Giant cell pneumonia in a leukemic child in remission
A Case Report

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Giant cell pneumonia is a rare and uncommon type of lung infection developing as a complication of measles, especially in immunocompromised patients, whether their immune systems are affected primarily or whether they have acquired immune defects. As well as being uncommon, it is also atypical because of absence of the characteristic rash and of absent or low antibody titers against measles in most of the cases. It is known that cellular immunity is more important than humoral immunity in the host response to measles, so hypogammaglobulinemic patients with normal cellular immunity usually recover uneventfully from measles and also have the characteristic rash. We report a case with giant cell pneumonia that was confirmed by postmortem histopathological examination. We especially want to point out that even in the absence of rash, with the clinical and radiological features of pneumonia, measles should be considered in a patient, whether in remission or not, receiving immunosuppressive treatment.

Key words: measles, pneumonia, leukemia, giant cell pneumonia, childhood.

Giant cell pneumonia is a rare and uncommon type of lung infection developing as a complication of measles, especially in immunocompromised patients, whether their immune systems are affected primarily or whether they have acquired immune defects[1-5]. As well as being uncommon, it is also atypical because of the absence of the characteristic rash and of absent or low antibody titers against measles in most of the cases[2,3,6]. It is known that cellular immunity is more important than humoral immunity in the host response to measles, so hypogammaglobulinemic patients with normal cellular immunity usually recover uneventfully from measles and also have the characteristic rash[2,3]. As a consequence of the increasing number of cellular immune deficiencies resulting from an increase in the number of children with malignancy that use chemotherapeutic drugs which prolong survival of the primary and secondary immunodeficiencies, giant cell pneumonia may become more frequent.

Here we report a case with giant cell pneumonia that was confirmed by postmortem histopathological examination. We especially want to point out that even in the absence of rash, with the clinical and radiological features of pneumonia, measles should be considered in a patient, whether in remission or not, receiving immunosuppressive treatment[4-9].

Case Report

A 10-year-old girl diagnosed as having acute lymphoblastic leukemia was in remission four years later following steroid, vincristine, daunomycin, asparaginase, etoposide, and cytarabine. Remission was maintained with methotrexate and 6-mercaptopurine together with steroid, vincristine, asparaginase and cytarabine. At the 95th week of the maintenance therapy she was seen in our infectious disease outpatient clinic with the complaints of fever, cough, malaise and dyspnea persisting for almost a week. As well as these complaints there was also an erythematous maculopapular rash, especially at the proximal parts of the arms and legs, together with a slight conjunctival hyperemia, and the body temperature was subfebrile. There was no Koplik spot, and immunization history for measles was uncertain. The mother stated that her daughter had not experienced a similar exanthematous disease

before. There was also partial alopecia, facial desquamation, postnasal and right external auditory purulent drainage, bilateral multiple micro-lymphadenopathies at cervical chain and widespread rales together with rare ronchi at both lungs, especially at basal areas. Other physical findings were unremarkable. Patient was hospitalized for parenteral therapy because of pneumonia and also because of suspected measles infection.

Laboratory studies revealed hemoglobin 11.3 g/dl, white blood cell count 12,800/mm^3 with 2% lymphocytes and 40% toxic granulation, thrombocyte count 188,000/mm^3, and erythrocyte sedimentation rate 120 mm/hr with normal renal and liver functions. Blood gas measurement included pCO_2 as 25.7 mmHg. At chest roentgenogram there was bilateral paracardiac infiltrates together with bilateral minimal pleural effusion (Fig. 1). Cultures were negative for any microbial agent.

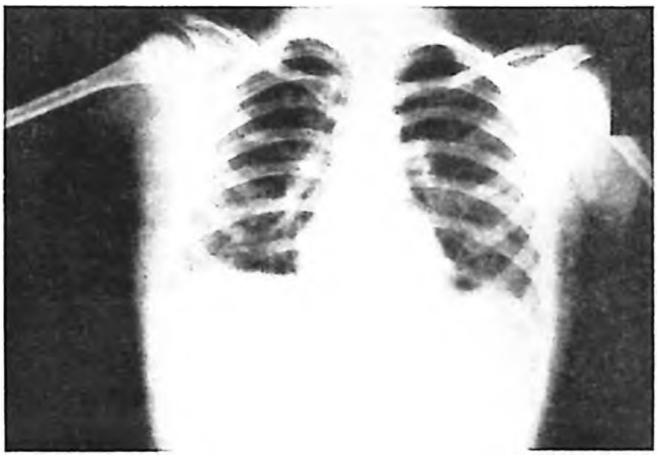

Fig. 1. Chest roentgenogram showing bilateral paracardiac infiltrates together with bilateral minimal pleural effusion on the first hospital day.

