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Case report

Disseminated infection of *Pneumocystis carinii* in a patient with the acquired immunodeficiency syndrome*

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Summary. This report describes the histopathology of a disseminated *Pneumocystis carinii* infecton in a 24-year-old Japanese male haemophiliac diagnosed as having the acquired immunodeficiency syndrome. He developed respiratory symptoms, and *Pneumocystis carinii* pneumonia was confirmed by transbronchial lung biopsy. On the 70th day of hospitalization the patient died. Autopsy findings revealed *Pneumocystis carinii* not only in the lungs but also in the stomach, jejunum, ileum, colon, mesoappendix, abdominal lymph nodes, diaphragm, and thyroid gland.

Key words: *Pneumocystis carinii* – Dissemination – Extrapulmonary infection

Introduction

According to the Centers for Disease Control (1985), *P. carinii* pneumonia is the most common clinical manifestation in patients with the acquired immunodeficiency syndrome (AIDS), appearing in almost two-thirds of the immunocompromised individuals. *P. carinii* infection is almost always confined to the lungs and extrapulmonary spread rarely has been documented. There are some early reports referring to extrapulmonary infection with this parasite in human (Anderson and Barrie 1960; Awen and Baltzan 1971; Barnett et al. 1969; Burke and Good 1973; Henderson et al. 1974; Hughes et al. 1973; Jarnum et al. 1968; LeGolvan and Heidelberger 1973; Pavlica 1962; Price and Hughes 1974; Rahimi 1974; Rossi et al. 1985; Zandanell 1954). Now, with the recent increase in the number of AIDS patients, extrapulmonary infection or dissemination of *P. carinii* is being reported more frequently (Carter et al. 1987; Coulman et al. 1987; Gagliardi et al. 1987; Gallant et al. 1988; Gherman et al. 1988; Grimes et al. 1987; Heyman and Rasmussen 1987; Kwok et al. 1982; Macher et al. 1987; Pilon et al. 1987; Schinella et al. 1987; Steigman et al. 1987; Unger et al. 1988). This report is an unusual case of widely disseminated *P. carinii* infection and describes the histopathology in detail, especially in small intestine, and lymph nodes.

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Case report

A 24-year-old Japanese male, B-haemophiliac, has received concentrated factor IX since 1978. During the year prior to admission, oral thrush and cough with sputum developed, along with intermittent diarrhoea and the patient was admitted to Kansai Rohsai Hospital on 5 July 1986, with minimal fever and an infiltrate in the left mid-lung field.

Laboratory evaluation on admission showed a WBC 5000/cmm with 89% neutrophils, 3% lymphocytes. Total protein was 4.5 g/dl, albumin 2.6 g/dl, globulin 1.9 g/dl (α_1 7.5%, α_2 17.5%, β 9.5%, γ 7.5%), CRP 1.5+. IgG 487 mg/dl (normal 700–1800), IgA not detectable (normal 110–370), IgM 52 mg/dl (normal 50–200). PaO_2 was 79.7 mmHg.

The serum contained antibodies to human immunodeficiency virus (by ELISA and IFA). Other anti-viral antibodies (CMV, HSV, HZV, EBV, ATLV). were negative except HBsAb (HBsAg negative). The T-helper/T-suppressor cell ratio (OKT4:6. 1%/OKT8:19.0%) was 0.32. *Candida* was detected from sputa but *P. carinii* was not found. The stool was strongly guaiac-positive and no pathogens were detected from the stool culture. Soon after admission, chest X-ray revealed bilateral opacification. A transbronchial lung biopsy (TBLB) was performed and *P. carinii* was detected by Grocott's methenamine silver stain. Although the patient was immediately treated with

trimethoprim-sulfamethoxazole, after slight improvement of his condition he died from pneumothorax from the left lung 70 days after admission. An autopsy was performed.

Results

P. carinii was found in 11 organs: lung, stomach, jejunum, ileum, colon, mesoappendix, diaphragm, thyroid gland, and mesenteric, coeliac, and peripancreatic lymph nodes, but not in the liver, spleen, or bone marrow. No other pathogenic bacteria, fungi, or parasites were found in the organs examined.

The lungs (left lobe 860 gm, right lobe 800 gm) were remarkably consolidated. Microscopically, alveolar septa were markedly thickened due to heavy fibroblastic proliferation and an intense infiltration of vacuolated macrophages, but there was only a mild infiltrate of lymphocytes with very few, if any, plasma cells. Foci of *P. carinii*, which were enclosed within scars, were observed sporadically (Fig. 1). The parasite was not found in alveolar septa, bronchioles, or the lumen and wall of blood vessels. No *P. carinii* were found in the hilar lymph nodes.

