Varicella Pneumonia in a Woman Receiving Methotrexate for Psoriatic Arthritis

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Varicella pneumonia accounts for the most severe complications of Varicella in adults. The mortality rate of Varicella pneumonia has been reported to be 30%, but may be significantly higher (50%) when the patient requires mechanical ventilation. Risk factors for developing Varicella pneumonia are smoking, immunosuppression, male gender, and pregnancy. The treatment of choice is intravenous acyclovir [1]. We present the case of a young woman admitted to our intensive care unit with a fulminant Varicella sepsis and pneumonia.

PATIENT DESCRIPTION

A 38 year old married woman, mother of three, was referred to the emergency department with increasing dyspnea and a vesicular rash. The ED physician elicited information that her children had had chickenpox 3 weeks earlier. Her rash had begun 3 days before admission, but shortness of breath appeared on the day of presentation. Her medical history was significant for psoriatic arthritis, which had been treated with methotrexate, and for smoking.

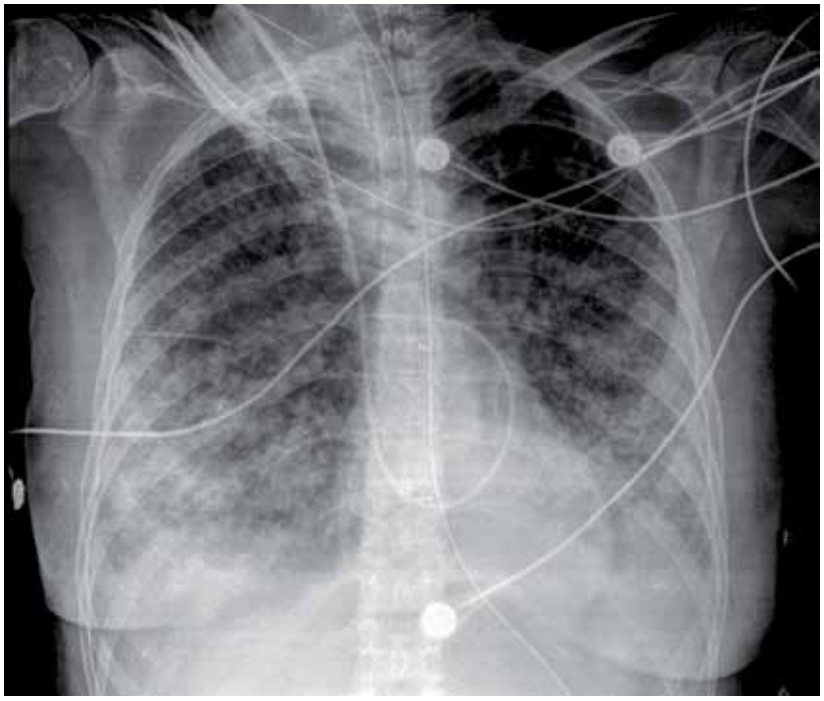
The patient's vital signs upon hospital admission were as follows: temperature 37.1°C, pulse rate 120 beats/minute, blood pressure 110/60 mmHg, oxygen saturation 92% (while breathing room air), and respiratory rate 25 per minute. Her vesicular rash was typified by lesions at various stages of progression and crusting. Auscultation to the lungs revealed bilateral rales. Physical examination was otherwise unremarkable. Chest radiography showed bilateral consolidation with a marked interstitial component [Figure]. Laboratory tests, on presentation, showed mild thrombocytopenia (126,000 x 10^3/μg) and mild hyponatremia (132 mEq/L).

The patient was admitted to the negative pressure suite in the internal medicine ward and was treated with intravenous acyclovir, ceftriaxone and azithromycin. Despite the treatment, her condition deteriorated; her respiratory rate rose to 40 bpm and although her oxygen saturation remained above 95% (with a face mask) she became agitated. She was admitted to the ICU 24 hours after hospital admission. Her admission vitals were heart rate 135 bpm, blood pressure 100/50 mmHg and saturated O_2 87%. Two hours later, her blood pressure dropped to 70/40, with a parallel drop in the ratio of arterial oxygen tension to inspired oxygen fraction (PaO_2/FiO_2) to 75. Following rapid fluid administration the patient was sedated and her trachea was intubated. After the intubation, the ratio of PaO_2/FiO_2 was 78. This hypoxemia required treatment with protective lung ventilation: high positive end-expiratory pressure (15 cmH_2O) and inverse-ratio

ED = emergency department

ICU = intensive care unit

Chest X-ray of the patient on the 3rd day



ventilation. When these did not suffice, inhaled nitric oxide was added at 16 ppm. A central venous line was inserted to administer noradrenaline (titrated to maintain blood pressure at a mean of 65 mmHg) and further fluid loading.