Despite initiation of therapy with sulbactam-ampicillin, because of tachypnea and low oxygen saturation at arterial blood gas studies together with enlargement of infiltrated areas at repeated chest roentgenograms taken the day following admission, therapy was changed to ciprofloxacin, vancomycin and amikacin. At the same time, despite negative fungal cultures, due to sudden worsening of patient's condition, amphotericin B was added to the therapy together with TMP-SMX against P. carinii pneumonia. A single high-dose vitamin A was given orally because of rash mostly resembling that seen in measles. On 3rd day of hospitalization her condition worsened further and she developed respiratory distress together with hypotension and tachycardia. It was learned that the antibodies against measles were negative. At chest X-ray there were fine but diffuse micronodular densities (Fig. 2). Arterial blood gas studies showed deep hypercarbia. Patient was intubated and mechanical ventilation was instituted. Intravenous fluids were then given according to central venous pressure measurements with positive inotropic agents. A high-dose steroid was also given because of the possibility of methotrexate pneumonia and also because of the possibility of infiltration by primary malignancy. But progressive worsening of respiratory insufficiency resulted in bradycardia and cardiac arrest and the patient died on the 4th day of hospitalization despite excessive effort. An autopsy was performed.

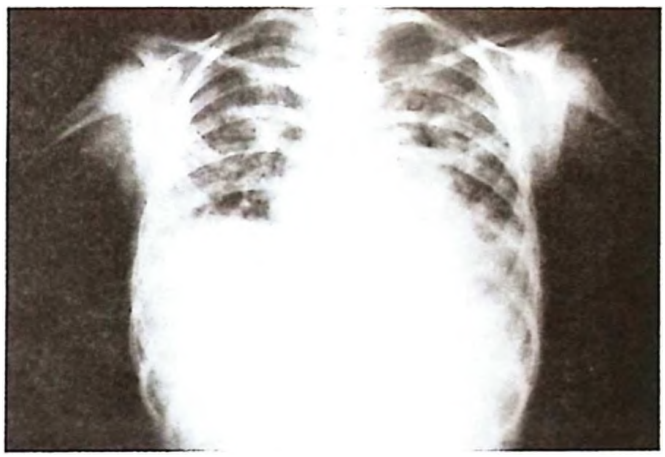

Fig. 2. Chest roentgenogram showing fine but diffuse micronodular densities on the third hospital day.

Postmortem Findigs: Postmortem studies were limited to the lungs, heart, thymus and incision materials of liver and kidney. Macroscopically, lungs were heavily consolidated and showed patchy hemorrhagic areas. Microscopic examination revealed a diffuse interstitial pneumonitis with giant cells and some areas of intraalveolar hemorrhage (Fig. 3). Numerous multinucleated giant cells were present and most of these giant cells demonstrated eosinophilic intranuclear and cytoplasmic inclusions typical of classic measles pneumonia. Bronchial and bronchiolar epithelial proliferation and squamous metaplasia were also seen. Hyaline membranes and alveolar hemorrhage were prominant in some areas. Thymus and lymph nodes showed lymphocyte depletion and atrophy. Congestion and fatty degeneration were noted in the liver. Microscopy of kidney revealed small areas of

glomerular and interstitial fibrosis, probably due to a previous pyelonephritis. No evidence of leukemic infiltration was present in any of the examined organs.

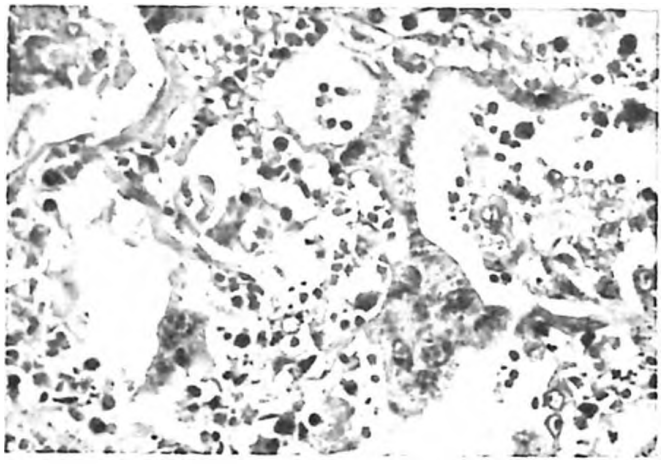

Fig. 3. Diffuse interstitial pneumonitis with giant cells (H & E X 132).

