CASE FOR DIAGNOSIS

Proteinuria, pancytopenia and hypoxaemic respiratory failure in a 28-year-old female

W. Berjaoui*, N. Dean*[#] and N. Dahle[†]

CASE REPORT

A previously healthy 28-yr-old Caucasian female presented to the emergency department with a 1-week history of generalised body swelling that was followed by pleuritic chest pain radiating to the patient's back. She had mild shortness of breath, cough and palpitations, but no fever, chills, nausea, vomiting or diarrhoea. No medications were taken except oral contraceptives. She denied any history of tobacco or alcohol use, recent travel or sick contacts.

The patient's vital signs were as follows: 1) blood pressure 135/94 mmHg; 2) body temperature 39.4°C; 3) respiratory rate 16 breaths·min⁻¹; 4) pulse 105 beats·min⁻¹; and 5) oxygen saturation 95%, while breathing room air. Her physical examination was remarkable for decreased breath sounds diffuse with minimal crackles, as well as facial swelling and pitting oedema of the lower extremities.

Pertinent laboratory results of the blood tests performed on admission are shown in table 1.

After significant respiratory distress, requiring noninvasive positive pressure ventilation, the patient was admitted to the intensive care unit and was started empirically on *i.v.* ceftriaxone, azithromycin and furosemide. Over the next few days, she remained febrile with worsening hypoxaemia. Her white blood cell count dropped to 2.2×10^9 cells·L⁻¹ with a haemoglobin level of 90 g·L⁻¹ and platelet count of 82×10^9 cells·L⁻¹. Chest radiography (fig. 1) and contrast-enhanced computed tomography (CT) scan of the thorax (fig. 2) were performed. Clear pleural fluid (500 mL) was aspirated by thoracentesis. Pleural fluid analysis was consistent with a transudative effusion (protein <20 g·L⁻¹; lactate dehydrogenase 313 IU with a serum level of 658 IU).

Bronchoscopy revealed mild mucosal erythema with mild increase in secretions. No endobronchial lesions were seen. Bronchoalveolar lavage (BAL) showed an increased number of lymphocytes. Cultures and special stains were negative.

TABLE 1 Laboratory results of the blood tests

Measurement	
Pa,O_2 kPa	8
Pa,CO_2 kPa	4
$PA-a,O_2$ kPa	3.9
Haemoglobin g·L ⁻¹	112
White blood cell count $\times 10^9$ cells·L ⁻¹	4.7
Platelet count $\times 10^9$ cells·L ⁻¹	112
D-dimer	2784 ⁺
C-reactive protein mg·L ⁻¹	16.3 [#]
Creatinine μ mol·L ⁻¹	100
β -Natriuretic peptide	>1300 ⁺
Serum protein g·L ⁻¹	71
Immunoglobulin electrophoresis	Normal
24-h urine protein g	1.65 ⁺
HCG, β -quantitative and serum qualitative	Negative
ANA, ANCA, anti-DNA, anti-GBM	Negative
Rheumatoid factor kIU·L ⁻¹	>7 (negative)
Complement component 3 mg·L ⁻¹	7 (normal)
Complement component 4 mg·L ⁻¹	0.8 (low)
HIV test	Negative
Urine <i>Streptococcus pneumoniae</i> antigen	Negative
Urine <i>Legionella</i> antigen	Negative
Antistreptolysin O antibody	Negative

Pa,O_2 : arterial oxygen tension; Pa,CO_2 : arterial carbon dioxide tension; $PA-a,O_2$: alveolar–arterial oxygen tension difference; HCG: human chorionic gonadotrophin; ANA: antinuclear antibody; ANCA: antineutrophilic cytoplasmic antibody; GBM: glomerular basement membrane. [#]: in room air; [†]: at 1,400-m altitude; ⁺: elevated. 1 mmHg=0.33 kPa.

An echocardiogram was normal. Right heart catheterisation showed a cardiac output of 10 L·min⁻¹, pulmonary pressure of 28/7 mmHg (mean 19 mmHg), pulmonary wedge pressure of 10 mmHg and a central venous pressure of 4 mmHg.

*Division of Pulmonary and Critical Care Medicine, Dept of Medicine, [†]School of Medicine, University of Utah, and [#]Division of Pulmonary and Critical Care Medicine, Dept of Medicine, LDS Hospital, Salt Lake City, UT, USA.

CORRESPONDENCE: W. Berjaoui, Division of Pulmonary and Critical Care Medicine, Dept of Medicine, University of Utah, 2600 North 1900 East, Salt Lake City, UT 84132-4701, USA. Fax: 1 8015853355. E-mail: Wael.Berjaoui@hsc.utah.edu

FIGURE 1. Supine antero-posterior chest radiograph.

FIGURE 2. Chest computed tomography scan at mid-chest level.

BEFORE TURNING THE PAGE, INTERPRET THE RADIOGRAPH AND COMPUTED TOMOGRAPHY SCAN, AND SUGGEST A DIAGNOSIS AND TREATMENT.

INTERPRETATION

Chest radiography

Portable supine antero-posterior chest radiography demonstrated diffuse parenchymal opacities with obliteration of the costophrenic sinus, suggesting the presence of bilateral pleural effusions. An air bronchogram is seen in the left lower lobe. Cardiomegaly is suggested by the ratio of the heart diameter to that of the chest, although this is a supine film (fig. 1).

Computed tomography

Contrast-enhanced CT scan of the thorax revealed moderate bilateral pleural effusions, and bilateral areas of airspace consolidation involving the lingula and lower lobe consistent with pneumonia. There was no evidence of central pulmonary emboli (fig. 2).

Diagnostic considerations

The current authors considered the following diagnoses: 1) vasculitis or collagen vascular diseases involving the lung and pleural tissues and causing a renal–pulmonary syndrome; 2) hydrostatic pulmonary oedema given the presence of bilateral transudative effusions and elevated β-natriuretic peptide; 3) immunodeficiency states; 4) bronchioalveolar carcinoma; and 5) viral pneumonia given the febrile presentation associated with BAL lymphocytosis and serum pancytopenia.

The negative vasculitis serology made the diagnosis of vasculitis less likely. The possibility of hydrostatic pulmonary oedema led the current authors to perform right heart catheterisation despite normal echocardiographic findings, but was excluded by the measured cardiac output of 10 L·min⁻¹ and normal capillary wedge pressure. Transudative pleural effusions have previously been reported in viral pneumonia, as appears to be the case in the presented patient [1]. Another possible explanation for the transudate is the significant proteinuria that caused the generalised oedema in the patient. The lack of history of recurrent infections and the negative HIV test made immunodeficiency status unlikely. The rapid changes in the chest radiograph, as well as the absence of airway abnormalities seen during bronchoscopy, negative pleural effusion cytology for malignancy and lack of smoking history ruled out bronchoalveolar carcinoma.

The following tests to investigate an infectious aetiology were carried out (table 2).

Diagnosis: Disseminated parvovirus B19 infection.

CLINICAL COURSE AND TREATMENT

The current patient improved with supportive therapy (oxygen, fluids and noninvasive positive ventilation) and was discharged home 1 week after admission. She was seen 2 weeks later in clinic where she had no symptoms, normal oxygen saturation and a normal chest radiograph.

DISCUSSION

Parvovirus B19 belongs to the parvoviridae family with a predilection to erythroid cells. Infection with parvovirus B19 occurs worldwide with >70% of adults having positive antibodies [2]. Transmission is commonly *via* respiratory droplets, and less commonly through vertical transmission from an infected mother to the foetus [3]. Parvovirus can also spread *via* blood products [4]. Children are the main source of

TABLE 2 Tests to investigate an infectious aetiology

Test	Result
Viral hepatitis profile	Negative
CMV PCR	Negative
HSV EIA	Negative
Mycoplasma pneumoniae antibody, IgM	Negative
Coccidioides antibody by complement fixation	Negative
Infectious mononucleosis screen	Negative
Rapid influenza A and B virus antigen	Negative
Parvovirus B19 antibodies[#]	
IgG IU	4.80
IgM IU	5.27
Parvovirus PCR	Positive

CMV: cytomegalovirus; HSV: Herpes simplex virus; EIA: enzyme immunoassay; Ig: immunoglobulin. [#]: laboratory cut-off is 0.89.

respiratory transmission with household contacts and day carers being at a higher risk. Transmission to healthcare workers seems to depend on the degree of contact [5, 6].

Parvovirus is a common human pathogen. It is known to cause severe illness in children, pregnant females, immunocompromised hosts, as well as patients with haematological diseases. However, severe illness in immunocompetent adults is not common. Most infections are asymptomatic. The most common manifestation is erythema infectiosum or “fifth disease”, which is a febrile exanthem. The disease tends to be more severe in adults. A clinically significant arthropathy is seen in 10–33% of infected individuals, being highest in middle-aged females and lowest in children [7]. Long-term sequelae are rare. Acute parvovirus infection during pregnancy, especially in the first trimester, can lead to miscarriage and hydrops foetalis [8].

Diagnosis is based on serological and DNA evidence. Enzyme immunoassay has a reported sensitivity of 89.1% and a specificity of 99.4%. Immunoglobulin (Ig)M antibodies usually appear within 7–10 days of exposure and can persist for several months. Therefore, low titres of IgM can be suggestive but not conclusive of acute infection. This is also true for parvovirus B19-specific DNA which can persist for years, especially in immunocompromised patients [9, 10].

Pulmonary involvement with parvovirus is extremely rare, especially in healthy individuals. Two cases were reported in immunocompromised children [11, 12]. The present authors could find only one previous case report of severe respiratory involvement in a previously healthy adult [13]; that patient was a middle-aged diabetic female with history of tobacco and intravenous drug abuse, which raises questions about the patient’s immunocompetency. Two mild cases of pulmonary involvement with parvovirus in healthy individuals causing pleuropneumonitis and pulmonary oedema, respectively, have been reported [14, 15].

The presented case appears to be the first report of severe pulmonary compromise in a completely healthy individual due to infection with parvovirus B19.

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