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Granulomatous Hepatitis*

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Hepatic granuloma which is of reticuloendothelial origin, is an inflamation of the liver. It consists of epitheloid cells, plasmocytes, lymphocytes, connective tissue, and sometimes giant cells.[1,2] These granulomas which are caused by infections, such as tuberculosis, sarcoidosis, brusellosis, parasitosis, and drugs,[3,7] are frequently seen in lobules and sometimes in portal tracts.[8,9] Quite often it is not possible to find the etiological factors.[6,8]

Clinically hepatomegaly,[6] jaundice, and fever are frequently seen.[10,12] Although laboratory findings are non-specific, abnormal liver function tests may be shown in some cases.[13]

We would like to present 10 cases of granulomatous hepatitis which were diagnosed from 1968 to 1975 in the Hacettepe Children's Medical Center, since this disease is relatively rare in childhood.

Case Reports

The clinical and laboratory findings of these cases; whose ages range from 7 months to 10 years, are condensed in Table I.

Case 1: M. K. (HCH 465570) was a 8.5 year old boy who was hospitalized with the complaints of fever and abdominal pain. He had had abdominal swelling and fever for 2 years and periumbilical pain for the last 15 days, without hematemesis, melena, jaundice or parasitosis.

Physical Examination: Temperature, 37°C, blood pressure, 110/60 mmHg, weight, 19 kg. His general condition was good. The liver and spleen were 4 cm and 8 cm palpable; respectively. Other systemic findings were not contributory. Normal laboratory studies included IVP, esophagogram, chest X-ray, Ca and P levels, bone marrow aspiration, and anti A

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TABLE I

CLINICAL AND LABORATORY FINDINGS OF GRANULOMATOUS HEPATITIS

Case No.	Age/Sex (year)	Fever duration	Liver cm	Spleen cm	Hb g/dl	WBC mm^3	SGOT KU (Nor. 0-50)	SGPT KU (Nor. 0-40)	Thymol t.U (Nor. 0-5)	CCF
1	8.5 M	2 yr.	4	8	9.37	4400	38	12	9	+
2	10 M	5 yrs.	6	2	10.8	9400	28	19	1	+
3	6 M	3 weeks	8	3	9.37	5200	36	11	1.5	+
4	5 M	2 yrs.	2	5	12	6640	38	22	3	+
5	7/12 F	1 week	8	7	10.16	4200	75	32	12	+
6	7 M	20 days	8	2	12.05	5400	31	41	4.2	+
7	6 M	–	8	2	10.6	6600	30	22	13.2	++
8	1 M	5 months	10	6	10.5	17000	270	390	8.3	+++
9	6 M	–	5	2	7.37	25800	34	20	9	+
10	4.5 M	–	2.5	–	11.73	9400	16	18	3	+

level (his blood group was B). Negative studies included, HbsAg, Latex, FANA; and stool examination. Brucellin agglutination was 1/320 positive. Needle biopsy of the liver showed granulomatous hepatitis. With the diagnosis of brucellosis he was given tetracycline (40 mg/kg) and streptomycine (35 mg/kg) for one month duration. A year later hepatosplenomegaly was still present without fever and the repeated liver biopsy showed no improvement in the granulomas.

Case 2: A. H. (HCH 172644) was a 10 year old Saudi Arabian boy who was hospitalized with the complaints of abdominal pain, swelling, bloody diarrhea, and at times fever, without jaundice or hematemesis.

Physical Examination: Temperature was 38°C, blood pressure 120/80 mmHg; weight 25 Kg. The liver and spleen were palpable 6 cm and 2 cm respectively. Other systemic findings were not contributory. Shistosoma mansoni eggs were seen in the stool. His blood group was A and anti B titration was 1/32 positive. Chest X-ray and esophagogram were normal. The liver biopsy revealed fibrosis and specific granolumas of shistosoma origin. Fuadin was started, 1.75 mg for two days then every other day, 2.5 mg. for 15 days.

Case 3: B. K. (HCH 559790), was a 6 year old boy who was hospitalized for abdominal swelling and fever of 3 weeks duration. Jaundice, hematemesis, melena; and parasitosis were not present.