Discussion

As mentioned previously, immunosuppressed patients cannot generate specific antibodies against measles and they are at high risk of developing measles giant cell pneumonia as a result of uncontrolled multiplication of measles virus in the respiratory tract[1,9]. This is one of the characteristic properties of giant cell pneumonia. The others are the persistence of virus without rash, no rise in antibody titer, having a hematologic malignancy (especially leukemia) and interstitial pneumonia with giant cells[9,10]. All these properties thus describe an unusual infection in a compromised host, and in some report an association is made between giant cell pneumonia and leukemia[5,9]. If the rash is regarded as a good predictor of cellular immunity, absence or short duration of the rash may be interpreted as a sign of immunosuppression[4]. Patient's primary disease and the chemotherapeutic treatment are two main factors for the immunocompromised state in leukemia. In children whose immune systems are working well, the measles infection has a time-limited course, but in immunocompromised patients, especially those with cellular immune defects, because of the long-standing viremia, secondary infections of measles could frequently be seen. Due to our patient's being in remission at the time of giant cell pneumonia, the chemotherapeutic treatment most likely had a major role in its development[4,6].

It was proposed that giant cell pneumonia is a reinfection of primary measles after an asymptomatic period, but the variability of that period between measles infection and giant cell pneumonia is still a question, together with the factors affecting this period[4,5,8]. In patients with short time periods, it may be a continuing primary infection of measles. Here the immune systems of patients gain importance because of their effect on the viremia period of measles; that is if a patient is more compromised, the time period becomes shorter[8,9]. In immunocompromised patients presenting with respiratory insufficiency and unresponsive to nonspecific therapy, measles should always be considered as a causative agent, even without a history of contact with measles, and without characteristic rash and specific antibody rise against measles. The diagnostic gold standard in these paients is "open lung biopsy"[3]. Rapid results could also be obtained by direct immunofluorescent studies of bronchoalveolar lavage specimens or nasopharyngeal secretion[7]. Otherwise, giant cell pneumonia is still going to be a postmortem diagnosis in future in spite of excessive effort to eradicate this infection.

Similar multinucleated giant cells in the lungs could be seen in some other diseases, especially with viral infections, but measles is the only virus producing multinucleated giant cells with both eosinophilic intranuclear and cytoplasmic inclusions[3,10]. Inclusion bodies seen with Respiratory syncytial virus, cytomegalovirus, herpesvirus and some parainfluenza strains are not eosinophilic and giant cells are also usually smaller with a different pattern[3]. Some granulomatous diseases may show multinucleated giant cells but these cells always lack inclusions[10]. The other important disease is methotrexate pneumonia, which should always be included in the differential diagnosis, especially in patients given methotrexate for any reason. It is also characterized by fever, cough, dyspnea and cyanosis together with fine scattered opacities on direct chest x-rays. The most important tool for making the differential diagnosis is a good response to steroids in the case of methotrexate pneumonia[7]. P. carinii pneumonia also presents itself with cough, malaise, slightly increased body temperature, and respiratory distress, the most frequently seen features of giant cell pneumonia, and it should also be included in the differential diagnosis[1,9].

Therapeutic measures for measles infection in compromised patients are still limited. Most often used today is the high-dose intravenous pooled immunoglobulin which, if given in early days of exposure (postexposure prophylaxis), may protect or modify measles infection. Ribavirin and also vitamin A supplementation have been considered to be beneficial in these patients in recent studies[3,4,7]. However, gammaglobulin, which can prevent or modify measles in normal hosts, is not protective in compromised patients[8]. However, there are some reports underlying the beneficial effects of high-dose gammaglobulin, especially for inhibiting viremia and thus inhibiting dissemination of virus[4,5,7].

In summary, one of the most important points to emphasize is that because of the possibility of severe measles infection in immunocompromised patients, it is important to complete the immunization chart of the patient before beginning chemotherapy in newly diagnosed patients. Also, if there is lung infection in such a child, possibilities of giant cell pneumonia should be considered even in a child with a complete immunization chart.

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