

Cytomegalovirus retinitis in AIDS

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Abstract

Cytomegalovirus retinitis is common in adults with AIDS but has been reported infrequently in children with perinatally acquired HIV infection. The cases are presented of two infants with vertically acquired HIV infection who developed disseminated cytomegalovirus infection and retinitis, and who posed difficult management issues.

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Infection with cytomegalovirus is extremely common in patients with AIDS, and can result in pneumonitis, hepatitis, colitis, and chorioretinitis. In adults the retina is the commonest site of clinical disease with cytomegalovirus retinitis occurring in 15-20% of AIDS patients.¹ In the paediatric population the incidence of cytomegalovirus retinitis appears to be much lower than in adults.² A recent review of cytomegalovirus infection in children with AIDS describes 38 cases of cytomegalovirus disease but found no retinitis.³ The only other previously published report describes two cases of cytomegalovirus retinitis from a series of 40 vertically infected children. Both died within six months of diagnosis.⁴ We describe two infants with AIDS, cytomegalovirus disease, and retinitis and discuss the difficulties encountered in the management of this complication.

Case reports

CASE 1

A 4 month old breast fed infant was admitted in respiratory failure after a one week history of cough, tachypnoea, and poor feeding. He required ventilation and a bronchoalveolar lavage demonstrated *Pneumocystis carinii* pneumonia. HIV-1 antibodies were detected on serological testing; HIV polymerase chain reaction was positive for *gag* and *pol* primers, and p24 antigen was detected at a concentration of 95 pg/ml. CD4 count was $0.073 \times 10^9/l$ (4% of a total lymphocyte count of $1.83 \times 10^9/l$). He made a good initial recovery after treatment with high dose co-trimoxazole (120 mg/kg/day), methylprednisolone, fluid restriction, and frusemide. Despite being extubated after three days, he still required high concentrations of oxygen via head box and deteriorated when attempts were made to decrease the steroid treatment. Two weeks after admission chest radiography showed persistent bilateral interstitial pneumonitis. Abnormal liver function test results prompted cytomegalovirus screening and early

antigen was detected in urine and nasopharyngeal secretions, though not in the buffy coat. Ophthalmological review revealed two white retinal exudates present in the left eye. The larger one was of several disc diameters in size and the smaller was a perivascular lesion (figure).

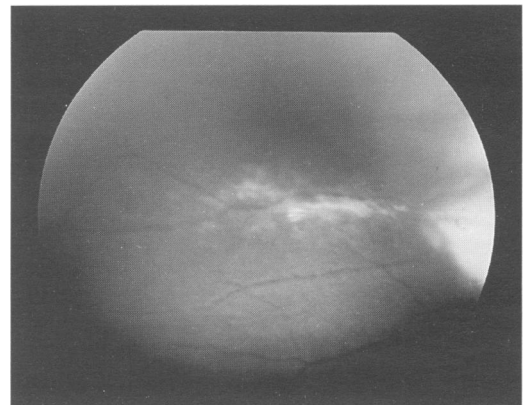
He was treated with ganciclovir 10 mg/kg/day in two divided doses after which his respiratory distress decreased and his liver function stabilised. There was no evidence of progression of the retinitis. He was discharged after three weeks of ganciclovir treatment on oral acyclovir, 600 mg/m²/dose four times a day as suppressive treatment as his mother refused the option of intravenous ganciclovir suppressive treatment via a central venous line daily for five days each week.

He was subsequently lost to follow up and died six months later, having been admitted to another London hospital with reactivated cytomegalovirus disease and pneumonitis.

CASE 2

An 8 month old girl was admitted with chronic cough, severe failure to thrive (weight falling from 50th to 3rd centile), generalised lymphadenopathy, and hepatosplenomegaly. She had been breast fed initially but was changed to bottle feeding at 3 months of age. Chest radiography revealed right upper lobe consolidation and hilar lymphadenopathy. HIV-1 serology, HIV polymerase chain reaction, and p24 antigen testing were positive. Mantoux testing (1 in 1000) was negative at 72 hours. CD4 count was $1.43 \times 10^9/l$ (19% of a total lymphocyte count of $7.5 \times 10^9/l$). Testing of nasopharyngeal aspirate for immunofluorescence to *P carinii* and respiratory viruses was negative.

She was treated initially with intravenous ceftazidime (150 mg/kg/day) and oral erythromycin, but this regimen was ineffective in



Perivascular focus of cytomegalovirus retinitis in child with AIDS (case 1).

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reducing her respiratory symptoms. Cytomegalovirus early antigen was detected in nasopharyngeal secretions and urine but not in the buffy coat. Ophthalmological review revealed unilateral grey/white discoloration of the retina of several disc diameters in size just inferior to the macula and a second infiltrate superior to the optic disc.

Induction treatment with intravenous ganciclovir (10 mg/kg/day for three weeks) was started and was effective in reducing her respiratory symptoms. Again, after discussion with the mother the option of a permanent central venous line for maintenance ganciclovir was rejected. Hence oral acyclovir 2400 mg/m²/day was started as cytomegalovirus suppressive treatment, as well as antiretroviral treatment with zidovudine, and *P carinii* pneumonia prophylaxis with co-trimoxazole.

On review at five months from diagnosis she remains generally well but some new perivascular lesions have appeared on the periphery of the longstanding infiltrates.

Discussion

These cases were consecutive presentations of infants with AIDS to our department. They were screened for cytomegalovirus infection because of suboptimal responses to treatment for *P carinii* pneumonia and presumed bacterial infection. In neither case was there evidence of congenital cytomegalovirus infection (both birth weights were above the 50th centile, no history of neonatal jaundice, no evidence of hearing impairment, and no intracranial calcification). Although no retinal biopsy samples were taken the diagnosis of cytomegalovirus retinitis was made clinically, based on the ophthalmological findings and clinical evidence of cytomegalovirus disease elsewhere as well as positive rapid tests for cytomegalovirus from urine, nasopharyngeal aspirate, and bronchoalveolar lavage fluid. There is strong evidence that these are cases of cytomegalovirus disease and retinitis.

The only detailed information available is from the adult experience where the high incidence of cytomegalovirus (95% of the homosexual population is infected) means that cytomegalovirus disease is a common accompaniment of severe HIV infection, especially when CD4 counts are less than 0.5 × 10⁹/l. Mean survival after a diagnosis of cytomegalovirus retinitis has been made is reported as 8.3 months.⁵ Treatment of sight threatening cytomegalovirus retinitis with either ganciclovir or foscarnet is effective in delaying disease progression.^{6,7} Neither drug eradicates

cytomegalovirus disease and relapse rates are very high if treatment is discontinued after induction alone. Maintenance treatment reduces the risk of recurrence to 18–54%¹ but at a cost to the quality of the patient's life.

These cases posed an ethical and therapeutic dilemma with regard to the long term administration of cytomegalovirus suppressive treatment with ganciclovir. The mothers in both cases declined the option of a central venous line insertion and infusions of ganciclovir five days each week for an indefinite period. Given recent data from the British Isles on the poor outcome and median survival of only three months of infants with perinatally acquired HIV infection and *P carinii* pneumonia,⁸ we felt unsure of the appropriateness of such treatment especially for the child described in case 1. Both sets of carers agreed to administer high dose oral acyclovir as cytomegalovirus prophylaxis. There is some evidence for the efficacy of acyclovir as cytomegalovirus suppressive treatment.⁹

The situation may be altered in the near future as studies with oral preparations of ganciclovir are progressing and suggest that the oral form retains much, if not all the activity of the intravenous preparation.¹⁰

It seems appropriate to screen all HIV infected children with evidence of cytomegalovirus infection for the presence of cytomegalovirus retinitis. Long term suppressive treatment for cytomegalovirus retinitis presents considerable problems at present.

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