The Turkish Journal of Pediatrics 29: 1987

GIANT CELL PNEUMONIA ASSOCIATED WITH HODGKIN'S DISEASE*

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Key words: giant cell pneumonia, Hecht's pneumonia, Hodgkin's disease, immunosuppression, measles

Giant cell pneumonia is an uncommon interstitial pneumonitis and is usually seen as a fatal complication of measles in patients with disturbed immunological function. Primary immune deficiencies, various reticuloendothelial system disorders and use of antimetabolites are the main predisposing factors for occurrence of this type of fatal pneumonia[1-3]. Since measles is still a commonly encountered childhood infection in many parts of the world, and in view of the increased use of immunosuppressives in the treatment of children with cancer, we would like to draw attention to this fatal disorder which occurred in a child with Hodgkin's disease who had been heavily treated with antimetabolites.

Case Report

I.L., a 7-year-old boy with a cervical mass was diagnosed as having mixed cellular type Hodgkin's disease stage IV. His past history was non-contributory, with uneventful polio and smallpox vaccinations but none for measles. Treatment with endoxan, vincristine, prednisolone and procarbazine was initiated with good response. Shortly after completion of the third step of the treatment protocol at home, he was diagnosed as having measles by a local physician. The duration of his rash was six days. One and a half months after the measles, he was hospitalized again with the complaints of fever, cough and dyspnea persisting for a week, and was found to have a fever of 38.5 °C, tachycardia, cyanosis, moderate respiratory distress with no audible rales, left cervical lymphadenopathy of 1 x 2 cm and slight hepatomegaly.

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Laboratory investigations revealed the following: Hemoglobin 10.6 g/dl; white blood cell count 1800/mm^3, with 4% lymphocytes; erythrocyte sedimentation rate 82 mm/hr; carbon dioxide content 25.6 mEq/L; blood electrolytes within normal limits. A chest roentgenogram disclosed a bilateral, rather diffuse reticulogranular appearance (Fig. 1). Fasting gastric fluid did not show acid-fast bacilli.

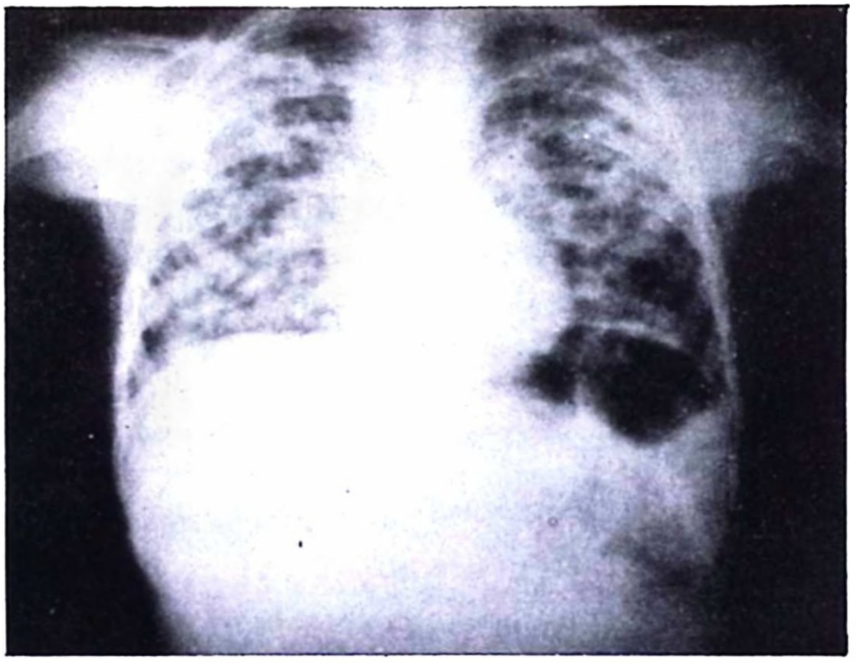

Fig. 1: Pulmonary manifestation of giant cell pneumonia.

Penicillin G and gentamicin were started intravenously. Despite therapy with oxygen and cold vapor, respiratory distress worsened, and confusion and hallucinations developed. A repeat chest roentgenogram at the 50th hour following admission revealed persistence of the same appearance. Additional intravenous vincristine and prednisolone therapy was introduced with no response and the patient expired in severe respiratory failure on the 3rd day of his second admission. Various cultures for fungi and bacteria yielded no growth.

Pathological examination: Lymph nodes showed total necrosis and obliteration of architecture without evidence of residual tumor. No metastasis was found in the kidney or liver. The lungs disclosed a heavy collection of fibrin with hyaline membrane-like formations and several multinucleated giant cells bearing eosinophilic intranuclear and rare cytoplasmic inclusion bodies (Fig. 2). Squamous metaplasia and proliferation of epithelial lining cells (occasionally with clump formation) were also noticed in some of the bronchi and bronchioli.

Direct immunofluorescent study of the lung with fluorescein-conjugated antiserum to measles antigen revealed staining of inclusions in the nuclei and cytoplasm of the giant cells.

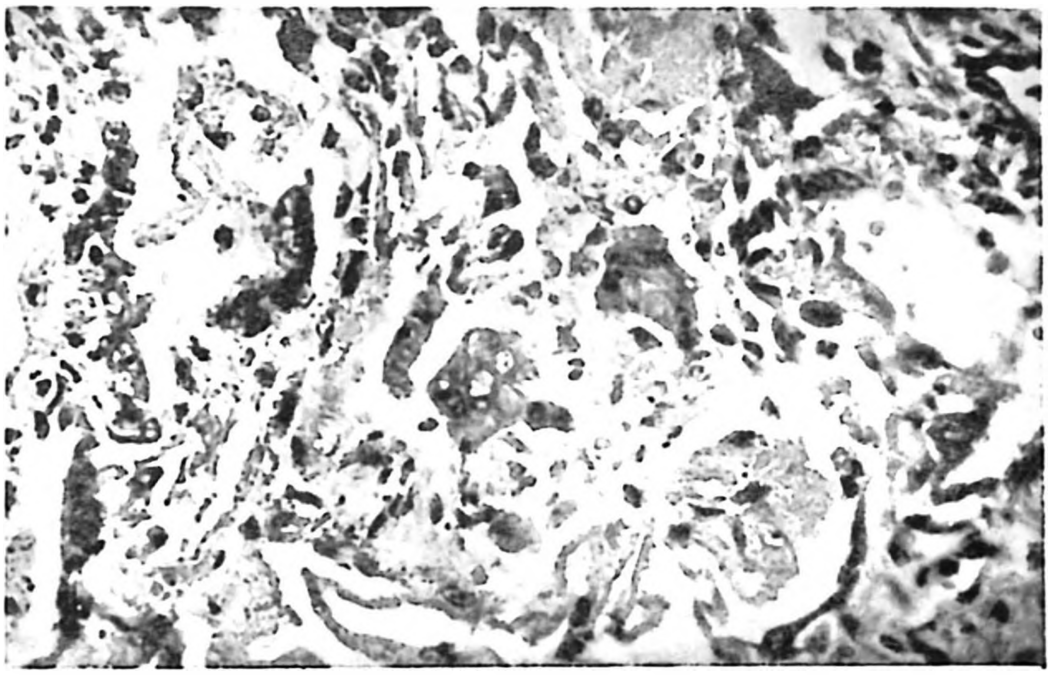

Fig. 2. Section of the lung showing multinucleated giant cells, bearing demonstrable intranuclear inclusions, clumps of fibrin and hyaline membrane-like formations (HE X 240).

Discussion

During measles viremia in the prodromal phase, the measles specific antibody is produced in patients with normal immunological status, viremia disappears after the rash becomes visible, and viral pneumonia does not occur, or if it does, it is mild. In contrast, immunocompromised children usually cannot attain adequate antibody levels. In general, there is no rash response and viremia continues, leading to a fatal measles-related disease, known also as Hecht's pneumonia[2,5,7].

The widespread therapeutic use of steroids and cytotoxic agents in various diseases is a predisposing factor for its occurrence[3,6,7]. If the exanthema is regarded as an index of cellular immunity, absence or short duration of the rash may be interpreted as an indication of the presence of immunosuppression. In the case presented, normal duration of the measles rash suggests that continued antineoplastic treatment may nevertheless have led to sufficient immunosuppression for the development of giant cell pneumonia. History of uncomplicated smallpox and oral poliomyelitis immunizations may indicate that the patient was at least adequately immunocompetent for some viruses prior to the onset of Hodgkin's disease. His primary disease and heavy antineoplastic treatment are the two contributory factors for the disturbed immunological functional state. Since he was in remission at the time of appearance of measles pneumonia, the immunosuppressive treatment administered most likely played a major role in its development.

Varying time intervals between the symptoms of measles and measles pneumonia are reported in some cases being as long as six months to one year[6]. Thus it is difficult to say whether this represents a continuing or an exogenous infection. The rather brief one and a half month interval in our case suggests the former. Hecht's pneumonia is not usually thought of and/or diagnosed while the patient is alive. History of exposure to measles in immunodepressed patients with respiratory distress must be searched for. Radiographically it is possible to find miliary and sometimes more massive condensates scattered in the lung.

Measles pneumonia is characterized by multinucleated giant cells with intranuclear and cytoplasmic inclusion bodies. Such cells in the peripheral respiratory tract in man appear to occur exclusively with measles virus and the inclusions contain specific virus antigen[4]. Histological diagnosis is based on the finding of these characteristic giant cells. Observation of giant cells by light microscopy led to demonstration of measles antigen in the lung; thus diagnosis was possible only after death in our case.

Results of treatment of this disease have been disappointing. Even though a recent study points out its inefficiency[6], there are reports of beneficial effects of high dose gamma globulin injections in inhibiting the viremia and thereby hindering the dissemination of measles[3]. Immunization of healthy children in the general pediatric population is mandatory to protect them from measles. In the case of unimmunized and immunosuppressed patients at risk, a prophylactic injection of high-dose gamma globulin may be effective at the first signs of a measles epidemic in the area or at the time of exposure.

Summary

Infectious complications occur with increasing frequency in patients with malignant diseases, since more effective immunosuppressive treatment is widely used. Even though giant cell pneumonia is rarely encountered among these complications of viral origin, it is worth considering this disease in the differential diagnosis of the complications occurring in the management of patients with cancer.

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