with the plasmacytic subtype. Patients with multicentric disease tend to be older (median age, 56 years). Multicentric disease is associated with "B" symptoms including fever and night sweats. Common laboratory abnormalities include anemia, hyperglobulinemia, hypalbuminemia, and an elevated sedimentation rate. Multicentric disease may be very aggressive and may require systemic chemotherapy. Despite aggressive treatment, the median survival time for multicentric disease is 26 months, compared with a nearly 100% 5-year survival with localized hyaline vascular lymph node hyperplasia.5

Both pleural and pericardial effusions have been described at presentation of Castleman’s disease, but as far as is known, there has been no report of a chylous effusion as an original presentation of Castleman’s disease.6,7 The most probable pathogenesis of the chylous effusion in the patient reported herein was a local lymphatic compression with impaired drainage into the thoracic duct, although alternative mechanisms are possible.

CONCLUSION

Castleman’s disease is an uncommon illness that can present with a variety of symptoms. Castleman’s disease should be considered in patients with mediastinal adenopathy or chylous effusions, or both.

REFERENCES


Pleural Fluid Characteristics in Hantavirus Pulmonary Syndrome*

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Hantavirus pulmonary syndrome (HPS), is a rodent-borne, acute, often fulminant cardiorespiratory ill-

*CHEST / 112 / 4 / OCTOBER, 1997 1133
ness. Noncardiogenic pulmonary edema is prominent in HPS as is cardiac dysfunction. Pleural effusions are commonly noted in patients with HPS and have been thought to be exudative. This report describes the prevalence and characteristics of pleural effusions by an assessment of chest radiographs for the presence of pleural fluid and reviews all pleural fluid specimens obtained from patients with HPS. Of 23 patients treated at the University of New Mexico Hospital for HPS, 22 had evidence of pleural fluid while 4 had sampling of their pleural fluid. Two samples met criteria for an exude by pleural fluid protein to serum protein ratio of more than 0.5; one was clearly a transudate and the other had inconsistent characteristics. The two exudative samples were obtained 7 days after admission, while the other 2 were obtained within 1 day of admission. Pleural fluid cultures were sterile, and the total of nucleated cells was less than 170/mm³, and predominately mononuclear. A hypothesis may be formulated that the pleural fluid in HPS is initially transudative, consistent with the observed cardiopulmonary dysfunction. However, following aggressive resuscitative efforts and as the acute illness resolves, fluid shifts occur as cardiac function normalizes; the pleural fluid may take on characteristics of an exudate.

(CHEST 1997; 112:1133-36)

Key words: exude; Four Corners virus; hantavirus; hantavirus pulmonary syndrome; Muerto Canyon virus; pleural effusion; sin nombre virus; transudate

Abbreviations: ECMO = extracorporeal membrane oxygenation; HPS = hantavirus pulmonary syndrome; LDH = lactate dehydrogenase; SNV = sin nombre virus

Several recent communications have described the clinicopathologic and epidemiologic characteristics of hantavirus pulmonary syndrome (HPS).1-5 The etiologic agent is a newly recognized hantavirus. The virus has not been officially named; however, it has been referred to as Four Corners virus, Muerto Canyon virus, and sin nombre (without name) virus (SNV). In this article the agent will be referred to as SNV. SNV is transmitted to humans via contact with infected deer mice (Peromyscus maniculatus). P. maniculatus has an exceptionally wide range, sparing only portions of the gulf states.6

As of May 31, 1996, 139 cases have been confirmed from 24 states, representing all regions of the United States, with a mortality rate of 49.6%. An additional 12 cases have been reported from Canada. The largest number of cases has occurred in the Four Corners region (shared border area between New Mexico, Arizona, Utah, and Colorado) of the United States. The University of New Mexico Hospital is the primary referral center for HPS in the Southwest and has the single largest clinical experience with this disease. To date, 23 patients have been treated, with a mortality rate of 34.8%. Five of the 8 deaths occurred in the first 2 months of the outbreak. Among the commonly described features of HPS are pulmonary edema and pleural effusion. The characteristics of these effusions have not been well elucidated. Included herein is a description of the pleural fluid and the radiologic appearance.

Methods

A retrospective, descriptive analysis of the radiologic and laboratory characteristics of pleural fluid from patients with HPS was performed. Medical charts and x-ray films of all 23 patients treated at the University of New Mexico Hospital were reviewed. All cases were confirmed by strip immunoassay (RIA) or Western blot analysis of serum antibody to the glycoprotein-1 protein of the SNV (viral outer membrane) envelope.6 An estimation of pleural fluid volume was made from standard portable anteroposterior chest radiographs and, when available, lateral decubitus chest radiographs. The quantity was defined as follows: minimal when silhouetting of the costophrenic angle only was present; mild when silhouetting of the costophrenic angle and fluid in the horizontal fissure occurred; moderate when more than 1 cm of fluid was shown on the anteroposterior film (from the costophrenic angle) or more than 2 cm layering (at greatest depth) on lateral decubitus was present; large when tube thoracostomy was required. Since this is a retrospective analysis, there was no standardization of patient positioning at the time the radiograph was obtained (supine and semierrict films) as well as the timing of subsequent chest x-ray films.

