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Veno-Occlusive Disease of the Liver and Australia Antigen*

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Veno-occlusive disease is primarily a disease of children which may occasionally affect adults.[1] Although the great bulk of the cases with this disease have been reported from Jamaica, scattered cases have been observed in Germany, Egypt, South Africa, India, Iraq as well as Turkey. [2–10] The characteristic pathologic features of the disease are obstruction of the smaller and medium-sized branches of the hepatic veins, centrolobuler congestion, and later fibrosis of the nonportal type.

Clinically, patients with the disease have ascites, hepatomegaly and, in long-standing cases, a cirrhosis which is indistinguishable from other types of cirrhosis.[11]

The cause of this disease is thought to a be a toxic agent. Although there is no uniformity of opinion as the nature of the toxic agent, bush-tea infusion and upper respiratory infections have been accused as the aetiological agents.[12 13]

Bras et al have experimentally produced a veno-occlusive disease-like picture in cattle fed with Crotalaria Fluva.[14] They believe that the Pyrrolizidine alkoloids present in this plant are the causative factors. Injections of these alkoloids into rabbit has produced histological changes identical to those found in humans with veno-occlusive disease.[15]

We report here a case of veno-occlusive disease in whom Australia antigen was found to be positive. The sera of the patient's mother and sister also showed the presence of Australia antigen.

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Case Report

This patient is a one-year-old boy who was hospitalized for abdominal enlargement, oedema and skin exanthemata. Maculo-papular exanthemata had started two months earlier, followed by hepatomegaly a month later. The infant's delivery was uneventful. There was no record of intake of plant extracts. Physical Examination: The liver was palpable 4 cms. below the costal margin. Ascites and peripheral oedema were present.

Laboratory tests: Hemoglobin: 8 gr. per 100 ml. WBC: 17.000 per mm^3, the blood smear showed polychromasia, anisocytosis, hypochromia. Reticulocytes: % 0.2. BUN: 13 mg. per 100 ml. prothrombin time: 19" (control: 13"), total serum proteins: 6.2 gr. per 100 ml. with 4.2 gr. albumin. SGOT: 75 Units, SGPT: 50 Units, Phosphorus: 4.6 mg per 100 ml., Thymol Turbidity: 3 Units, Alkaline phosphatase: 4.7 Bodansky units, CCF: (++). Total Cholesterol was 100 mg. per 100 ml. serum Iron: 38 micrograms per 100 ml., iron-binding capacity: 445 micrograms per 100 ml.

Abdominal taps showed clear fluid with no tumor cells in it. Australia antigen was detected in the serum by Ouchterlony technique.[16] Complement fixation test was also positive for the same antigen. Teleradio-

