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Journal of Cardiovascular Emergencies 2023
DOI: 10.2478/jce-2023-0020

CASE REPORT

A Severe Case of Hantavirus Cardiopulmonary Syndrome in a Patient Presenting as STEMI

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ABSTRACT

Hantavirus cardiopulmonary syndrome (HCPS) is a rare disease caused by Hantaviruses, that are transmitted from rodents to humans through aerosols. In some patients, HCPS can have a severe evolution, with rapid progression to respiratory distress and cardiogenic shock. We present the case of a 56-year-old female patient who was transferred to our hospital with ST-segment elevation myocardial infarction (STEMI) and acute respiratory distress syndrome (ARDS). The coronary angiography showed normal epicardial coronary arteries and the lung computed tomography (CT) raised the suspicion of tracheoesophageal fistula, which was soon refuted by an upper digestive endoscopy. Initially, the evolution was very severe, requiring mechanical ventilation, hemodynamic support, and broad-spectrum antibiotics. Later, serological testing revealed an acute infection with Hantavirus Dobrava type. The patient lives in a rural environment, working in a wheat mill. Despite the severe presentation, the evolution was favorable, with complete remission of the pulmonary and myocardial damage after 2 weeks. We emphasize the importance of HCPS suspicion and specific testing in the early phase of the disease, as well as early admission to an intensive care unit, which is crucial in severe cases and can improve survival in a patient without any specific symptoms or a clear diagnosis.

Keywords: Hantavirus, cardiopulmonary syndrome, STEMI

ARTICLE HISTORY

Received: October 8, 2023
Accepted: November 1, 2023

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INTRODUCTION

Hantavirus infection is one of the rare causes of hemorrhagic fever, with a global incidence of 200,000 cases per year and low mortality rate (5%).[1]

Hantavirus cardiopulmonary syndrome (HCPS) is a rare, severe disease caused by Hantaviruses – a genus from the Bunyavirales order.[2] The main virus reservoir is represented by rodents, and the transmission to humans occurs via the aerosol route, with most cases arising in rural environment.[1] The initial clinical presentation is often non-specific, and the correct diagnosis is usually delayed.

CASE PRESENTATION

We present the case of a 56-year-old female patient without any past medical history, residing in a rural environment. She was admitted to a local hospital for asthenia, abdominal pain, nausea, and vomiting. Three days later, she developed additional chest pain and shortness of breath. The patient was afebrile, with a peripheral oxygen saturation (SpO2) of 85%, normal blood pressure and heart rate. Myocardial necrosis and heart failure markers were highly elevated (hs-cTnI 2,953 ng/L, NT-proBNP > 30,000 pg/mL), and the electrocardiogram showed slight ST-segment elevation in the lateral leads (Figure 1). The transthoracic echocardiography revealed hypokinesia of the interventricular septum and lateral wall, with a left ventricular ejection fraction (LVEF) of 35%, as well as moderate mitral and tricuspid regurgitation. Therefore, the patient was transferred to our hospital for lateral STEMI and further additional investigations. Additionally, a chest CT was performed, raising the suspicion of a tracheoesophageal fistula.

On admission to our hospital, the patient was in a critical condition, with a clinical, electrical, and echocardiographic picture of STEMI and ARDS. Given the patient's worsening condition, we decided to perform endotracheal intubation and protective mechanical ventilation, followed by immediate coronary angiography, without evidence of obstructive coronary artery disease (Figure 2).

We immediately reperformed the chest CT, which revealed a 'ground glass' aspect of both lungs, diffuse alveolar and interstitial densification and bilateral pleural effusion (Figure 3A). Moreover, the suspicion of a fistula between the esophagus and the trachea (Figure 3B), as on the previous CT, was maintained. Hence, we considered the diagnosis of aspiration pneumonia caused by the tracheoesophageal fistula, thus explaining both the respiratory and digestive symptoms. However, the upper digestive endoscopy described only an erythematous esophageal mucosa, disproving the diagnosis of tracheoesophageal fistula. The blood tests showed severe metabolic acidosis, marked thrombocytopenia with a platelet count (PLT) of 18,000/mm3, hemoglobin 10.1 g/dL, leukocyte count 11,100/mm3, AST 75 IU/L, ALT 55 IU/L, creatinine 2.68 mg/dL, hematuria and proteinuria.

