Fever and dyspnoea in a young man with a rash

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A 36-year-old male smoker presented with a 7-day history of fever, chills and malaise. He admitted to increasing dyspnoea over the past 2 days. There was no history of cough, nausea or vomiting. The patient had developed crops of erythematous pruritic vesicles on his face, trunk, and extremities 5 days prior to admission. He admitted to being exposed to a child with a similar rash, and his own three sons had developed a similar rash.

On examination he appeared to be severely ill. Skin examination revealed multiple vesicular lesions with crusting, mostly on his chest, back, and extremities. An arterial blood gas revealed pH 7.42, pO_2 6.63 kPa, pCO_2 4.03 kPa, and O_2 saturation of 87% on room air. He was febrile with a temperature of 39°C. His lungs were clear to auscultation bilaterally. Routine blood tests were normal except for neutrophil leucocytosis (white blood cells of $10 \times 10^9/l$ with 89% neutrophils, 3.3% lymphocytes, 6.4% monocytes, 0.1% eosinophil, and 0.8% basophil). His chest X-ray is shown in the figure.

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Figure Chest X-ray

Questions

- 1 What is the differential diagnosis?
- 2 What treatment would you advise?
- 3 What are the risk factors and other complications associated with this condition?

Answers

QUESTION 1

There are many causes of diffuse nodular shadowing on chest X-ray (box 1). The patient's rash was suggestive of chicken-pox. His three sons also had this diagnosis. A diagnosis of presumptive varicella pneumonia was based on the patient's response to intravenous acyclovir and laboratory findings which included negative findings for tuberculosis, legionella, cryptococcosis, and pneumocystis carinii pneumonitis. Blood and sputum cultures and sputum cytology were also negative. The patient refused fiberoptic bronchoscopy. After 7 days of treatment with acyclovir, his condition greatly improved and he was discharged.

Principle causes of diffuse nodular shadowing

- metastatic carcinoma to lungs
- lymphoma
- alveolar cell carcinoma
- sarcoidosis
- tuberculosis
- fungal diseases (histoplasmosis; cryptococcosis; coccidioidomycosis; blastomycosis)
- pneumoconiosis
- varicella pneumonia
- systemic vasculitis (Wegener's granulomatosis and peri-arteritis nodosa)
- collagen vascular disease (including rheumatoid nodules and systemic lupus erythematosus)
- septic emboli
- arteriovenous malformations
- haemosiderosis (including Goodpasture's disease)
- amyloidosis
- cryptogenic organising pneumonia/bronchiolitis obliterans organising pneumonia
- alveolar proteinosis
- pneumocystis carinii pneumonitis
- Kaposi's sarcoma

Box 1

QUESTION 2

Acyclovir is preferred over vidarabine for treatment. It has been more effective in shortening the cutaneous course of varicella infection in the immunocompromised patient. Other advantages of acyclovir are reduced haematopoietic and neurological toxic reactions, shorter infusion time, and increased solubility. Vidarabine and foscarnet have also been used to treat varicella infection, but with much less success. The recommended doses of these drugs are listed in box 2.

QUESTION 3

The identification of several risk factors for adult varicella pneumonia is of special interest for possible chemoprophylaxis (box 3). Reports have shown an increased risk for varicella pneumonia in patients after prolonged treatment with corticosteroids, cytotoxic or radiation therapy. In addition, it has been reported that

Antiviral treatment for varicella infections

Varicella pneumonitis

- acyclovir, iv 30 mg/kg/day every 8 h or
 - vidarabine, iv 10 mg/kg/day every 12 h or
 - foscarnet, iv 40 mg/kg/day every 12 h
- (duration depends on clinical course)

Varicella in the immunocompromised host

- acyclovir, iv 30 mg/kg/day every 8 h for 5–7 days or
- vidarabine, iv 10 mg/kg/day every 12 h for 5–7 days or
- foscarnet, iv 40 mg/kg/day every 12 h for 5–7 days