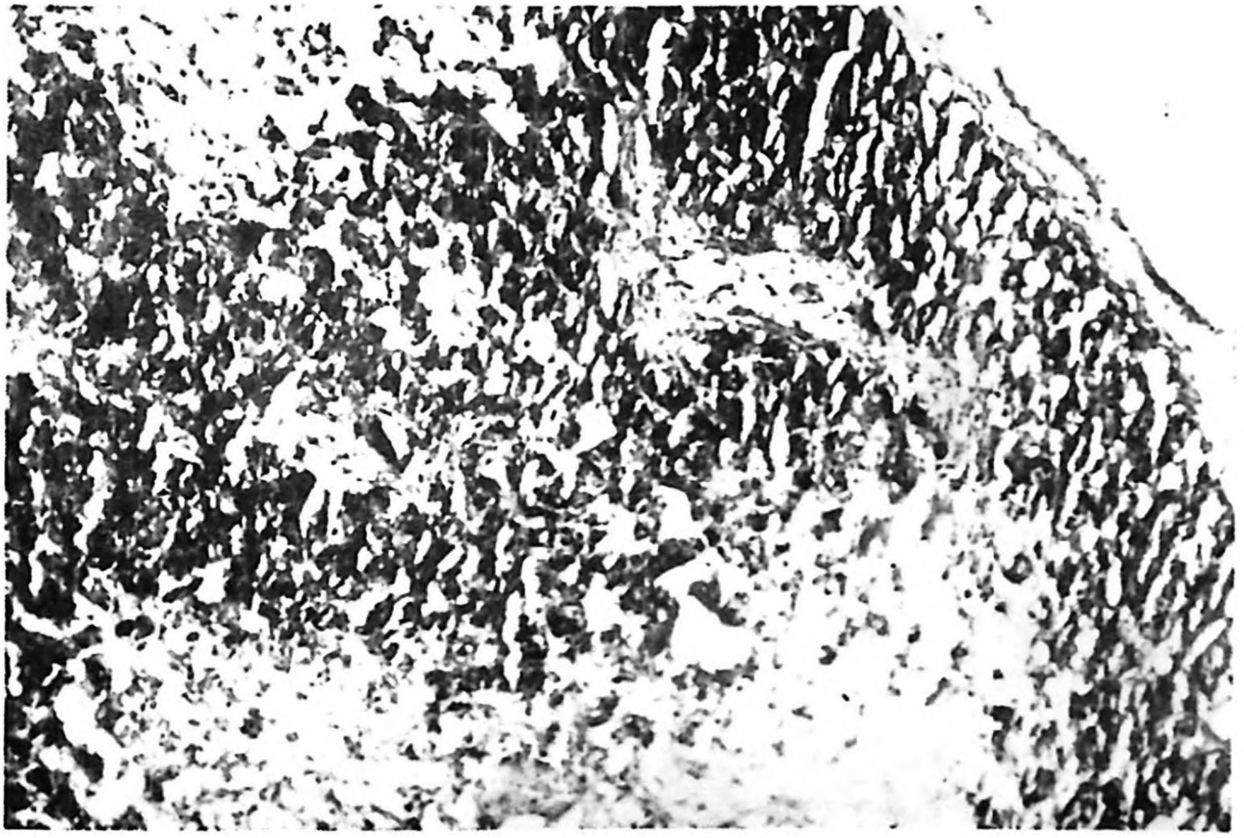

Figure 1
Centro-lobular hemorrhagic necrosis: Needle biopsy of liver. H+E.

gram revealed cardiac enlargement and there was low voltage and evidence of right atrial enlargement and right ventricular hypertrophy on the E.K.G.

Needle biopsy of the liver (Figures 1, 2, 3) showed central lobular sinusoidal dilatation and hemorrhagic necrosis of the hepatic paranchymal cells. In one area fibrous thickening and obliteration of a central vein was noted. No thrombosis, fibrosis, bileduct proliferation or regenerative nodules were seen. However in a few foci mild inflammatory cell reaction in portal areas was present.

Since the Serum Hepatitis Antigen was positive in the patient, the members of his family were investigated. Although there was no history of hepatitis, icterus or transfusions, the same antigen was shown to be present in the sera of both the patient's mother and his seven year old sister by diffusion and complement fixation techniques. The father's

