The Turkish Journal of Pediatrics
Volume 22 / Nos. 1-2 / Jan.-April 1980 / pp. 28 - 31

Syndrome Mimicking Histiocytic Medullary Reticulosis Due to Diphenylhydantion Therapy*

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Diphenylhydantoin could be responsible for a variety of hematological, reticuloendothelial and metabolic reactions.[1] Recently we have observed a patient in whom a syndrome mimicking histiocytic medullary reticulosis (HMR) developed during diphenylhydantoin administration.

Case Report

A 10-year-old girl was admitted to the Hacettepe Children's Hospital in March 1980, complaining of pallor, epistaxis and jaundice. Five months prior to admission she was started diphenylhydantoin (2 X 100 mg/day) with the diagnosis of posttraumatic epilepsy. Within ten days she developed erythematous rash on the trunk and abdomen which was diagnosed as a scarlet fever by her family physician. Two days later, she developed jaundice and her urine became dark. The anticonvulsant drug was stopped. The rash had faded within a few days, but jaundice persisted for 1.5 months. Diphenylhydantoin treatment was resumed and within 10 days she developed fever, skin rash, severe epistaxis, jaundice and visual blurring. When she was first seen by us with the above complaints on March 11, she appeared pale, seriously ill, and she had progressive weight loss accompanied by increasing weakness.

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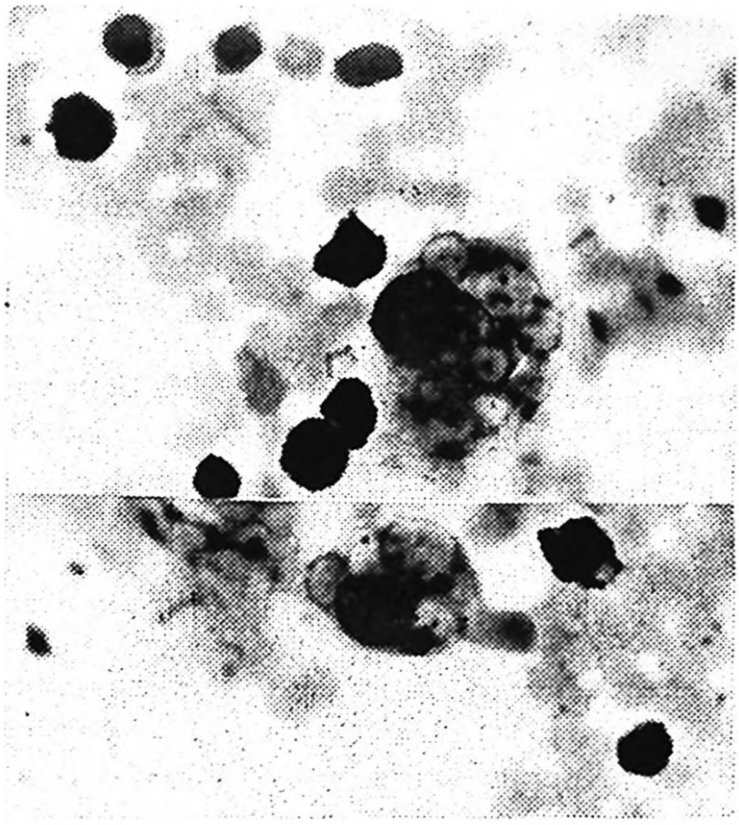

Figure 1
A typical histiocytes with Erythrophagocytosis

On physical examination she had jaundice, bilateral retinal and subconjuctival hemorrhage, and her liver was palpable 5 cm below the costal margin. On the lower extremities there were a desquamative skin lesions. physical findings including neurological examination did not disclose any other abnormality. Blood examination revealed haemoglobin 6.3 g/dl., Hct 19 %, WBC 2.6 X 10^9/L, with 14 % polymorph leucocytes, 86 % lymphocytes, and platelet count was 20 X 10^9/L. Bone marrow aspiration smears disclosed moderate hypocellularity with proponderance of lymphocytic, myelocytic cells and abnormal histiocytes with abundant foamy and vacuolated cytoplasm containing phagocytised erythrocytes, leucocytes and platelets (Figure 1). Plasma cels were also found in increased numbers. Test for urinary bilirubin was positive. Investigations revealed serum bilirubin 8.1 mg/dl., direct bilirubin 5.3 mg/dl., total protein 7.4 g/dl., albumin 4.8 g/dl., SGOT 75 U, SGPT 250 U, alkaline phosphatase 7.6 BU, serum immunoglobulin results were within normal limits. HB_s Ag and anti-HB_s, the direct and indirect Coombs tests were negative. The patient was transfused and the anticonvulsant drug was discontinued. Although the admission diagnosis was HMR her general condition improved dramatically, her low grade fever subsided and jaundice decreased within a short period of time but her pancytopenia persisted. On the 20th day of admission a repeat bone

marrow examination showed hypercellularity with an increased number of erythroid precursors which showed megaloblastic changes; the abnormal phagocytic histiocytes were found decreased. Therapy with oral folic acid (500 mcg/day) resulted in striking improvement in her appetite and general condition within a few days. By the tenth day, reticulocytes reached 5.2 per cent, and WBC and platelet counts reached normal values. Subsequent bone narow aspiration smears were normal and folic acid therapy was discontinued after fourty days. She was in excellent health when the patient was last seen in June 1980 with the exception of visual blurring. Whole blood counts were normal. Since no epileptic attacks were observed during this period of time, anticonvulsant therapy was not resumed.

Discussion

HMR is described as a rapidly fatal syndrome characterized by rapid weight loss, fever, jaundice, hepatosplenomegaly accompanied by progressive pancytopenia and abnormal histiocytes in the reticuloendothelial system associated with erythrocyte, granulocyte and platelet phagocytosis. Recently, a number of cases with HMR have been described due to viral,[2] bacterial,[3] and possibly with parasitic infections[4] Schumacher and Stass reported a case of gastric carcinoma that simulated HMR with erythrocytic, granulocytic and platelet phagocytosis by bone marrow histiocytes.[5] In our patient, the first clinical impression on admission was HMR because of fever, jaundice, hepatomegaly cutaneus lesions and severe pancytopenia with strikingly increased number of phagocytic histiocytes. Although it is well documented that megaloblastic anemia[6] and pancytopenia[7] as rare complication develop due to anticonvulsant therapy; but abnormal phagocytic histiocytes in bone marrow as seen our patient have never been described previously.

As a complication of diphenylhydantoin therapy reticuloendothelial reactions mimicking malignant lymphoma[8] infectious mononucleosis-like syndrome and hepatitis are well documented in the literature.[9, 10] An observation in our patient who had all signs and symptoms of HMR including eryhrocytic, granulocytic, and platelet phagocytosis by bone marrow histiocytes, indicated that complications of diphenylhydantoin therapy should be considered, in the differential diagnosis of HMR among the other etiological factors.

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