Less than 24 h from admission, the patient's condition further worsened, developing hemodynamic instability, with a need for high doses of inotropes and vasopressors. The clinical aspect was not only of septic shock but also of a cardiogenic shock with severe EFVS depression. Four days after admission, the echocardiography showed a new small pericardial effusion (8 mm) located posterior to the left ventricle, and the repeated lung CT revealed the expansion of bilateral pneumonic densifications and an increase in pleural effusion volume (Figure 3C). The leukocytosis in-

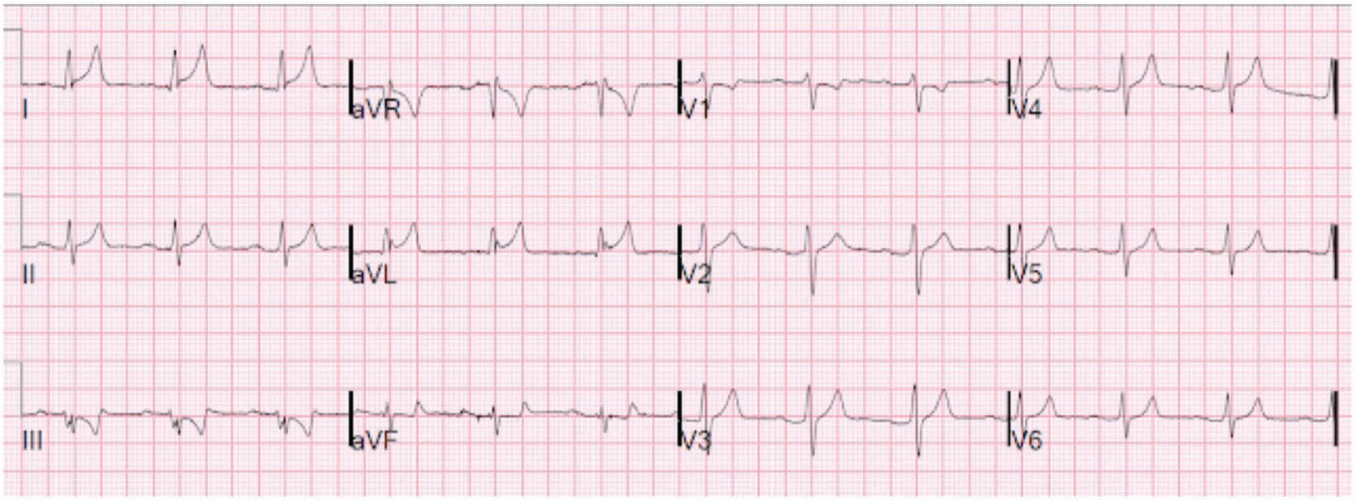

FIGURE 1. Electrocardiogram: sinus rhythm, slight ST–segment elevation in DI, aVL

