A Case of Legionnaires’ Disease with Extensive Concurrent Deep Vein Thrombosis

YASEEN S. SAMMAN, MOHAMED A. ABDELAAL, SIRAJ O. WALI, ABDULLAH H. ALMALKI and MUNTASIR M. ABDELAALZ

From the Department of Medicine, King Khalid National Guard Hospital, Jeddah, Saudi Arabia

INTRODUCTION

Legionella was first identified as the aetiological agent of the 1976 epidemic of acute respiratory disease that occurred in Philadelphia at the National Convention of American Legion (1). Legionella is a genus of fastidious flagellated aerobic Gram-negative coccobacilli which includes at least 43 distinct species and 63 serogroups. Human infection with serogroups 1, 4 and 6 accounts for 80–90% of cases of pneumonia due to Legionella pneumophila (2). Among patients with nosocomial pneumonia, the reported incidence of Legionella infection has varied from 1% to 40% (3). Worldwide, legionellosis accounts for 2–15% of all cases of community-acquired pneumonia (CAP) severe enough to require hospitalization (4). Legionnaires’ disease is a severe form of legionellosis with a wide spectrum of extrapulmonary manifestations such as involvement of the gastrointestinal tract, kidneys, central nervous system, liver, spleen, myocardium, bone marrow and lymph nodes (5, 6). Legionnaires’ disease is associated with a significant mortality rate of about 20% (6). Delay in administration of appropriate therapy has been associated with increased mortality (7).

Although a case of Legionnaires’ disease associated with deep venous thrombosis (DVT) was reported in 1980 (8), extensive MEDLINE search showed no further report of such an association. We describe here a case of Legionnaires’ disease presenting with concurrent extensive right upper limb DVT with no identifiable hypercoagulable state, raising the possibility of association between legionellosis and venous thrombosis.

CASE REPORT

A 37-y-old male presented with community-acquired pneumonia and extensive upper limb deep vein thrombosis. The diagnosis of Legionella pneumonia was made based on a positive direct immunofluorescence of the bronchial wash. An extensive investigation for hypercoagulable states was negative. The possible association between Legionella infection and deep vein thrombosis is highlighted.

Y. S. Samman, Respiratory Section, Department of Medicine, King Khalid National Guard Hospital, PO Box 9515, Jeddah 21423, Saudi Arabia (Tel. +966 2 624 0000 extn 137213, fax. +966 3 624 7234 or 624 0000 extn 1573, e-mail. sammanys@ngha.med.sa)
Two weeks after discontinuation of warfarin therapy, PT, APTT, TT and fibrinogen level and antithrombin III and protein C activity were all within reference range. Total protein S, measured by polyclonal ELISA (9) and free protein S, measured directly in plasma by ELISA using 2 monoclonal antibodies specific for free protein S (10), were both normal. Levels of anticardiolipin antibodies (IgG and IgM), as measured by ELISA technique, were within reference range. Plasminogen activity using amidolysis of chromogenic substrate and plasminogen inhibitor activity, by 2-stage indirect enzymatic assay, were normal. Reverse hybridization assay for combined molecular genetic analysis of point mutations 1691 A in factor V and 20 210 in factor II using thrombotype test (F Hoffman-La Roche AG, CH-4002 Basel, Switzerland) according to the manufacturer's instructions was negative. Total homocysteine concentration was 15 μmol/l (reference range 7–17), when measured in citrated plasma by automated high pressure liquid chromatography on fasting blood specimen collected into EDTA tube and promptly separated and stored frozen at −80°C (11).

**DISCUSSION**

Although some symptoms and signs are typical of legionellosis, none reliably distinguishes it from other forms of CAP (3, 4). The diagnosis of Legionella pneumonia in this patient was based on the result of direct immunofluorescent staining of the bronchial wash.

Identification of Gram-negative coccobacilli in respiratory secretions is an important clue to the diagnosis (12, 13). Several staining techniques have been described for identification of the organism in lung specimens, e.g. Gimenez or Dieterie Silver impregnation techniques and Wolbach modification of the Giemsa Stain (14, 15). The most reliable method of identifying Legionella is by direct immunofluorescent or immunohistochemical staining of respiratory tract secretions or tissue (16, 17). Serological methods using ELISA and microagglutination depend on a 4-fold increase in antibody titre over 4 to 8 weeks for diagnosis.

Legionnaires’ disease shows a propensity for older men with a male to female ratio of 2:3:1 and most cases occur in patients with preexisting diseases, e.g. malignancy, renal failure and immunodeficiency states (18). Our patient was only 37 y old and was previously healthy. The source of infection in our patient remains speculative but probably related to contaminated water or cooling towers.