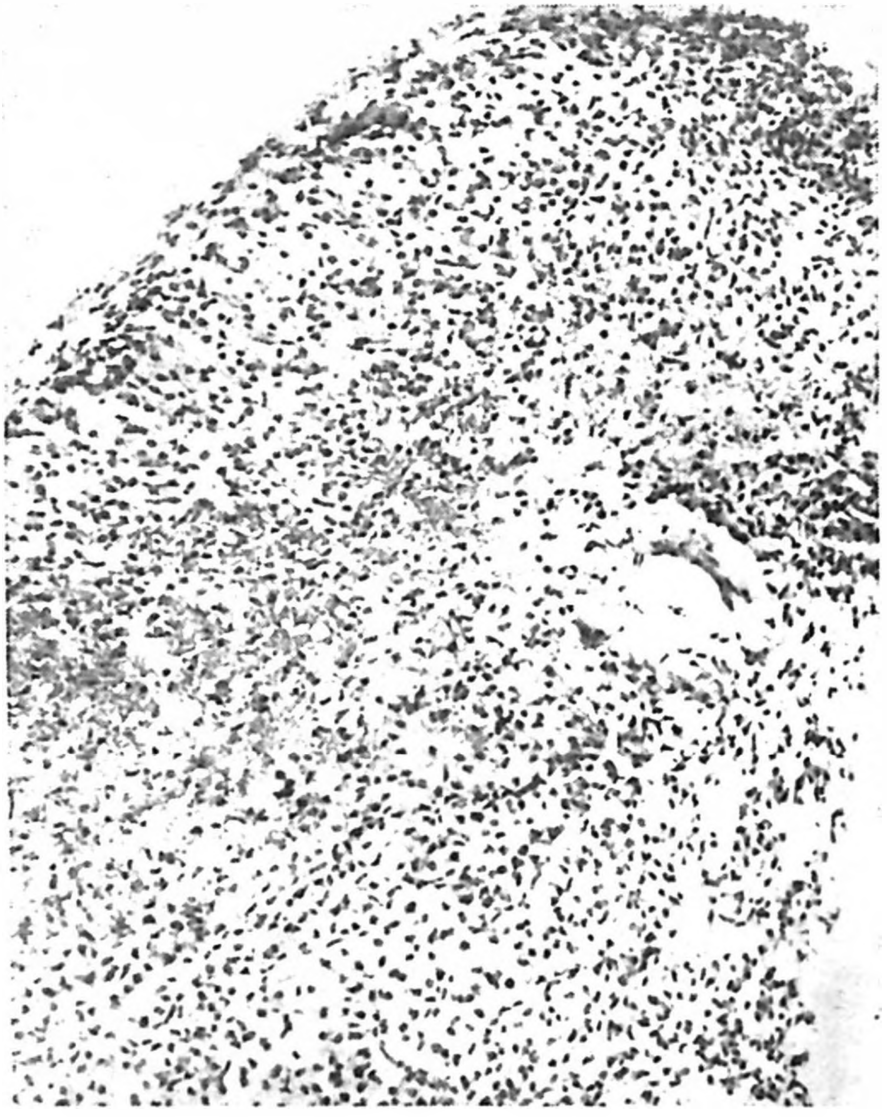

Figure 2
Fibrous thickening of the wall of central vein.