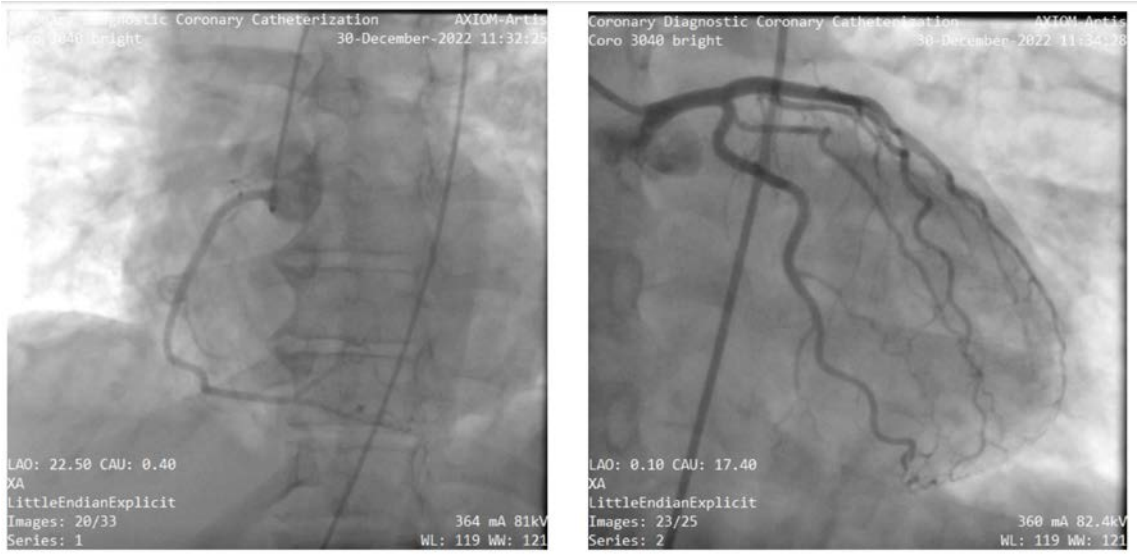

FIGURE 2. Coronary angiography: normal epicardial coronary arteries

creased progressively, reaching a maximum of 26,000/mm3 on day 4, concomitantly with the increase of inflammatory markers (high procalcitonin, C reactive protein × 22 ULN, erythrocyte sedimentation rate × 6 ULN). During the first 4 days, the PLT constantly remained below 20,000/mm3 despite the administration of 10 units of platelet concentrate. Additionally, the hemoglobin level dropped to a minimum of 6.9 g/dL, without evidence of any active bleeding.

We performed serological testing for a wide variety of viruses and bacteria – HIV, HBV, HCV, SARS-CoV-2, MERS-CoV, Influenza A and B, Parainfluenza, SRV, Adenovirus, Enteroviruses, Human metapneumovirus, Hantaviruses, *Bordetella pertussis* and *Bordetella parapertussis*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Coxiella burnetii* – all with negative results, except for an increase in IgM antibodies titer

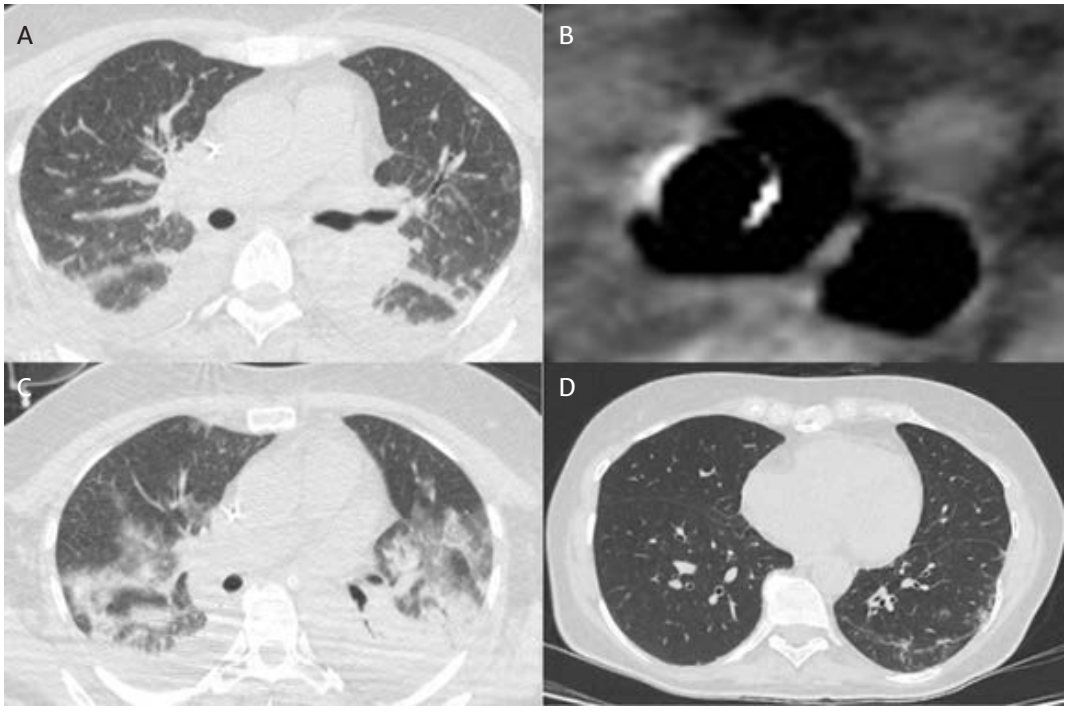

FIGURE 3. Chest CT. **A** – On admission: "ground glass" aspect, diffuse alveolar and interstitial densification, bilateral pleural effusion; **B** – Eso-tracheal communication; **C** – Day 4: expansion of bilateral pneumonic densifications, increase in pleural effusion; **D** – Day 14: complete recovery

for Hantavirus Dobrava type. Thus, a positive diagnosis of acute Hantavirus infection complicated with HCPS was established. Moreover, the blood cultures were positive for *Klebsiella pneumoniae*.

