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A 55-Year-Old Couple Both Returning from Chile and Argentina With Acute Respiratory Distress Syndrome

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Clinical Presentation

History

A 55-year-old Swiss couple, both fitness instructors, travelled for 3 months from Ecuador to Chile. The last month of their trip they spent hiking, camping and taking occasional mud baths in the Chile-Argentinian border region. On their flight back to Switzerland, the husband developed a fever (39°C, 102.2°F), myalgias and generalized weakness that did not respond to symptomatic treatment. At presentation at the hospital in Switzerland 4 days later, he continued to be febrile and felt too weak to walk to the toilet unassisted or even hold up a newspaper. He developed shortness of breath with oxygen desaturation and bilateral interstitial infiltrates were seen on chest x-ray (Fig. 90.1).

The respiratory pathogen panel from a nasopharyngeal swab (including influenza A/B, parainfluenza, RSV, adenovirus, rhinovirus, bocavirus, coronavirus and human metapneumovirus) as well as an HIV test came back negative. The following day he was transferred to the intensive care unit for non-invasive ventilator support.

Three weeks later, his wife presented with similar complaints and was admitted to the same hospital. She deteriorated rapidly over the 24 hours after admission, developed cardiorespiratory failure and fulfilled fast-entry criteria for extracorporeal membrane oxygenation (ECMO). Furthermore, she experienced multi-organ failure requiring hemodialysis, and she developed profuse bleeding from puncture sites in the context of disseminated intravascular coagulation. During the following days, she required mass transfusions of blood products.

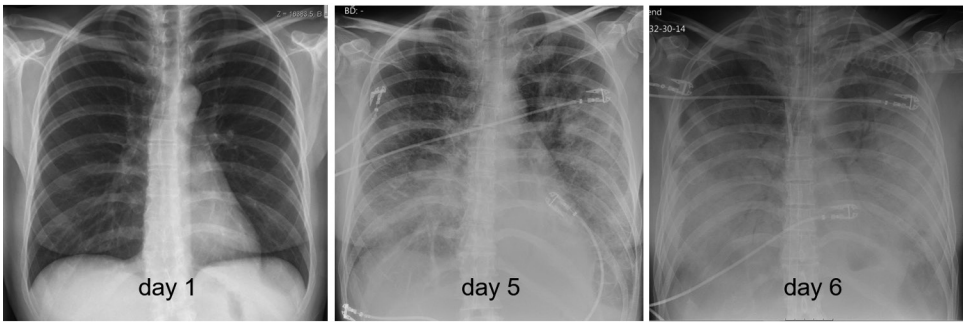
Clinical Findings

Husband: BP 90/55 mmHg, pulse 120 beats per minute, oxygen saturation 94% on ambient air, and temperature 39°C (102.2°F). No abnormal findings on cardiopulmonary auscultation.

Wife on admission (3 weeks after her husband's admission): normal blood pressure, heart rate and oxygen saturation, temperature 38.6°C (101.5°F). No abnormal findings on auscultation.

Laboratory Results

Husband, on admission: WCC 7.3 G/L (reference: 3.0–10.5), 35% band neutrophils; platelets 48 G/L (reference: 150–450); CRP 68 mg/L (reference: <5); glomerular



• **Fig. 90.1** Chest x-ray findings of the female patient on day 1, day 5 and day 6 of admission.

filtration rate >90 mL/min (reference: >90 mL/min); transaminases normal.

Wife, on admission: WCC 1.88 G/L; platelets 98 G/L; CRP 7 mg/L; glomerular filtration rate >90 mL/min; transaminases normal.

Chest radiography at presentation was normal in both patients; however, during the course of the disease both developed extensive bilateral infiltrates with pleural effusions.

Questions

1. What is your differential diagnosis for this couple?
2. How would you manage these patients clinically? Is there any need to consider particular hospital hygiene precautions?

Discussion

A previously healthy Swiss couple in their mid-50s present with varying degrees of cardiorespiratory failure of 2 and 21 days, respectively, after their return from a 3-month trip down the western coast of South America. They spent the last month travelling along the Chile-Argentinian border. The cardiorespiratory collapse in the female patient occurs precipitously and requires ECMO treatment.

Answer to Question 1

What Is Your Differential Diagnosis for This Couple?

Conditions that may present with acute respiratory distress syndrome (ARDS) and possible multi-organ failure after travel to South America include influenza and other respiratory viruses. Of the viral infections, New World hantaviruses cause cardiopulmonary disease; their incubation period is comparatively long and human-to-human transmission has been described, which could explain why husband and wife presented 3 weeks apart.

