Cytomegalovirus myocarditis

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A patient with myocarditis and a significant rise in cytomegalovirus complement-fixing antibody is described. Investigations for other aetiological factors were negative, and it is suggested that the virus was the cause of the myocarditis.

*Infection with human cytomegalovirus is common and world wide. In this country about 55 per cent of the population show evidence of past infection by the age of 35, and thereafter primary infection is rare (Stern, 1968). This virus is rarely recognized as a cause of overt disease, and it is difficult to prove cause and effect when the infection is associated with another common condition. Furthermore, the virus may lie dormant in the cells of the host until relit by a concurrent debilitating illness. Therefore a rise in cytomegalovirus titre may indicate a primary infection, or reactivation of latent virus by an unassociated illness.

Congenital cytomegalovirus infection may cause cytomegalic inclusion disease, microcephaly, and mental deficiency (Lamb, 1971), and acquired infection may lead to pneumonia (Carlström *et al.*, 1968), hepatocellular jaundice (Lamb and Stern, 1966), hepatitis (Toghill *et al.*, 1967), pericarditis (Räsänen and Saikku, 1967), aseptic meningitis and polyneuritis (Klemola *et al.*, 1967a), acute haemolytic anaemia (Coombs, 1968), cytomegalovirus mononucleosis (Klemola and Kääriäinen, 1965), postperfusion syndrome (Kääriäinen, Klemola, and Paloheimo, 1966), and a disseminated infection in immunosuppressed and debilitated patients (Rifkind, Goodman, and Hill, 1967). In the following case we suggest that cytomegalovirus infection was the cause of myocarditis.

Case report

A white woman, aged 60, was admitted to the Bristol General Hospital on 5 October 1970. She had been in excellent health until three weeks previously when she developed a head cold which progressed to dry cough and wheezing. She then became increasingly breathless and had repeated

attacks of paroxysmal nocturnal dyspnoea. She had no chest pain.

Past medical history Scarlet fever aged 12, anterior repair aged 38, Keller's operation aged 48, dilatation and curettage aged 56, and 3 normal pregnancies. No cardiac abnormalities were noticed at these times.

Family history Two sisters with hypertension, no other cardiac disease.

Clinical examination Ill, febrile (38.2°C), and dyspnoeic at rest. Pulse regular, 130/min, blood pressure 150/90 mmHg, and jugular venous pressure raised 5 cm above the sternal angle, with equal 'a' and 'v' waves. On auscultation there was gallop rhythm with pansystolic and mid-diastolic murmurs at the apex. There was no opening snap. There were fine râles at both lung bases. The rest of the examination was normal.

The electrocardiogram showed sinus tachycardia, left bundle-branch block, and left ventricular hypertrophy. The chest x-ray showed cardiomegaly and pulmonary congestion (Fig. 1).

Progress With bed rest, digoxin, and diuretics, the signs of heart failure disappeared, though the gallop rhythm and murmurs persisted. Serial chest x-rays showed a progressive reduction in cardiac size to within normal limits (Fig. 2). She was discharged, feeling well, on 25 November 1970, but her symptoms soon recurred despite a restricted regimen and she was readmitted on 14 February 1971. She had signs of recurrent heart failure with the jugular venous pressure raised 10 cm above the sternal angle. The electrocardiograms were unchanged, but the chest x-rays showed an increase in cardiac size (Fig. 3).

Investigations Haemoglobin 13.4 g/100 ml. White cell count 10,700/mm³, cholesterol 238 mg/100 ml, serum thyroxine 5.3 µg/100 ml, latex fixation test, lupus erythematosus cells, Wasser-

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FIG. 1 Chest x-ray on admission showing cardiomegaly and pulmonary congestion.

FIG. 2 X-ray after initial therapy, showing reduction of heart size and clearing of lungs.

FIG. 3 X-ray on readmission, showing further increase in cardiac size.

mann reaction, Coombs test, midstream urine, and throat swabs were all negative. Serum alanine-aminotransferase 9 and 19 units. Toxoplasma dye test, antistreptolysin titres, and paired sera for Paul-Bunnell test, mumps 'S' and 'V', psittacosis, mycoplasma, Q fever, and influenza were all negative. No virus was isolated from the faeces on human embryo fibroblasts or kidney cells, or from urine or throat swabs or human embryo fibroblast culture.

Cardiac catheterization and cytomegalovirus results are shown in Tables 1 and 2.

Treatment The patient failed to respond to digoxin and diuretics, and continued to show signs of active disease with a tachycardia, high ESR, reactive lymphocytes, and a high cytomegalovirus titre. Because of the recurrence of failure and evidence of persistent activity she was given cytosine arabinose, an antiviral agent, in an attempt to eradicate the virus. The dosage was 5 mg/kg intravenously for one day, and 3 mg/kg for four days. Apart from a fall in her jugular venous pressure, which was accompanied by a fall in the cytomegalovirus titre, there was no change in her condition. She experienced no side effects from the treatment. She was finally discharged on 8 March 1971, and has remained symptom free on a very restricted regimen, with persisting cardiomegaly, gallop, mitral murmurs, and left bundle-branch block.

Discussion

Myocardial involvement in cytomegalovirus infection has been reported in 4 cases, in 3 of which there were no cardiac symptoms or signs apart from T wave changes on the electrocardiogram (Klemola *et al.*, 1967b; Sterner *et al.*, 1970). A diagnosis of lymphadenopathy and myocarditis was made in the other case (Sterner *et al.*, 1970) but few other clinical details are given. This patient was a 27-year-old woman, who had a fourfold rise in cytomegalovirus complement fixing antibody, but no reactive lymphocytes or virus isolation. She recovered completely. Our patient clearly had myocarditis, and the fourfold rise in antibody titre indicates that the patient was infected with cytomegalovirus. In the absence of other aetiological factors it is suggested that the two were causally related.

Antiviral therapy was considered because of the severity and persistence of the myocarditis in our patient. Floxuridine has been used in cytomegalovirus pneumonia with some improvement (Cangir *et al.*, 1967), and idoxuridine in cytomegalic inclusion disease, with a reduction in excretion of the virus (Conchie, Barton, and Tobin, 1968). Idoxuridine has also been used with varied success in treatment of encephalitis due to the related herpes simplex virus (Evans *et al.*, 1967;

TABLE 1

Date	ESR	Globulins	Blood film	Cyto-megalo-virus	Paul-Bunnell	Mumps 'S' and 'V'	Psittacosis	Mycoplasma	Influenza A	Q fever	ASOT
6 October 1970	23			1/96	Negative	Negative	Negative	Negative	Negative	Negative	200
15 October 1970	38	3.4									200
29 October 1970	25										200
10 November 1970	48	3.9		1/256							
20 November 1970				1/384							
30 December 1970			Reactive lymphocytes								
6 January 1971	49		Reactive lymphocytes	1/384		Negative	Negative	Negative	Negative	Negative	
27 January 1971											200
10 February 1971	21	2.9		1/384	Negative						200
16 February 1971	42										
Cytosine arabinose started											
22 February 1971	44	2.3		1/384							
25 February 1971	32			1/256							
1 March 1971		2.0		1/192							

Buckley and MacCullum, 1967; Silk and Roome, 1970). Because of its toxicity we were reluctant to use this and gave the newer antiviral agent, cytosine arabinose, which has been used successfully to treat generalized herpes infections (Juel-Jensen, 1970). No clinical benefit occurred in our patient.

It was of interest that the patient had mitral incompetence as shown by the physical signs and selectively high indirect left atrial pressures with a giant V wave (see Table 2). This may have been the functional result of left ventricular damage or direct damage to the valve as has been suggested to occur in other types of viral myocarditis (Burch and Colcolough, 1969).

