inclusion bodies were not seen in any of the tissues examined.

The patient's 3-year-old daughter was admitted to hospital two weeks after her father, suffering from a

brief febrile illness without neurological involvement. Her serology indicated a CMV infection. The CMV complement fixation titre was 1 in 160 and IgM and IgG specific antibody were demonstrated.

Discussion

CMV infection is most commonly seen in neonates, following intra-uterine infection. Adult infection was usually only recognized in debilitating diseases producing immuno-deficiency and in organ transplant recipients. However, population studies have shown that 33% or more of adults have antibodies to CMV (Stern and Elek, 1965), suggesting that this is a common infection producing little symptomatic disease. A case of CMV infection in a young adult, resembling infectious mononucleosis was first described in 1965 (Klemola and Kaariainen), and many more cases have been described subsequently. In this condition, later termed CMV mononucleosis (Klemola *et al.*, 1967a), there are atypical mononuclear cells in the peripheral blood but the Paul Bunnell test is negative. The clinical picture is of a mild, non-specific febrile illness, usually without tonsillitis or marked lymphadenopathy. Minor abnormalities of liver function tests are commonly seen. Occasionally, specific organ involvement may dominate the clinical picture, such as frank hepatitis (Lamb and Stern, 1966), myocarditis (Ball and Archer, 1976) or chorio-retinitis (Chawla *et al.*, 1976). Atypical mononuclear cells have not always been seen in these cases.

A case of CMV infection in association with the Guillain-Barré syndrome was first reported by Klemola *et al.* (1967b). Leonard and Tobin (1971) described nine cases and Jordan *et al.* (1973) added a further case. Atypical mononuclear cells were found in only five of these eleven cases. The majority of these cases occurred in young adults, in whom the illness was relatively mild and the recovery complete. There was one fatality occurring in a 21-year-old woman who had profound weakness, requiring assisted ventilation, and who developed a panophthalmitis and diabetes mellitus secondary to pancreatitis. The CSF protein levels were normal in three of these cases, and only moderately elevated in the remainder (0.92–4 g/l), and there was no pleocytosis. Abnormalities of liver function tests were noted in four of these eleven cases. Tobin *et al.* (1974) reported two cases in young adults but without full laboratory data.

The effect of corticosteroids in adult CMV infection is unknown. They may lead to increased sensitivity to the virus (Krech, Jung and Jung, 1971). Seven of the previously reported cases of Guillain-Barré syndrome due to CMV infection received steroid therapy, without apparent ill effect. However, in a series of thirteen adult patients with

evidence of CMV infection at post-mortem, eight were receiving steroid therapy (Evans and Williams, 1968). The benefit of steroid therapy in the Guillain-Barré syndrome has yet to be proved (Leading Article, 1975) and, in view of the fatal outcome of the present case, should perhaps be avoided in cases due to CMV infection. Since virological proof of CMV infection only becomes available at a late stage of a patient's illness, earlier evidence should be sought, such as the presence of abnormal liver function tests and abnormal mononuclear cells in the peripheral blood, with a negative Paul Bunnell test.

Acknowledgment

We thank Dr M. H. Oelbaum for permission to report this case.

References

- BALL, S.G. & ARCHER, G.J. (1976) Myocarditis complicating cytomegalovirus mononucleosis. *Postgraduate Medical Journal*, **52**, 102.
- LEADING ARTICLE (1975) Guillain-Barré syndrome. *British Medical Journal*, **3**, 190.
- CHAWLA, H.B., FORD, M.J., MUNRO, J.F., SCORGIE, R.E. & WATSON, A.R. (1976) Ocular involvement in cytomegalovirus infection in a previously healthy adult. *British Medical Journal*, **2**, 281.
- EVANS, D.J. & WILLIAMS, E.D. (1968) Cytomegalic inclusion disease in the adult. *Journal of Clinical Pathology*, **21**, 391.
- JORDAN, M.C., ROUSSEAU, W.E., STEWART, J.A., NOBLE, G.R. & CHIN, T.D.Y. (1973) Spontaneous cytomegalovirus mononucleosis. *Annals of Internal Medicine*, **79**, 153.
- KLEMOLA, E. & KAARIANEN, L. (1965) Cytomegalovirus as a possible cause of a disease resembling infectious mononucleosis. *British Medical Journal*, **2**, 1099.
- KLEMOLA, E., KAARIANEN, L., VON ESSEN, R., HALTIA, K., KOIVUNIEMI, A. & VON BONSDORFF, C.-H. (1967a) Further studies on cytomegalovirus mononucleosis in previously healthy individuals. *Acta medica Scandinavica*, **182**, 311.
- KLEMOLA, E., WECKMAN, N., HALTIA, K. & KAARIANEN, L. (1967b) The Guillain-Barré syndrome associated with acquired cytomegalovirus infection. *Acta medica Scandinavica*, **181**, 603.
- KRECH, U., JUNG, M. & JUNG, F. (1971) In: *Cytomegalovirus Infections of Man*. Karger, Basle.
- LAMB, S.G. & STERN, H. (1966) Cytomegalovirus mononucleosis with jaundice as presenting sign. *Lancet*, **ii**, 1089.
- LEONARD, J.C. & TOBIN, J.O'H. (1971) Polyneuritis associated with cytomegalovirus infections. *Quarterly Journal of Medicine*, **159**, 435.
- STERN, H. & ELEK, S.D. (1965) The incidence of infection with cytomegalovirus in a normal population. *Journal of Hygiene*, **63**, 79.
- TOBIN, J.O'H., MACDONALD, H., DOYCE, L. & TAYLOR, J.E. (1974) Unsuspected cytomegalic mononucleosis. *British Medical Journal*, **2**, 385.

Postgraduate Medical Journal (February 1978) **54**, 114-115.

Phenobarbital dyskinesia

S. L. LIGHTMAN
M.A., M.R.C.P.

Middlesex Hospital, London W1N 8AA

Summary

A patient was admitted to hospital following an overdose of phenobarbital. During her recovery she developed both chorea and torsion dystonia which could only be related to her high plasma phenobarbital levels.

DIPHENYLHYDANTOIN (phenytoin) overdose is a well recorded cause of chorea and dystonia. A case is now reported of a patient who showed these features after phenobarbital alone. This is thought to be the first report of such an occurrence.

Case report

A 36-year-old nurse was brought by ambulance to the casualty department, having been found semi-comatose at a reception centre in central London. She was known to have a personality disorder and

was on treatment with diazepam 15 mg/day and dichloralphenazone 1300 mg at night, prescribed on a daily basis to obviate the danger of overdosage.

On admission she responded in a co-ordinated fashion to painful stimuli but was unresponsive to verbal commands. Her cardiovascular, respiratory and abdominal systems were unremarkable, and in her central nervous system no focal abnormalities could be detected. Her pupils were equal and reacted well to light, she had no doll's eye movements and her fundi were clear. Her reflexes were all present and equal and her plantars flexor.

The following day she was still very drowsy and only arousable by painful stimuli, and it was only 36 hours after admission that she woke up. At this time she was alert and orientated, and while lying in bed she was seen to have choreic movements about the eyes and mouth, and torsion movements at the