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CASE REPORT

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Histiocytosis in a 7 year old boy, a diagnostic dilemma.

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Abstract Histiocytoses are a group of rare disorders which are characterized by the infiltration/ accumulation of histiocytic cells in affected tissues. Their mode of clinical presentation varies greatly and can represent a diagnostic challenge in our environment where there is a paucity of diagnostic facilities. This report is on a 7 year old boy with probable Histiocytosis who initially presented with signs and symptoms suggestive of pulmonary tuberculosis. Difficulties in reaching a conclusive diagnosis of the type of histiocytosis coupled with financial limitations contributed to the eventual demise of this patient.

Key words: Histiocytosis, tuberculosis, diagnostic facilities.

Introduction

Histiocytosis refers to a group of rare disorders which are characterized by the accumulation and infiltration of monocytes, macrophages and dendritic cells in affected tissues.[1] This excludes diseases in which infiltration of these cells occurs in response to a primary pathology. There are three major classes of the disease-Langerhans cell histiocytosis(Histiocytosis X),Malignant Histiocytosis syndrome(T-cell lymphoma) and Non –Langerhans cell histiocytosis(haemophagocytic syndrome).[2] Clinical presentation varies greatly and in our environment where there is paucity of diagnostic facilities, this disease could present a diagnostic challenge.

Case report

The patient A .R .U, was a seven and a half year old boy who presented with a one month history of fever, cough and difficulty in breathing. Cough was non productive, non paroxysmal and worse at night. There was no history of contact with any person with chronic cough and the patient was not a known asthmatic. Difficulty in breathing was noticed at about the same time as the cough, was associated with wheezing, worse at night and also worsened by exertion. Fever was initially low grade, then high grade and intermittent. It had no variation with time of day.

Physical examination at initial presentation revealed a well nourished boy, not pale and afebrile. His respiratory rate was 32cpm with bilateral rhonchi in both hemithoraces. He had a hepatomegaly of 5cm below the right costal margin which was smooth, soft and tender. The initial full blood count result showed a packed cell volume of 28 percent, total white cell count of 14,800/ mm^3 with a neutrophilia of 92 percent and lymphocytes of eight percent. In addition, the presence of neutrophilic toxic granulations was noted. Malaria parasites were present in the blood film. Based on these findings, an initial assessment of malaria and sepsis, to rule out asthma was made and the patient was treated with antimalarials and antibiotics and nebulised with salbutamol together with oral steroids.

Despite the above treatment, the patient continued to deteriorate, was losing weight, remained febrile and dyspnoeic and was observed to have generalized lymphadenopathy. A working diagnosis of disseminated tuberculosis was made and further investigations carried out included a chest x-ray and abdominal ultrasound scan which revealed hilar/hepatic masses and a negative Mantoux reaction. A lymph node biopsy was performed and sent for histology. The tissue sections showed a sinusoidal proliferation (Fig. 1) composed of histiocytes with atypical features and occasional haemophagocytic forms consistent with malignant histiocytosis. Due to lack of facilities for electron microscopy in this environment, ultrastructural findings of Birbeck granules could not be demonstrated but a bone marrow aspirate showed marrow infiltration by histiocytic cells displaying haemophagocytosis.

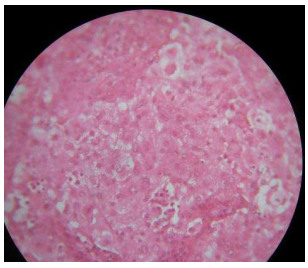

Fig 1: Sheets of histiocytes filling the sinusoids

The patient was commenced on cytotoxic therapy with intravenous cyclophosphamide 1000mg/M^2 day one, vincristine 1.4mg/M^2

day one, doxorubicin 50mg/M^2 day one and oral Prednisolone 15mg 12hrly x 5/7. The course interval was 21 days and a total of five courses were envisaged but drug administration was erratic and patient compliance poor due to financial constraints.

The patient did not show any remarkable clinical improvement and eventually succumbed to the disease six months after presentation.

Discussion

Histiocytoses as a group of disorders are very rare with an incidence of 4-5.4/million population.[3]Males are more commonly affected than females with a male to female ratio of 1.5:1.[3] Our patient was male. The disease is seen in all age groups with peak incidence in childhood seen between ages 1-3years.[3] However, other studies have shown age at diagnosis to range between nine months to 15years [3] with our patient falling into this age bracket. Much effort has gone into the elucidation and classification of these disorders[2] though their pathophysiology remains an enigma. Factors which have been implicated in the aetiology and pathophysiology of these disorders include viral infections[5], cellular and immune dysfunction[6,] genetic factors[7] and neoplastic mechanisms amongst others.

Because of the multisystemic involvement[4] that characterizes them, they can clinically mimic several other more common diseases with tuberculosis being a major differential diagnosis in our environment. Perhaps due to the rarity of this condition, histiocytosis was not among our initial list of differential diagnoses. Pulmonary involvement in histiocytosis occurs in 20-40percent of patients who may manifest with symptoms such as cough, tachypnoea and dyspnoea[8] and a male predominance is observed as was seen in our patient. He presented with a triad of fever, cough and dyspnoea together with generalized lymphadenopathy and in particular, prominent cervical lymphadenopathy.

The chest x-ray did not help in distinguishing this disease condition from tuberculosis as nodular infiltration, pleural effusion and pneumothorax are also known to occur in histiocytosis.[8] We had to rely on histology of the biopsied lymph nodes and the bone marrow biopsy. A major drawback in the management of this patient was our inability to arrive at a definitive conclusion of the type of histiocytosis which requires the use of electron microscopy and immunohistochemistry to do so.[9] Chemotherapy is used for multisystemic disease with local or constitutional symptoms as was seen in this patient. The paucity in our diagnostic facilities coupled with the patient's financial incapacitation was responsible for the delay in onset of appropriate therapy and all these contributed to the untimely demise of this young patient.

Conclusion

We present a case of a 7 year old boy with malignant histiocytosis, which was eventually fatal despite chemotherapeutic intervention. Although histiocytosis is very rare, it is of paramount importance that clinicians suspect this disease as well as other neoplasms in all cases of generalized lymphadenopathy and investigate these patients appropriately.

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