Vidarabine in fulminating chickenpox pneumonia

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Chickenpox (varicella), a common and usually mild infection of childhood, is frequently more serious in adults. The principal complication of adult varicella is pneumonia which may be fatal in a fifth of cases. We describe two patients with rapidly fulminating varicella pneumonia who responded to vidarabine therapy.

Case reports

CASE ONE
A 34-year-old teacher, previously in good health, was admitted with rapidly progressive shortness of breath complicating varicella. He first became unwell four days before admission with fever, sweats, and anorexia. The varicella eruption appeared the next day and spread rapidly to cover his body and face. Two days before admission he developed severe, dull central chest pain, a dry cough, and increasing dyspnoea. His two daughters, aged 3 and 5 years, had had varicella, six and three weeks previously. On examination he looked ill and was covered with the lesions of haemorrhagic varicella. His temperature was 39.2°C, pulse 110 beats/minute, blood pressure normal, respiratory rate 30/minute, and he was centrally cyanosed. He had bilateral crepitations at both lung bases. The liver was tender and enlarged 3 cm below the costal margin.

Investigations revealed a total white count of 13 700 × 10⁹/litre (8905 neutrophils; 4247 lymphocytes; 548 plasma cells) and the platelet count was reduced to 64 000 × 10⁹/litre. Other investigations failed to show evidence of a consumptive coagulopathy. The electrolytes were normal but liver function tests were markedly abnormal; alkaline phosphatase 638 IU/l (normal 46-190), γ glutamyl transpeptidase 92 IU/l (normal 6-28), glutamyl pyruvic alanine transferase 57 IU/l (normal 2-21), and a normal bilirubin. The chest radiograph showed extensive bilateral alveolar shadowing and his arterial blood gases while breathing air were Pao₂ 4.2 kPa, Paco₂ 5.0 kPa, and pH 7.53. Fifty per cent oxygen by mask increased his Pao₂ to 6.1 kPa. Electron microscopy of vesicular fluid revealed herpes-like virus particles. However tissue culture failed to isolate a virus from either the fluid or a throat swab. Testing of paired sera for complement fixing antibodies against varicella-zoster showed a diagnostic rise from zero, to a titre of 128 18 days after admission. Blood and sputum cultures failed to yield any pathogens. Intravenous erythromycin was started and subsequently tobramycin and flucloxacinill were added. However his clinical state, chest radiograph, and arterial blood gases deteriorated. Fifteen hours after admission

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Figure Case 1. Chest radiographs taken a day after starting vidarabine (13.11.80) and eight days later (21.11.80).
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Treatment with intravenous vidarabine, 15 mg/kg/day, was begun and continued for seven days.

Thirty-five hours after admission he required mechanical ventilation and an inspired oxygen concentration of 100% with five centimetres of positive end-expiratory pressure was needed to maintain a PaO₂ of 9.1 kPa. The following day, his arterial oxygen began to improve. No fresh skin lesions were seen two days after starting vidarabine and the radiograph showed clearing. He steadily improved (figure), was weaned from ventilation following day, and was discharged from hospital 19 days after admission. When seen one month later he was well and his pulmonary shadowing had almost resolved. Lung function studies showed normal lung volumes and a transfer factor of 71% of predicted.

CASE TWO
A previously well 37-year-old factory worker contracted varicella from his three children. Three days after the onset of the rash, he developed a dry cough, left pleural pain, and rapidly increasing shortness of breath and was admitted to hospital. On examination he was covered with a varicella rash, his temperature was 39.0°C and pulse rate 110 beats/minute. His liver was enlarged and tender. The respiratory rate was 38/minute and his chest was clear to auscultation. Investigations revealed a total white count of 10 300 × 10⁹/litre (3150 neutrophils; 4944 lymphocytes; 206 monocytes) and a platelet count of 101 000 × 10⁹/litre. Liver function tests were abnormal. The chest film showed patchy alveolar shadowing throughout both lung fields and his arterial gases were PaO₂ 7.7 kPa, PaCO₂ 4.3 kPa, and pH 7.44 while breathing air.

Electronmicroscopy of blister fluid and serial serum complement fixation tests confirmed a varicella infection. Blood and throat swab cultures were negative.

Treatment with intravenous vidarabine (15 mg kg day for five days) together with intravenous erythromycin were started shortly after admission. His chest radiograph had deteriorated by the next day and new skin vesicles appeared. However two days after admission he started to improve, his temperature settled and no new skin lesions appeared after the third day. His chest film was virtually normal when he was discharged home, eight days after admission.

Discussion
A previously fit man (case one) developed haemorrhagic varicella complicated by fulminating pneumonia, thrombocytopenia, and hepatitis. Within five days of becoming ill he required artificial ventilation with 100% inspired oxygen to maintain adequate oxygenation. Recovery from this severity of varicella pneumonia has not been reported before and it was almost certainly attributable to his prompt treatment with vidarabine. The second patient, although less severely affected, made a similar excellent response to vidarabine.

Primary varicella pneumonia occurs in 16-33% of adults developing chickenpox, with a reported 20% mortality in patients admitted to hospital. Before the availability of antiviral chemotherapy, treatment of such cases was supportive.

Vidarabine has been shown to be effective in severe herpes virus infections particularly in immunosuppressed patients. However its use in varicella pneumonia has only been reported twice, neither patient being ill enough to require mechanical ventilation.

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