Despite an echocardiogram that showed good bilateral ventricular function and filling, urine output continued to decrease. A pulmonary artery catheter was inserted; central venous pressure was 12 mmHg, pulmonary occlusion pressure 13 mmHg, cardiac index 3.75 L/min/m^2, systemic vascular resistance index 1100 dyn s/c^5/c^2 and mixed venous saturation (SvO_2) 61%. The rate of crystalloid infusion was decreased and the dose of noradrenaline was increased. A blood sample was sent for cortisol measurement (16 mmol/L) and therapy with intravenous hydrocortisone (50 mg 4 times a day) was initiated.

Both the history of methotrexate use and the clinical deterioration despite broad-spectrum antibiotic coverage prompted further investigation. Thus, 36 hours after intubation the patient underwent diagnostic broncho-alveolar lavage. Initial staining of the lavage fluid was negative for routine and acid-fast bacteria, as well as for *Pneumocystis jiroveci*. Atypical cells in the peripheral blood smear prompted further hematological testing, but neither peripheral blood nor bone marrow demonstrated clonal cell proliferation.

On the following day the patient began to improve rapidly. She was weaned from noradrenaline within 72 hours and the intravenous fluids were gradually changed to nasogastric feeding. On the morning of the third day, the lavage fluid polymerase chain reaction for viruses returned highly positive for Varicella. Also positive were blood tests for antinuclear antibody titers (1:400, in nucleolar pattern) and cryoglobulins, raising the possibility of an underlying disease other than psoriatic arthritis.

The patient was extubated after 9 days of mechanical ventilation and was transferred 2 days later to the internal medicine ward. The rest of her recovery was uneventful and she was discharged home 4 days later.

COMMENT

Immunosuppression is a risk factor of Varicella pneumonia [1]. This patient had received methotrexate immunosuppressive therapy for psoriatic arthritis. The role of immunosuppressive medications for treating inflammatory diseases is increasing. This immunosuppressive therapy can expose patients to a variety of infections. To note, the increasing use of anti-tumor necrosis factor antibodies can lead to reactivation of Varicella zoster. TNFα, which has a role in cellular immunity, can inhibit the replication of the virus, and therefore immunosuppressive therapy can predispose to this infection [2].

While treating this patient, we encountered three main adjunctive treatment dilemmas of critical care: Should systemic steroids be administered? Would the patient benefit from treatment with immune globulin or Varicella zoster immunoglobulin? What is the time frame to consider an extracorporeal membrane oxygenator?

Two studies (not randomized or controlled) describe the use of steroids in Varicella pneumonia. The first was a retrospective chart review of 19 adult patients admitted with Varicella pneumonia. The 10 patients, who received corticosteroids, although sicker, had improved oxygenation and a trend towards a shorter duration on mechanical ventilation [1]. In the second study, 6 of the 15 ICU patients with Varicella pneumonitis who received hydrocortisone had shorter ICU and hospital stays and all survived, in contrast to the rest of the patients, of whom four died [1,3].

We debated the value of intravenous immunoglobulin or VZIG as an adjunct therapy. Our decision not to administer immunoglobulins was based on the lack of recommendations regarding use of immunoglobulins after severe infection, and the late presentation (the patient presented more than 3 days after appearance of the skin eruption). The VZIG could be given only intramuscularly, and the existing literature does not mention giving it therapeutically but only prophylactically. In addition, concerns were raised regarding the effect of an intravenous protein with high oncotic pressure on extravascular lung water. Others have chosen to act differently; in a case series of 17 immunocompromised children with hematological malignancies and Varicella infection, 5 received immunoglobulin within less than 3 days of skin eruption and none died, 7 were treated after 3 days and 3 of them died [4].

We found a single case series of patients with Varicella pneumonia treated with an ECMO. Eight of 14 ECMO patients survived [5]. We did contact our national ECMO center to notify them of our patient shortly after her ICU admission (< 24 hours). However, since clinical turnaround occurred within less than 72 hours a final decision was never required. In our case, clinical improvement occurred following intensive supportive care.

We believe these adjunct therapies should be considered when treating Varicella pneumonia patients in the intensive care unit.

TNFα = tumor necrosis factor-alpha
VZIG = Varicella zoster immunoglobulin

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ECMO = extracorporeal membrane oxygenator