The spectrum of legionellosis varies from Pontiac fever, which is usually a mild influenza-like illness, to severe fulminating cases of Legionnaires’ disease with frequent occurrence of a variety of extra-pulmonary manifestations (3, 15, 19, 20). Our patient presented with severe CAP, due to Legionella, and developed hypoxaemia, disturbed liver function tests and renal impairment. In addition, he had an extensive DVT in the upper limb. In 1980, Segnemst et al. (8) reported a case of legionellosis that was complicated with DVT. Unlike our patient, DVT occurred in the lower limb 4 weeks after the diagnosis of Legionnaires’ disease and no test was cited in the report to exclude a coexisting thrombophilia (8). In contrast, our patient presented concurrently with Legionella CAP and DVT at an unusual site in the absence of any demonstrable hypercoagulable state, raising the possibility of an association between Legionnaires’ disease and DVT.

Septicaemia frequently results in disturbance of haemostatic mechanisms (21, 22). Endotoxin, a lipopolysaccharide present in the outer membrane of Gram-negative bacteria, plays an important role in the development of the clinical and laboratory manifestations of septicemia (22). Tissue factor, an integral membrane glycoprotein of the subendothelial component of the vessel wall comes into contact with blood and hence activates the coagulation cascade via intrinsic pathway, after there has been damage to the vessel wall by the bacteria. Moreover, vascular endothelial cells and monocytes can both be induced to express tissue factor by interleukin-I and bacterial endotoxin (22). Vasculitis and thrombosis of small vessels of the lungs have been described in several reports of Legionella pneumonia (23, 24). Acquired antithrombin deficiency is commonly found in sepsis (25) and may occur in venous thrombosis associated with sepsis, although not investigated in the acute phase of the present case.

In conclusion, DVT may be an extrapulmonary manifestation associated with Legionnaires’ disease.

**REFERENCES**

Successful Treatment of Pulmonary Mucormycosis in an Allogenic Bone-marrow Transplant Recipient with Combined Medical and Surgical Therapy

JULIETTE PAVIE1, MATTHIEU LAFAURIE1, CLAIRE LACROIX2, ANNE MARIE ZAGDANSKI3, DENIS DEBROSSE3, GÉRARD SOCIÉ4, FRANCIS DEROUIN2, ELIANE GLUCKMAN4 and JEAN MICHEL MOLINA1

From the 1Service des Maladies Infectieuses et Tropicales, 2Laboratoire de Mycologie et Parasitologie, 3Service de Radiologie, 4Service de Greffe de Moëlle, Hôtel Saint Louis, Assistance Publique-Hôpitaux de Paris, and 5Service de Chirurgie Thoracique, Institut Mutualiste Montsouris, Paris, France

Mucormycosis is a rare, but severe, complication in allogenic bone-marrow recipients with a mortality rate of about 80%. Moreover, its incidence appears to have increased during the past decade. We report a case of pulmonary and nasal mucormycosis in a 55-y-old patient, which occurred 1 y after BMT. Treatment combining 4 months of amphotericin B, early surgical resection of infected tissue and discontinuation of immunosuppressive treatment allowed the cure of this mould infection.

INTRODUCTION

Mucormycosis is an opportunistic infection due to moulds from the order Mucorales, in the Zygomycetes class. It is a rare but severe infection in allogenic bone-marrow recipients. The mortality rate is about 80% (1). Its incidence, in this population, appears to have increased during the past decade with 7 cases reported between 1985 and 1989, 8 between 1990 and 1995, and 14 between 1995 and 1999 in the same institution (2).

Main risk factors associated with the development of mucormycosis after bone-marrow transplantation (BMT) include underlying myelodysplastic syndrome, recipient of an allogenic BMT from an HLA-mismatched or unrelated donor, severe acute graft-vs-host disease, and immunosuppressive treatment including steroids (2, 3). Neutropenia is observed in only half of the cases (2). Infection with Zygomycetes occurs more frequently late (i.e. >90 d) after transplantation.

We report a case of pulmonary mucormycosis in a patient who underwent allogenic BMT 1 y earlier. Outcome was favourable after medico-surgical treatment and discontinuation of immunosuppressive therapy.

CASE REPORT

A 55-y-old male was diagnosed with a low grade non-Hodgkin's lymphoma in March 1994. After 3 relapses treated by chemotherapy and radiotherapy, allogenic stem cell transplantation was performed with an HLA-identical donor after a non-myeloablative conditioning regimen (cyclophosphamide, fludarabine and ATG sera) in November 2000. Seven months later, because of relapse, he received chemotherapy (including cyclophosphamide and etoposide), anti-