Pneumococcal pneumonia should also be in the differential diagnosis as a common cause of community-acquired pneumonia worldwide. Rickettsial diseases have to be considered: of the spotted-fever group, in particular *Rickettsia rickettsiae,* which notoriously causes severe disease should be on the list of differentials; and scrub typhus, which was long thought to be limited to Asia, has recently been described from Chile. Pulmonary plague is also focally endemic in South America. Fungal infections (Histoplasmosis, Cryptococcosis) also have to be considered. Severe malaria may cause ARDS and is a possibility, too.

Given the bleeding tendency seen in the wife, most viral haemorrhagic fevers can be excluded based on the incubation time alone, which is well below 21 days for most endemic viral haemorrhagic fevers (yellow fever, dengue and the New World arenaviruses, e.g. Junín virus and Machupo virus). There is only one exception to this rule, which is hantavirus infections: their incubation time may be up to 35 days.

Answer to Question 2

How Would You Manage These Patients Clinically? Is There Any Need to Consider Particular Hospital Hygiene Precautions?

Both patients should be referred to a tertiary care setting, which is equipped to handle ARDS and haemorrhagic fevers. Clinically, securing cardiorespiratory function is the main priority. Broad-spectrum antibiotics are indicated as empirical treatment until further results are back.

Although the aetiology is still unclear, a patient with respiratory symptoms must be treated under standard hygiene and droplet precautions (at least) to prevent potential nosocomial transmission. Depending on local hospital hygiene requirements, airborne precautions may be required.

The Case Continued…

Both patients were confirmed by PCR and serology to be infected with Andesvirus (ANDV), a New World species of the family *Hantaviridae,* belonging to the order of *Bunyavirales.* The New World hantaviruses are the causative agent of the Hantavirus Cardiopulmonary Syndrome (HCPS).

The husband was treated with non-invasive ventilation for 5 days. He made a full recovery after a month of rehabilitation. His wife experienced a dramatic course with nearly a full month on ECMO treatment. Multi-organ failure requiring renal replacement therapy and haemorrhagic complications with mass transfusions of blood products ensued. As a result of bleeding complications at the inguinal ECMO insertion sites (compartment syndrome and leg ischemia) ECMO was replaced centrally (Fig. 90.2). After additional bleeding complications at inguinal and thoracic insertion sites, she underwent several surgical interventions. Nosocomial infections followed, and she remained in intensive care for 5 months and an additional 12 months in rehabilitation. The mode of transmission remained unclear; both human-to-human-transmission and acquisition from a common source were possible.

• **Fig. 90.2** Computed tomography of the chest (lung window) of the female patient on day 13 showing extensive and dense dorsal infiltrations and the centrally placed ECMO cannulae.

SUMMARY BOX

Hantavirus Cardiopulmonary Syndrome (HCPS)

HCPS is caused by ANDV. This New World hantavirus is endemic in the border region between Chile and Argentina. The vast majority of infections occur through inhalation of excreta from the long-tailed pygmy rice rat *(Oligoryzomys longicaudatus),* the reservoir host. Accordingly, outdoor activities are the major risk factor for acquiring ANDV infection.

The incubation period is typically 2 to 3 weeks (range 7–39 days) in case of common exposure.

After non-specific prodromal symptoms over 2 to 8 days, the clinical course varies from a mild disease to its most severe form, HCPS, which is characterized by microvascular leakage and is mainly attributed to host immune response. It presents with rapidly progressing respiratory failure and precipitous haemodynamic instability because of cardiogenic shock and consecutive pulmonary oedema. Capillary leak leads to hypovolemia, which may further impair cardiac and renal function. A haemorrhagic course may occur, although uncommon.

Diagnosis is confirmed by RT-PCR from whole blood or by serology, either with presence of specific IgM antibodies or at least a 4-fold increase in IgG titres in paired samples.

There is no specific treatment or vaccine against ANDV. The use of ribavirin and corticosteroids in ANDV infection still remains to be elucidated. Organ supportive therapy is therefore the mainstay of treatment. Patients should be transferred to a tertiary intensive care unit immediately upon suspicion of ANDV infection, because ECMO support might be required. Case fatality rate in patients with HCPS attributable to ANDV is 20% to 40%.

ANDV is the only hantavirus for which person-to-person transmission has been described, though this occurs very rarely. Nosocomial outbreaks were first reported in 1995. The incubation period in such a scenario is usually around 20 days. Person-to-person transmission is much less common than infection by inhalation of rodent excreta and occurs through close interpersonal contacts in the hospital setting (caring for a person with respiratory or haemorrhagic symptoms) or at home (such as sexual contacts, deep kissing or sharing the same bed).

In the nosocomial setting, standard hygiene and droplet precautions should be adopted, and it is recommended to treat the patients in a single room. During aerosol-generating procedures, however, healthcare workers are advised to wear high-efficiency respirator masks and ocular protection.

Further Reading

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