Varicella in the immunocompetent host

- acyclovir, po 800 mg five times a day for 5 days

Box 2

Risk factors for adult varicella pneumonia

- pregnancy
- smokers
- immunosuppressed individuals
- cancer
- older individuals
- severe cutaneous/haemorrhagic rash
- chronic obstructive pulmonary disease

Box 3

conventional 'low-dose' corticosteroid therapy (<2 mg/kg or 5–20 mg daily), and short-term steroid therapy for acute asthma attacks may predispose patients to disseminated varicella.¹

The US Food and Drug Administration have warned that patients on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox and, if exposed, obtain medical advice. The UK Committee on Safety of Medicines has recently recommended that all patients taking systemic corticosteroids for purposes other than replacement should be regarded as at risk of severe varicella zoster unless there is a history of previous chicken pox. Even then, a clinical history of chicken pox is not necessarily reliable, and testing of all such patient to identify the seronegative cases at risk might be wise, albeit expensive.² The Joint Committee on Vaccination and Immunization has recommended that immunosuppressed patients who have been receiving steroids at a daily dose of 2 mg/kg for more than a week within 3 months of direct contact with chicken pox should be passively immunized with varicella zoster immunoglobins if they do not already have antibodies to varicella zoster. Similar recommendations seem appropriate with other immunosuppressive agents, especially when several agents are combined.

The only identifiable risk factors for this patient was that he had smoked 50 cigarettes/day for the past 10 years and he had a severe cutaneous disease. Further investigation revealed him to be HIV positive with a CD4

Other complications of varicella infection

- encephalitis
- Guillain-Barre syndrome
- glomerulonephritis
- arthritis
- hepatitis
- pancreatitis
- myocarditis
- venous thrombosis
- thrombocytopenia
- orchitis
- conjunctivitis, iritis, uveitis, keratitis
- Henoch-Schonlein purpura

Box 4

count of 0. He denied any history of intravenous drug use or high-risk sexual behaviour. Eight months later, this patient developed varicella retinopathy and progressive outer retinal necrosis (PORN syndrome), which resulted in permanent visual loss. PORN is a distinct form of necrotizing herpetic retinopathy that has been reported with increasing frequency in AIDS patients. Varicella zoster virus is currently the only agent that has been associated with the disease.

Various complications of varicella infection may occur (box 4). The most common and serious complication is varicella pneumonia.

Discussion

Varicella is usually a benign childhood disease, while in the adult it may be complicated by pneumonia with high morbidity and mortality rates. Varicella is one of the most common transmittable diseases. However less than 2%

of 3–4 million annual cases in the US occur in adults. The most common complications of adult varicella are pulmonary manifestations, especially pneumonia (incidence rate 10–50%).³ Ninety per cent of pulmonary manifestations of varicella occur after the age of 19 years, mainly in the third decade. Untreated adult varicella pneumonia is fatal in approximately 10% of cases.⁴

Pneumonia occurs early in the course of varicella, within 1–6 days after the onset of the rash. Varicella pneumonia should be considered in any adult with chicken pox who complains of dyspnoea, cough and fever. Physical findings usually correlate poorly with the degree of pneumonia.

Chest X-rays of varicella pneumonia can vary; abnormal findings are seen in about 16% of cases with primary varicella.⁵ Findings may include a patchy, diffuse air-space consolidation or diffuse interstitial infiltrates that may be nodular, with the severity correlating with the diffuseness of the rash. The infiltrate can be associated with a proteinaceous exudate, oedema and hyaline membrane formation which can progress to respiratory distress syndrome. In the later stages, diffuse pulmonary microcalcifications of 2–3 mm in diameter have been described.⁵

Aggressive and early treatment with acyclovir seems to prevent the potentially catastrophic consequences of varicella pneumonia. Oral acyclovir chemoprophylaxis may have some benefit in high-risk populations with chicken pox.

Final diagnosis

Varicella pneumonia.

Keywords: chicken pox; varicella pneumonia; acyclovir

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