The treatment was mainly supportive: mechanical ventilation, hemodynamic support, veno-venous hemodiafiltration, broad-spectrum antibiotics, and repeated transfusions of platelet concentrate and erythrocyte mass. Under treatment, the patient's evolution was favorable, with progressive ventilation weaning and extubating on day 10, and no further need for hemodynamic support. Two weeks after admission, the echocardiography showed a fully recovered LVEF of 50–55% with persistence of the small pericardial effusion. Furthermore, the lung CT revealed complete remission of the pulmonary lesions and no pleural effusion (Figure 3D).

The patient was discharged with persistent asthenia, moderate anemia, and residual inflammatory syndrome. Six weeks after the acute event, a cardiac magnetic resonance was performed, which did not reveal inflammatory or fibrotic changes suggestive of myocarditis. At the 3-month follow-up the patient was fully recovered, with normalization of Hb and PLT levels, no inflammatory syndrome, a LVEF of 60%, as well as the remission of the pericardial effusion.

DISCUSSION

HCPS is a rare disease, with an increasing incidence in America and Europe in the last few years. Considering the prodromal, non-specific phase, the diagnosis is often delayed; an exposure to rodents or travel history to rural areas should alert the physician regarding the possibility of this particular disease. If HCPS is suspected, transfer from local hospitals to tertiary centers should be facilitated as soon as possible. In our case, the fact that HCPS presented as STEMI led to the rapid transfer of the patient to a tertiary center, hence benefiting from early intensive care measures.

The incubation period is followed by a prodromal, non-specific phase, with fever, chills, headache, abdominal pain, nausea, and vomiting, which can last up to 5 days. Laboratory findings include thrombocytopenia, leukocytosis or leukopenia, abnormal liver and renal function, proteinuria, and hematuria. Interestingly, in a small cohort observational study, thrombocytopenia was associated with a higher risk of clinical progression.[3] Approximately 50% of the infections evolve to a cardiopulmonary phase that is caused by a pulmonary capillary leakage and can rapidly progress to ARDS. In addition, depression of cardiac function ensues, which complicates the picture with cardiogenic shock. The dominant opinion is that the primary cardiac lesion is functional rather than structural, but histologic and immune-histochemical evidence from a small study suggests a concomitant Hantavirus-induced myocarditis.[3]

The diagnosis of certainty requires specific serological testing. The treatment remains largely supportive, with the need for mechanical ventilation, vasoactive drug support, and even extracorporeal membrane oxygenation in severe cases.[1–5] The overall mortality rate is 35–40%, with most of the deaths occurring within 24 h of hospital admission.[5]

Despite the high morbidity and case-fatality rates, no vaccine or drug is currently proven to be preventive or therapeutic. Ribavirin was proven not effective in patients with acute HCPS, while passive immunotherapy with neutralizing antibodies (Nabs) is showing encouraging results.[6]

The impact of the disease on the myocardium is mostly functional, but there is some evidence of a direct cytotoxic effect leading to a specific Hantavirus-induced myocarditis. Therefore, we highlight the importance of serological testing for Hantavirus in patients with acute myocarditis, especially if they reside in a rural environment or are exposed to rodents. Despite the development of cardiogenic shock in severe cases, the evolution can be favorable, with complete recovery of LVEF, as was the case in our patient. In contrast to the adult ARDS seen in other systemic infections, respiratory failure in HCPS resolves within a few days. The importance of infection with *Klebsiella pneumoniae* in our case is debatable.

Although some patients may have a long recovery time, with persisting fatigue, myalgia and dyspnea for months, no lasting complications have been reported.[6]

There is currently no vaccine available and treatment remains largely supportive.[7] Very different concepts are currently pursued to either prevent or treat human Hantavirus infections. It remains challenging and interesting to see which of the current concepts will provide a net clinical benefit.

CONCLUSIONS

HCPS is a severe disease, in which early suspicion and diagnosis, followed by rapid transfer to an intensive care center is crucial and can improve survival. Even in severe cases, the evolution may be favorable under supportive treatment, with complete recovery after the acute phase.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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