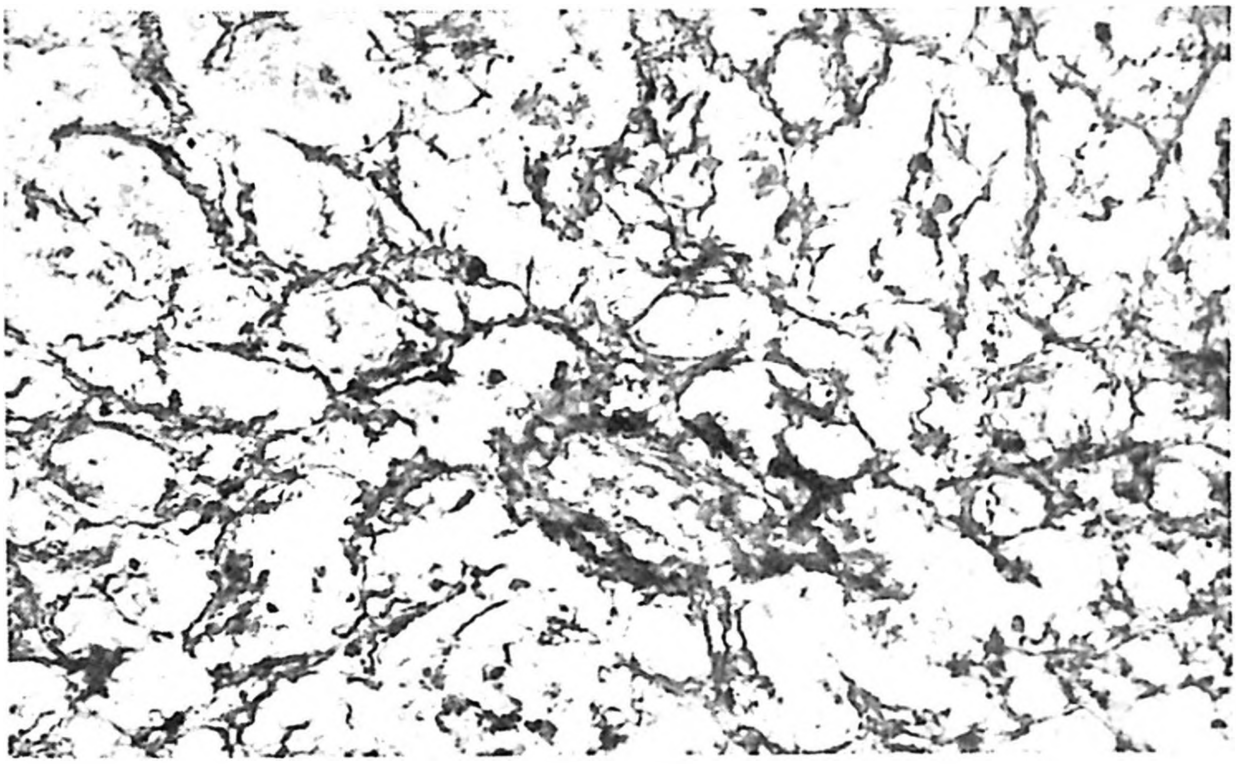

Figure 3
Thickened and obliterated central vein. Reticular stain.

serum contained no antigen. Liver function tests showed the following results:

TABLE I

Name	SGOT	SGPT	Thymol turbidity	Alkaline phosphatase	CCF
L. T. (sister)	38	22	5.4	7.0	++
F. T. (mother)	460	720	6.1	4.1	++
I. T. (father)	8	16	5.8	3.1	++

Since the mother was pregnant, no attempt for liver biopsy was made.

The patient was discharged with improvement after his oedema was controlled with diuretics, and heart failure treated with digitalis.

Discussion

Cirrhosis of the liver is common in children in parts of India and in Jamaica, where it usually occurs as result of vena-occlusive disease of the liver. Clinically, the disease is primarily seen in children between two and five years, but it may occur at any age.

The presenting features are huge ascites with hepatomegaly resulting from severe hepatic venous congestion. During the early phases splenic enlargement is absent since the pressure is directly reflected upon the liver paranchyma. Morphologically, obstruction occurs in the small and medium-sized branches of the hepatic vein (in contrast to the involvement of larger-sized vessels in Budd-Chiari syndrome). Obstruction is thought to be resulting from intimal fibrous proliferation, this latter leading to centro-lobular congestion and necrosis and finally to fibrosis of the non-portal type.

The pathogenesis of the disease is believed to be related to toxic effects on the hepatic veins. The hepato-toxic action of home-prepared herbal infusions known as "Bush tea" has been demonstrated in experimental animals.

The case presented in this communication, is, to the best of our knowledge, the first patient with veno-occlusive disease in whom Serum Hepatitis Antigen was found to be positive. There was definitely no history of ingestion of plant infusions. As different from the other cases of veno-occlusive disease in the literature, our patient had evidence of cardiac pathology as well. Normal heart sounds, the absence of murmur, the E.C.G. and X-Ray changes are all in favor of a myocardial disease. Here one can speculate that the liver and heart pathology might have been produced by the same infection.

We think that viral infections may be considered as possible agents causing veno-occlusive disease besides the toxins, and therefore report this case with the hope that it may trigger some interest towards investigations in this direction.

Summary

A case of veno-occlusive disease in whom Australia Antigen was found to be positive, is presented. The possibility of viral infections being among the etiological agents of this disease is discussed and the related literature is reviewed.

REFERENCES

1. Stuart, K. L., and Bras, G. :Veno-occlusive disease of the liver, Quarterly Journal of Medicine 26: 291-315, 1957.
2. Bras, G., