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Fatal Infectious Mononucleosis*

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Infectious mononucleosis (I. M.) has been regarded as a benign, self-limited disease and a very rare cause of death. Recorded fatalities have resulted mainly form respiratory paralysis arising from neurologic complications, splenic rupture, secondary infections and, on exceptional occasions, liver failure. The real mortality rate in I. M. is probably less than 1 per 3000 cases.[1]

Most recently four familial fatal I.M. cases were reported, seemingly related to an X-linked inheritance. We would like to present such a case because of its rarity.

Case Report

A. D. (HCH 512646). A 12 year old boy was admitted to Hacettepe Children's Hospital with the complaints of fever, headache, sore throat, prostration and nausea of 20 days duration. He was the fifth product of unrelated parents and his two brothers died with similar complaints at 2.5 and 5 years of age.

On physical examination he looked pale and acutely sick with a mild fever (37.9° C), tachycardia (124/min) and tachypnea (27/min). His cervical, axillary and inguinal lymph nodes were palpable (1x1 cm) and he had subicterus. The liver and spleen were 4 and 2 cm below the respective costal margins. The rest of the physical findings were not contributory.

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Laboratory Findings: Indicated mild anemia (9.0 g/dl) and leukocytosis (13.200 / μ l). Platelets were normal on the peripheral smear; differential showed 11 % granulocytes, 5 % monocytes, 13 % lymphocytes and 71 % Downey type atypical lymphocytes. An urinalysis was normal. SGOT (1010), SGPT (96 U) thymol turbidity (25.2 U), bilirubin (3.4 mg/dl, conjugated 2.5 mg/dl), alkaline phosphatase (17.3 B.U.) PT (18 secs., control 12 secs) were abnormal (Table I) and IgM was elevated (540 mg/dl). Blood sugar (80 mg/dl), ammonia (90 γ/dl), EEG, EKG, L. P., bone marrow and throat culture findings were normal.

TABLE I

SOME IMPORTANT LABORATORY FINDINGS OF THE PATIENT

	1st Day	4th Days	6th Days
Serum Bilirubin (mg/dl total/Conjugated)	3.4/2.8	9./6.2	11.8/7.3
SGOT (Karmen U)	1010	–	400
SGPT (Karmen U)	96	–	100
Thymol (U)	25.2	–	10.2
Alkaline Phosphatase	17.3	–	19.2
Blood Ammonia (γ/dl)	90	–	92

His condition deteriorated fast with a deepening of jaundice and he died within a week. Postmortem examination revealed mononuclear cell infiltration of all the organs without any evidence of fulminant hepatitis. (Permission for the examination of the brain was not obtained).

Discussion

The diagnosis of I. M. in this case was substantiated on clinical features, such as fever, pharyngitis, tonsillitis, lymph node enlargement and splenomegaly; absolute lymphocytosis was characterized by the presence of atypical lymphocytes, and elevated IgM levels. Positive heterophyl agglutination which is specific for the disease, is often found not positive in childhood, as in this case. Current evidence supports the concept that the Epstein-Barr (E-B.) virus is a causative agent[5, 6] of I. M. and antibodies to this virus appear in the serum within 5 to 7 days after the onset of the clinical disease.[4]

The histological changes in I. M. may be impressive but they are not specific for the disease. Nelson and Darragh[8] described three phases of liver involvement in I. M., all detected by percutaneous liver biopsy in 22 patients. Those three stages are portal exudates consisting almost entirely of mononuclear cells, invasion of sinusoids by mononuclear cells and areas of scattered focal necrosis filled with monocuclear cells. Rather massive infiltration of every organ including the liver was impressive in our case. In addition to sinusoidal mononuclear infiltration, without parenchymal cell necrosis, fairly extensive portal exudates of these cells were marked. There have been only 4 cases of I. M. reported in the literature up to 1975 whose death was related to liver failure.[9-12]

Although our pattient died in deepened jaundice, the morphological findings of the liver as described above were not compatible with massive hepatic necrosis. The clinical course and the morphologic findings of the liver of this patient do not resemble the Reye syndrome, hemolytic uremic syndrome or disseminated intravascular coagulation with hepatic necrosis which were reported as complications of infectious mononucleosis.[13,14] Pulmonary infiltration of mononuclear cells was also impressive but we believe that this was the representation of general involvement of the organs differing from Fermaglich's patient with pulmonary involvement of infectious mononucleosis.[15]

Our patient's clinical and morphological findings were very much compatible with fatal infectious mononucleosis syndrome.[2-4] Purtilo suggests that this is a phenotype of an X-linked recessive lymphoproliferative syndrome related to E-B virus.[4] B-lymphocytes in I. M. are infected by the virus, but the typical atypical lymphocytes (Downey cells) in the peripheral blood are T cells,[16] whose function is depressed in the very early period of the disease. More recently, it has been shown that the T cells in peripheral blood of I. M. are mostly helper T cells,[18] which help in the cleaning of infected B cells by the virus genom. It is accepted that in fatal I. M. syndrome there is intrinsic defect of both B and T cells inherited by the X chromosome.[4,9] As a result of these defects the antibody to E-B virus could not be formed, at least adequately, and the proliferation of the infected B cells could not be clared by the host.

The family history of this patients was compatible with the above diagnosis. His two brothers also died with similar illnesses at 2.5 and 5 years of age. Further observations of these patients may help identify the importance of inter-relations between B and T lymphocytes in this rare syndrome.

Summary

A 12 year old boy with clinical and peripheral blood findings of I. M. died within a week of the disease in deepened jaundice without massive hepatic necrosis. Postmortem studies showed infiltration of all the organs by mononuclear cells. It is our belief that he had all the clinical and morphological evidence of fatal I. M. syndrome in which B and T cell's intrinisic defect is suggested.

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