In the small intestine although there were no abnormalities macroscopically in the jejenum, a yellow necrotic lesion, about 10 cm in width and extending for the full circumference of the bowel, was observed on the serosal side of the ileal wall, about 25 cm from the ileocecal valve. It was cheesy and resembled a caseous necrotic lesion. The corresponding mucosal surface was normal. Microscopically, a small eosinophilic *P. carinii* lesion in the jejunal propria mucosa was found, which extended deep into the mucosa, but the mucosal surface around the lesion was normal (Fig. 2). No remarkable changes were observed in the mucosa of the ileum. In the muscle layers of the propria and the subserosa of the jejunum and ileum, there was widespread destruction caused by infiltrative lesions, which were surrounded by foamy histiocytes. The lesions were eosinophilic and acellular with the H & E stain (Fig. 3), and numerous *P. carinii* cysts were found with the GMS stain (Fig. 4).

Lymph nodes: The mesenteric lymph nodes were soft and enlarged up to 4 cm in diameter. When cut, cheesy areas resembling caseous necrotic lesion were seen. Microscopically, there was lymphoid depletion and angiomatous transformation in the paracortex. Eosinophilic material identical to that observed in the intestine was seen in and around massive necrotic lesions with calcification (Fig. 5) and *P. carinii* was confirmed with the GMS stain. Vacuolated macrophages, foreign body giant cells, small numbers of neutrophils, and fibroblastic proliferation were observed around the necrotic foci. *P. carinii* cysts were also seen in some marginal and intermediate sinuses and in the lumen of some afferent lymphatics (Fig. 6). Although coeliac and peripancreatic lymph nodes showed no macroscopic abnormalities, the histopathologic findings were similar to those seen in the mesenteric lymph node.

P. carinii lesions were small and localized and there were no remarkable changes both macroscopically and microscopically in other *P. carinii*-positive organs. The skin was normal. Neither the brain nor the eyes were available for examination.

Discussion

In the present case report, the widespread dissemination of *P. carinii* in the peritoneal viscera, jejunal

Fig. 1. Foci of *P. carinii* enclosed within scar (*arrowheads*). Severe fibrosis and marked interstitial thickening are seen. GMS with H & E, double stain. × 70. *Inset:* High magnification of the focus showing *P. carinii* cysts (*arrows*). GMS stain. × 690

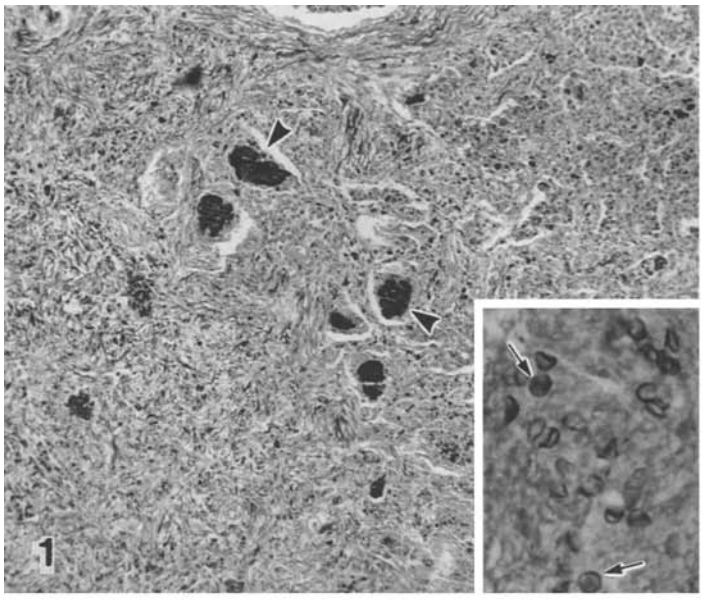
Fig. 2. Eosinophilic material in propria mucosa of the jejenum having the similar appearance as seen in the lung (*arrowhead*). Several foam cells are observed in the material. Note that the mucosal change around the material is minimal. H & E stain. × 160