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TABLE 2 Right heart catheterization (18 February 1971)

	Pressure (mmHg) reference point: midchest	
	Phasic	Mean
Right atrium	a = 13 v = 13	9
Right ventricle	72/13	
Pulmonary artery	72/38	56
Pulmonary artery wedge	a = 50 v = 70	40
Arterial oxygen saturation	88%	
Right atrial oxygen saturation	52%	

References

- Buckley, T. F., and MacCullum, F. O. (1967). Herpes simplex virus encephalitis treated with idoxuridine. *British Heart Journal*, **2**, 419.
- Burch, G. E., and Colcolough, H. L. (1969). Viral valvulitis. *American Heart Journal*, **78**, 119.
- Cangir, A., Sullivan, M. P., Sutow, W. W., and Taylor, G. (1967). Cytomegalovirus syndrome in children with acute leukaemia. *Journal of the American Medical Association*, **201**, 612.
- Carlström, G., Alden, J., Belfrage, S., Hendenström, G., Holmberg, L., Nordbring, F., and Sterner, G. (1968). Acquired cytomegalovirus infection. *British Medical Journal*, **2**, 521.
- Conchie, A. F., Barton, B. W., and Tobin, J. O'H. (1968). Congenital cytomegalovirus treated with idoxuridine. *British Medical Journal*, **4**, 162.
- Coombs, R. R. H. (1968). Cytomegalic inclusion-body disease associated with acquired autoimmune haemolytic anaemia. *British Medical Journal*, **2**, 743.
- Evans, A. D., Gray, O. P., Miller, M. H., Verrier Jones, E. R., Weeks, R. D., and Wells, C. E. C. (1967). Herpes simplex encephalitis treated with intravenous idoxuridine. *British Medical Journal*, **2**, 407.
- Juel-Jensen, B. E. (1970). Severe generalised primary herpes treated with cytarabine. *British Medical Journal*, **2**, 154.
- Kääriäinen, L., Klemola, E., and Paloheimo, J. (1966). Rise of cytomegalovirus antibodies in an infectious-mononucleosis-like syndrome after infusion. *British Medical Journal*, **1**, 1270.
- Klemola, E., and Kääriäinen, L. (1965). Cytomegalovirus as a cause of a disease resembling infectious mononucleosis. *British Medical Journal*, **2**, 1099.
- Klemola, E., Kääriäinen, L., Von Essen, R., Haltia, K., Koivuniemi, A., and Von Bonsdorff, C. H. (1967a). Further studies in cytomegalovirus mononucleosis in previously healthy individuals. *Acta Medica Scandinavica*, **182**, 311.
- Klemola, E., Weckman, N., Haltia, K., and Kääriäinen, L. (1967b). The Guillain-Barré syndrome associated with acquired cytomegalovirus infection. *Acta Medica Scandinavica*, **181**, 603.
- Lamb, S. G. (1971). Cytomegalovirus infections. *British Journal of Hospital Medicine*, **5**, 347.

- Lamb, S. G., and Stern, H. (1966). Cytomegalovirus mononucleosis with jaundice as presenting sign. *Lancet*, **2**, 1003.
- Räsänen, V., and Saikku, P. (1967). Cytomegalovirus hepatitis. *Lancet*, **2**, 772.
- Rifkind, D., Goodman, N., and Hill, R. B., Jr. (1967). The clinical significance of cytomegalovirus infection in renal transplant recipients. *Annals of Internal Medicine*, **66**, 1116.
- Silk, B. R., and Roome, A. P. C. H. (1970). Herpes encephalitis treated with intravenous idoxuridine. *Lancet*, **1**, 411.
- Stern, H. (1968). Isolation of cytomegalovirus and clinical manifestations at different ages. *British Medical Journal*, **1**, 665.
- Stern, G., Agell, B.-O., Wahren, B., and Espmark, A. (1970). Acquired cytomegalovirus infection in older children and adults. *Scandinavian Journal of Infectious Diseases*, **2**, 95.
- Toghill, P. J., Bailey, M. E., Williams, R., Zeegen, R., and Bown, R. (1967). Cytomegalovirus hepatitis in the adult. *Lancet*, **1**, 1351.

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