Physical Examination: Temperature 37°C, blood pressure 90/60 mmHg. The liver was 8 cm and the spleen 3 cm palpable. Normal laboratory studies included chest X-ray, esophagogram, IVP, Ca, and P levels. Brucella group agglutination was negative. The liver biopsy showed chronic granulomatous hepatitis.

Case 4: M. P. (HCH 680738) was a 5 year old boy who was hospitalized for abdominal swelling and intermittent fever of 2 years duration, without jaundice, hematemesis and melena.

Physical Examination: Tempareture 37°C, blood pressure 100/70 mmHg, weight 17 kg. The liver was 2 cm and the spleens 5 cm palpable. Other systemic findings were not contributory. Normal laboratory studies included esophagogram and bone marrow aspiration. An IVP showed a double collecting system. The liver biopsy showed granulomatous hepatitis.

Case 5: S. D. (HCH 522357) was a 7 month old girl who was hospitalized for fever and cough. She had had pneumonia at 1 week of age. She did not have hematemesis or melena.

Physical Examination: Temperature 38°C, blood pressure 100/50 mmHg, and weight was 8 kg. The liver was 8 cm and the spleen 7 cm palpable below the respective costal margins. Other physical findings were not contributory. Normal laboratory studies included esophagogram, IVP, sweat chloride, anti A anti B titration (1/16), and stool examination. The patient died abruptly in 2 days and granulomatous hepatitis was observed in necropsy.

Case 6: (Y. G. 5905779), was a 7 year old boy who was hospitalized with the complaints of abdominal pain and fever. Jaundice, hematemesis and melena were not present.

Physical Examination: Temperature, was 38°C, blood pressure 90/60 mmHg, weight 24 kg. The liver was 8 cm and the spleen 2 cm palpable. Other physical findings were not contributory. Normal laboratory studies included esophagogram, bone marrow, and duodenal aspiration, and brucella group agglutination. IVP revealed hydroureter, most likely related to the infection. There was hymenolepis nana in the stool. The needle biopsy showed granulomas and piperazine citrate was started (75 mg/kg).

Case 7 M. G. (HCH 633025) was a 6 year old boy who was hospitalized with the complaints of abdominal swelling, night sweating and parasitic infection.

Physical Examination: Temperature 37°C, blood pressure 110/70 mmHg, weight 19 kg. The liver was 8 cm and the spleen 2 cm palpable. Other physical findings were not contributory. Normal laboratory studies included chest x-ray, esophagogram, IVP and bone marrow aspiration and Brucella agglutination. The liver biopsy showed granulomas; (Figures 1, 2).

Case 8: T. A. (HCH 178324) was a 1 year old boy who was hospitalized for fever, abdominal swelling, jaundice, dark urine and pale stools of 15 days duration.

Physical Examination: Temperature, 37°C, blood pressure 115/65 mmHg, and weight 9 kg. The scleras were subicteric and there were rales over the lungs. The liver was 10 cm and the spleen 6 cm palpable. Other physical findings were not contributory. Normal laboratory studies included lung x-ray, esophagogram, IVP, sweat chloride and bone marrow aspiration. Negative studies included VDRL, brucella agglutination, and PPD. The liver needle biopsy showed granulomatous hepatitis and infantile cirrhosis.