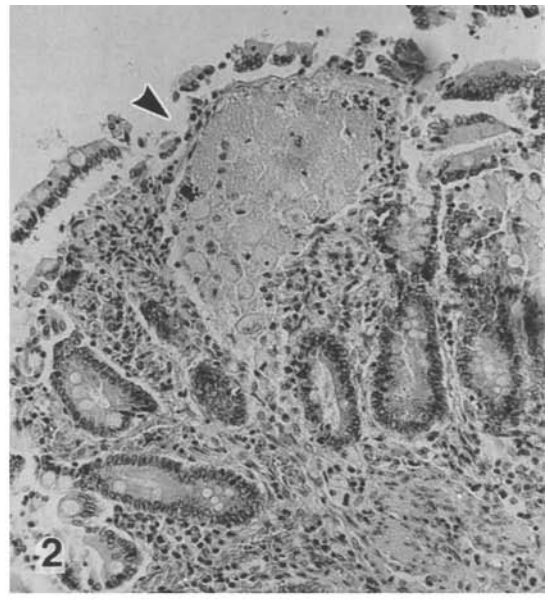
Fig. 3. Longitudinal section of the ileum containing eosinophilic material (*asterisk*) with conspicuous tissue damage. The lesion extends from the muscle layer to the subserosa. Mucosa is on the right. H & E stain. × 60

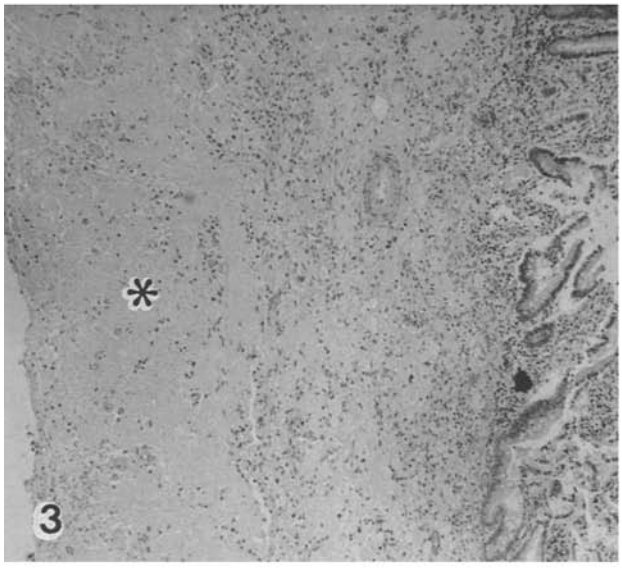
Fig. 4. Severe infiltrative GMS-positive lesions in the muscle layer and subserosa of the ileum (*arrows*). GMS stain. × 60. *Inset:* High magnification of the focus showing *P. carinii* organism. *Arrows* indicate classical *P. carinii* cysts with parentheses-like structure. Mucosa is on the right. GMS stain. × 670

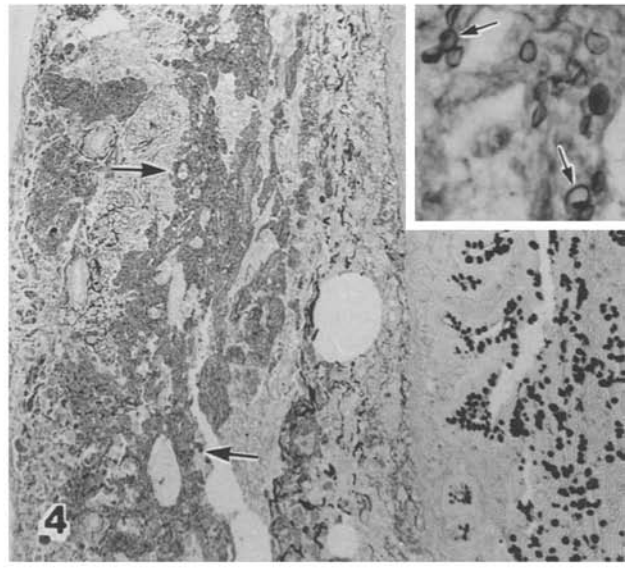
Fig. 5. Massive necrotic lesion (*arrowhead*) with calcification (*arrow*) in the mesentery lymph node with lymphoid depletion. *P. carinii* cysts are seen in and around the lesion when stained with GMS method. Giant cells (at the center) and angiomatous change (on the right) are seen. × 35