Diagnostic thoracentesis was performed in 4 of the 23 patients, and fluid was evaluated for total protein value, lactate dehydrogenase (LDH), and glucose content, WBC and differential cell counts, pH value, Gram stain, and microbiologic culture. Simultaneous serum measurements were obtained. Effusions were categorized as transudates or exudates according to Light’s criteria.7 Briefly, an exudate has a pleural fluid to serum protein ratio of more than 0.5; pleural fluid to serum LDH value ratio of more than 0.6; or pleural fluid LDH level of more than two thirds the upper normal serum limit. If these criteria were not met, the effusion was classified as a transudate.

Results

Chest radiographs from the first 48 h after admission were reviewed. Twenty-one of 23 patients had radiographs which demonstrated the presence of pleural fluid on admission and the development of an effusion over the next 24 h in an additional patient. One patient did not have identifiable fluid at any time during the hospital course, 2 demonstrated minimal fluid, 12 showed mild amounts, and 8 had moderate amounts. Fluid in the minor fissure was a characteristic noted in 12 of 23 (52.2%) patients. Effusions of similar size were present bilaterally in most patients. Maximum size of effusion was achieved over the subsequent 24 to 48 h. Time of resolution of effusion was variable; most effusions diminished to a minimal size by 96 h. Three patients had a large effusion which resolved after placement of bilateral chest tubes in 1 and after 10 and 14 days, respectively, in the other two. Uncertainty

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Manuscript received June 10, 1996; revision accepted March 2, 1997.

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about the time course of resolution is due to the fact that 7 of the 23 patients died within the first 24 h of observation. Neither patient with a minimal effusion died; 5 of 12 (41.7%) with mild effusions died and 3 of 8 (37.5%) with moderate effusions died. A large effusion and two moderate-sized effusions were documented in the three patients who required extracorporeal membrane oxygenation (ECMO) for salvage treatment of refractory cardiogenic shock. Pleural fluid quantity did not impair respiratory dynamics except for one patient (patient B) who required insertion of bilateral chest tubes to facilitate weaning from mechanical ventilation.

A diagnostic thoracentesis was performed on 4 patients (Table 1). One patient (C) had bilateral thoracentesis on 2 separate occasions. Patients B and C had thoracentesis after successful ECMO for cardiogenic shock and both had documented return of normal cardiac function prior to termination of ECMO. Pleural fluid LDH level ranged from 357 to 1,554 IU/L, with a pleural fluid LDH to serum LDH ratio of 0.29 to 0.52, and total protein value ranged from 1.9 to 3.7 g/dL, with a pleural fluid to serum protein ratio of 0.35 to 0.61. The pleural fluid met criteria for an exudate in 2 samples on the basis of a pleural fluid to serum protein ratio of more than 0.5, and in 4 on the basis of a pleural fluid LDH level greater than two thirds the upper normal serum limit (normal range, 300 to 600 IU/L). One of these 4 subjects, patient A, had a value just over two thirds the upper limit at 403 IU/L. Pleural fluid to serum LDH ratio was below 0.6 in all samples. The initial thoracentesis on day 7, for patient C, narrowly met criteria for an exudate on the basis of a protein ratio and LDH level, while on day 12 the only criterion for exudate was the LDH level. The pH value ranged from 7.39 to 7.51. Total nucleated cells ranged from 70 to 181/mm³, predominately lymphocytes and monocytes. All microbiologic stains and cultures were negative for organisms. Pleural fluid glucose results were similar to serum values. Pleural fluid to serum glucose ratio ranged from 0.90 to 1.14.

**DISCUSSION**

HPS, the consequence of SNV infection, is an acute and frequently fatal respiratory disease. It results in various degrees of cardiopulmonary dysfunction, ranging from fulminant shock and rapid death to mild hypoxemia with stable hemodynamics. Shock induced by SNV infection is atypical for sepsis in that systemic vascular resistance is high and cardiac output is generally depressed and consistent with cardiogenic shock or hypovolemic shock. A profound capillary leak occurs, most notably in the lung. This is evidenced by the presence of noncardiogenic pulmonary edema, as defined by the tracheal aspirate fluid total protein, albumin, and LDH values which are nearly identical to serum values. Pleural effusions could be caused by the cardiac dysfunction, or alternatively may be due to the profound vascular leak.

