Pneumocystis carinii Pneumonia in Acute Lymphatic Leukaemia*

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SUMMARY

A case report of a patient who developed fatal pneumocystis pneumonia while in remission from acute lymphatic leukaemia is presented. Clinical and aetiological aspects of this rare infection are discussed. Attention is drawn to diagnostic pitfalls encountered in leukaemia.

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Pneumocystis carinii is an organism which causes a diffuse pulmonary alveolar infestation in man. The organism was recognized and classified as a protozoan 60 years ago by Chagas and Carini.[1,2] This rare and usually fatal disease occurs in young babies,[3,4] or in individuals whose capacity for resistance to infection has been compromised because of hypogammaglobulinaemia,[5,6] drug therapy[7] or disease of the haematologic or lymphoid system.[8,9]

Only a few cases have been diagnosed antemortem in the United States of America.[6,10] The clinical picture is usually characterized by (*a*) insidious onset of tachypnoea with progression to cyanosis and severe dyspnoea, (*b*) minimal auscultatory findings in the lungs and (*c*) progressive pneumonitis, consisting at first of soft patchy infiltrates with eventual consolidation spreading from the hilum to the periphery. Reported cases of *Pneumocystis carinii* with underlying lymphoreticular disease have almost uniformly ended in death;[8,9] there have been 4 reports in the literature of adults with lymphoreticular disease where the *Pneumocystis carinii* infection responded to pentamidine treatment.[6,11-13]

The following is thought to be the first case of pneumocystis pneumonia reported in the South African literature. In this case the diagnosis was made postmortem, and the *Pneumocystis carinii* demonstrated on histological examination of the lung.

CASE REPORT

A 3-year-old White boy suddenly became ill during the night with acute abdominal pain and a very painful, swollen arm. Within a week he was limping with swollen ankles and knees; at this stage he was admitted to hospital. Examination showed him to be in acute pain, with normal temperature, tonsillar adenopathy and a palpable liver and spleen. His haematological examination showed a haemoglobin value of 12·8 g/100 ml, white blood cell count of 10 000/mm³ with 70% polymorphonuclear cells, 29% lymphocytes and 1% basophils. Platelets were 'adequate', sedimentation rate was 34 mm/hour (Westergren), the Heaf test was normal and the antistreptolysin titre was less than 12 units.

At this stage the patient was treated with antibiotics, corticosteroids and gammaglobulin, to which he seemed to respond, and after some improvement he was discharged. Three weeks later he was readmitted, the hepatosplenomegaly had increased and the haematological examination showed: haemoglobin 9 g/100 ml, white blood cells 3 200/mm³, with 18% polymorphonuclear cells, 75% lymphocytes, 5% monocytes, 1% eosinophils, and 1% basophils. A marrow aspiration from the iliac crest was done and microscopic examination of the smears confirmed the diagnosis of acute lymphatic leukaemia.

At this stage the patient was referred to our clinic. It was then a month since his illness had started. On admission to our clinic we found the following: haemoglobin 7·4 g/100 ml, white blood cells 3 700/mm³ with 8% blasts in the peripheral blood and 90% blasts in the bone marrow. The liver and spleen were enlarged. Blood urea was 31 mg/100 ml, uric acid was 4·8 mg/100 ml, creatinine was 0·7 mg/100 ml, total serum protein was 7·2 g/100 ml, with 3·0 g/100 ml albumin and 4·2 g/100 ml globulin. The gammaglobulin was 1·53 g/100 ml and no abnormal bands were detected on immune-electrophoresis. Bilirubin was less than 0·5%, SGOT was 12 Caboud units, alkaline phosphatase was 8·8 KA units, fasting blood sugar was 96 mg/100 ml, serum amylase was 123 mg/100 ml and fibrinogen was 418 mg/100 ml.

Treatment

Treatment was started with asparaginase 1 000 units/kg daily 5x, vincristine 2 mg/m² thrice weekly and prednisone 120 mg/m² daily 15x. The patient responded rapidly to treatment. His performance status was normal by day 3 of treatment, appetite was normal by day 5, the spleen was no longer palpable by day 8 and the liver no longer palpable by day 15. By day 8 there were only 2% blasts in the peripheral blood, with 20% blasts in the marrow. The blasts in the marrow rapidly decreased to 6% on day 15 to 4% on day 22. On day 8 the serum albumin was 3·5 g/100 ml. On day 15 the albumin was 2·9 g/100 ml and the globulin 1·5 g/100 ml.

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Judged by accepted criteria of clinical and haematological response the patient was considered to be in complete remission. A month after his antileukaemia treatment was started he was allowed to go home. Maintenance treatment was started with oral methotrexate.

The patient returned to our clinic 2 months after the start of treatment for a planned reinduction injection of Daunomycin, vincristine and also oral prednisone. At this stage he was still in complete remission as confirmed by bone marrow and cerebrospinal fluid examination.

Two weeks later he developed insidious symptoms of respiratory infection. He was treated with antibiotics but became progressively worse. A week after onset of the 'pneumonia' he was again sent to our department. On arrival at our clinic he was found to be gravely ill with tachypnoea, cyanosis and hyperpyrexia and signs of cardiac failure. Bone marrow examination and full blood count were within normal limits. He died within 24 hours of admission.

Postmortem Findings

On postmortem examination no sign of leukaemia or leukaemic infiltrate could be found. Both lungs showed consolidation, there was some cardiac dilatation and hypertrophy. On histologic examination *Pneumocystis carinii* was found in the lungs.

DISCUSSION

This case is a typical example of one of the obstacles to complete control over leukaemia, namely infection. *Pneumocystis carinii* is found in rabbits, dogs, goats and other animals. The mode of transmission of this ubiquitous organism is still unproved though it is reasonable to assume that the infected airborne particles are inhaled directly into the lung. Pneumocystis pneumonia occurs almost exclusively in individuals whose capacity for resistance to infection has been compromised because of hypogammaglobulinaemia, drug therapy or lymphoreticular disease. Although most patients die during exacerbation of disease, Nathorst-Windahl *et al.*[14] reported the case of a 4-year-old girl who died of this infection despite remission of the basic disease process. The case reported here was also in complete remission when he developed the fatal pneumocystis pneumonia.

In this patient factors necessary for susceptibility to *Pneumocystis carinii* were present. The quiescent stage of leukaemia tends to diminish its importance as a primary factor in the aetiology of the infection. An immune-deficit due to lymphoreticular disease as well as antileukaemic therapy is suspected to be of primary importance in the aetiology of the pneumonia. This case illustrates the need for further investigation on the effects of cancer chemotherapy on immunologic capacity, it serves further to draw attention to certain diagnostic pitfalls:

(*a*) The patient had been ill for a month, and was treated with antibiotics, gammaglobulin and corticosteroids, before his bone marrow examination revealed that he had leukaemia. The leukaemia had been completely controlled for more than 2 months when chest symptoms became prominent.

(*b*) Diagnosis of the complicating infection is extremely difficult to establish. At present open lung biopsy is the only way to prove that *Pneumocystis carinii* is the causative organism; this carries a grave risk for the patient with severe alveolar capillary block and possibly defective clotting mechanism.

Each individual with acute leukaemia presents a diagnostic as well as a therapeutic challenge.

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