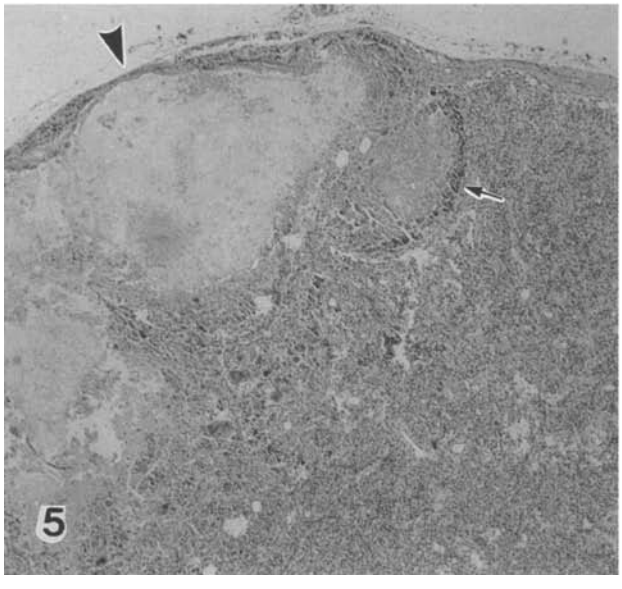
Fig. 6. GMS-positive material containing *P. carinii* cysts (*arrows*) in the lumen of a subcapsular afferent lymphatic. GMS with H & E, double stain. × 440

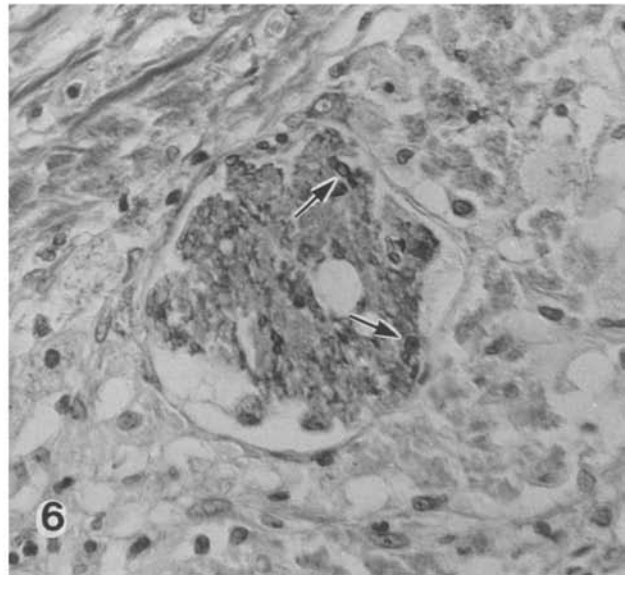












propria mucosa, and thyroid gland indicates haematogenous spread, while the masses of parasites found in the lymph nodes, especially in the afferent lymphatic vessels, suggest lymphatic transport. Almost all previous reports of extrapulmonary foci had concurrent pulmonary infection, as did our patient. It therefore seems reasonable to conclude that the organisms spread from the lungs to other organs via both haematogenous and lymphatic routes as suggested by other investigators (Anderson and Barrie 1960; Awen and Baltzan 1971; Barnett et al. 1969; Coulman et al. 1987; Grimes et al. 1987; Henderson et al. 1974; Heyman and Rasmussen 1987; LeGolvan and Heidelberger 1973; Pilon et al. 1987; Steigman et al. 1987; Unger et al. 1988).

Eosinophilic "honey-comb" material (H & E stain), which is known to consist of masses of *P. carinii* trophozoites, precysts, cysts, bound immunoglobulins and complement (Brzosko et al. 1976; Frenkel 1976), was observed in all the extrapulmonary lesions in the present case. The infiltrative and enlarging lesions seen in the small intestine and lymph nodes suggest that the organisms were proliferating actively in these anaerobic extrapulmonary sites. It is obvious therefore that *P. carinii* is able to survive and proliferate in both aerobic and anaerobic environments and the extrapulmonary environments may not be as unsuitable for the organism as previously supposed. The reason why *P. carinii* usually seems to be limited to alveolar spaces may simply be that it is quite difficult for the supposedly noninvasive organism to migrate from the alveoli, which are the only site for the entry of *P. carinii*. Should an opportunity for dissemination occur, the organism probably has enough potential to run its life cycle in various sites.

The reasons for disseminated *P. carinii* infection remain unknown. One possibility may be that hypogammaglobulinaemia permits the successful migration of parasites from the lung to extrapulmonary sites. In about 40% of the cases of extrapulmonary *P. carinii* infection reported to date, diminished levels of immunoglobulins were detected, as was the case with our patient who was profoundly hypogammaglobulinaemic.

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