In previous reports, the incidence of pleural effusions in HPS ranges from 23.5% (4 of 17 patients) to 78.6% (11 of 14 patients). The rate of 23.5% may perhaps be an underestimate of the prevalence since effusion was not specifically looked for by the Center for Disease Control and Prevention chart review while this study specifically sought to document their occurrence by reviewing the radiographs. The series reported herein includes 14 of the

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**Table 1—Pleural Fluid Characteristics of Four Patients With Hantavirus Pulmonary Syndrome**

<table>
<thead>
<tr>
<th>Timing of Sample</th>
<th>Total Protein, g/dL</th>
<th>Total Protein Ratio</th>
<th>LDH, IU/L</th>
<th>LDH Ratio</th>
<th>Glucose, mg/dL</th>
<th>pH</th>
<th>TNC/ mm³</th>
<th>PMN, %</th>
<th>Lymphocytes, %</th>
<th>Monocytes, %</th>
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<tbody>
<tr>
<td>Patient A</td>
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<tr>
<td>Day 1 Pleural</td>
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<td>0.46</td>
<td>403</td>
<td>0.31</td>
<td>121</td>
<td>7.51</td>
<td>70</td>
<td>1</td>
<td>16</td>
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<tr>
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<td>1302</td>
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<tr>
<td>Day 7 Pleural</td>
<td>3.7</td>
<td>0.61</td>
<td>1554</td>
<td>0.52</td>
<td>228</td>
<td>7.42</td>
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<td>25</td>
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<td>Day 12 Pleural</td>
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<td>0.35</td>
<td>717</td>
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<tr>
<td>Day 7 Pleural</td>
<td>2.2</td>
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<td>447</td>
<td>0.29</td>
<td>97</td>
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<td>0.36</td>
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*Abbreviations: TNC=total nucleated cells; PMN=polymorphonuclear leukocytes.*
patients from the study which resulted in an estimate of 78.6% prevalence. All radiographs were reviewed from patients treated at University of New Mexico Health Sciences Center and found evidence of pleural fluid, even if of minimal amount, in 22 of 23 (95.6%) patients during the course of their illness. In an autopsy review of HPS, thus representing the sickest of patients, all subjects had large bilateral serous pleural effusions ranging between a total of 210 to 8,420 mL. Histologically, all lungs had varying amounts of intraalveolar and septal edema, and all but one had slight to moderate interstitial infiltrates of mononuclear cells. The respiratory epithelia were intact, capillary endothelial cells were enlarged without evidence of necrosis, and no evidence of vasculitis or thrombosis was detected.

The pleural fluid characteristics have not been previously described but were thought to be exudative on the basis of capillary leak.7 In this communication, samples A and D were obtained within 1 day of admission. Sample D clearly was a transudate, while sample A had borderline criteria for an exudate, with an absolute LDH level of 403 IU/L (exudate criteria, two thirds the upper serum limit, 400 IU/L) and is classified a transudate. The presence of a transudate in these two samples could be explained by volume resuscitation and depressed cardiac function. A pulmonary artery catheter was placed in 1 of these subjects (patient D) which revealed a nadir cardiac index of 3.8 L/min/m². Hemodynamic data from other patients have documented very low cardiac output during the acute phase of HPS.8 With recovery of acute cardiopulmonary dysfunction and diuresis, the effusion may be minimal to characteristics of an exudate.9,10 Two patients (B and C) had profound cardiopulmonary dysfunction with a predicted mortality of 100% (lactate level, greater than 4 mmol/L),4 yet they survived because ECMO was instituted. Sample B, obtained 7 days after admission and successful treatment with ECMO, was exudative, with pleural fluid protein to serum protein ratio greater than 0.5. The initial thoracentesis done on day 7 for patient C narrowly met criteria for an exudate by the protein ratio and LDH level while on day 12 the only criterion for exudate was LDH.

Pleural fluid quantity did not appear to impair respiratory dynamics except for patient B who required insertion of bilateral chest tubes to facilitate weaning from mechanical ventilation.

In conclusion, the vast majority of patients with HPS have evidence of pleural effusion on chest radiographs. The pleural fluid characteristics appear to be transudative during the initial phase of the illness, coincident with the period of maximal cardiopulmonary dysfunction. As cardiac function normalizes during recovery, the pleural fluid characteristics may change to those of an exudate but may remain transudative. It is important to note that ECMO therapy could have influenced the pleural fluid characteristics and could have contributed to the transformation of the transudate into an exudate. On a cautionary note, it is possible that the small number of patient samples obtained may not reflect the true nature of the effusions in HPS, and clearly, as new cases occur, acquisition of more pleural fluid samples will be important to describe better the pleural fluid characteristic.

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Bronchoscopic Balloon Dilatation in the Combined Management of Postintubation Stenosis of the Trachea in Adults*

Marc Noppen, MD, PhD, FCCP; Marc Schlessor, MD; Marc Meyson, MD; Jan D’Haese, MD; Rudi Peche, MD; and Walter Vincken, MD, PhD, FCCP

Bronchoscopic balloon dilatation (BBD) using angioplasty balloon catheters has been employed successfully in the treatment of tracheobronchial stenoses in children and has worked with variable success in adults with bronchial stenosis. In adults with tracheal stenosis, BBD only has been reported anecdotally. In this study, experience with BBD using a valvuloplasty balloon catheter in the combined treatment (with Nd-YAG laser photoablation and stenting) of severe benign postintubation tracheal stenoses in

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