Figure 1
Noncascation granulomas are seen in the lobules. H. E. X 90

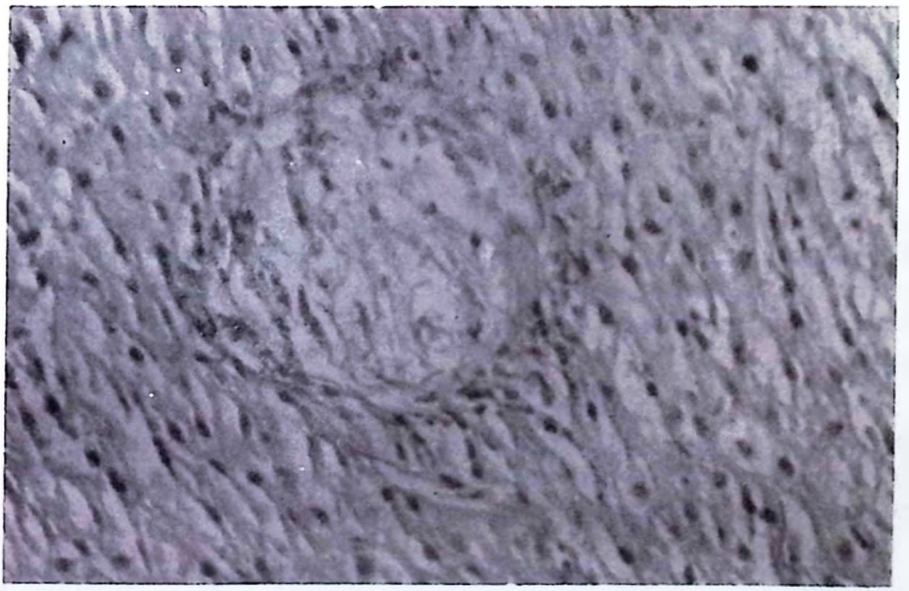

Figure 2
Epitheloid and inflammatory cells are prominently seen in the granuloma. H.E. X 230.

Case 9: B. K. (HCH 483539), was a 6 year old boy who was hospitalized with the complaints of periumblical pain and fever of one week duration. He had had jaundice 35-40 days previously and at that time his urine was dark but stool colour was normal. Hematemesis and melena were not present. Twenty days prior to admission he had passed ascariasis.

Physical Examination: Temperature was 37°C, blood pressure, 90/70 mmHg; and weight 16 kg. The liver was 5 cm and the spleen 2 cm palpable; respectively. The other physical findings and chest X-ray were normal. There was eosinophilia 10 % in the blood smear, and 50 % in the bone marrow aspiration. There was trichuristrichura in the stool. His blood group was A, anti B titration was 1/256 positive. The liver needle hiopsy showed parasitic granulomatous hepatitis. Toxocara infection was diagnosed and hexyl resorchionol was stared, 5 mg/kg.

Case 10: A. I. (HCH 441714) was a 4.5 year old boy who was hospitalized with the complaints of periumblical abdominal pain which passed after defecation. Jaundice and parasitic infection were not present.

Physical Examination: Temperature, was 36.5°C, and weight 19 kg. The liver was 2.5 cm palpable. Other physical findings were normal. There was eosinophilia 60 percent in the blood smear and 50 percent in the bone marrow aspiration. Blood group was A, and anti B titration was 1/256 positive. The chest X-ray was normal. The liver biopsy showed eosinophilia and granuloma. Toxocariasis was diagnosed and Combantrin was started, 10 mg/kg.

Discussion

Tuberculosis, brucellosis, ascariasis, amebiasis, histoplasmosis, Hodgkin's disease, malaria, Q fever, sarcoidosis, shistosomiasis, syphilis, toxocariasis, infectious mononucleosis, cytomegalovirus diseases, and drugs can cause granulomatous hepatitis without clinical and biochemical changes.[1, 9, 13]

Persistent and intermittent fever is an important finding in these patients[10, 11] and jaundice may be observed. Varying degrees of hepatopslenomegaly can be present according to the etiological factors and portal hypertension may be produced by massive granulomas.[4]

Although biochemical findings are nonspecific, mild elevation of transaminases and alkaline phosphatase may be observed. Normal transaminases and hepatosplenomegaly were present in all cases, except for one each.

In two cases toxocariasis was diagnosed with hypergamma-globulinemia, eosinophilia, elevated anti A, anti B titration and specific tissue reaction. In case II, from Saudi Arabia, shistosomiasis was diagnosed following stool examination and observation of specific granulomas in the liver. Although brucellosis was strongly considered in one case because of high agglutination titer, his granulomas did not disappear following specific therapy. Tuberculosis was not found in any of our cases. Since the drug history was not obtained in any of the cases, granulomatous hepatitis related to allopurinol, sulfadimetoxine were not considered as an etiological factors in any of our patients.[8, 9, 14]

In seven of our patients with fever, the etiologic factors could not be documented as in some of the cases in literature.[15] This disease in general has a good prognosis with spontaneous healing of the granulomas.[10] Prednisone can be used symptomatically.[7]

Summary

Ten cases with granulomatous hepatitis were presented and the clinical and laboratory findings of this disease are discussed. A short review of the literature is also given.

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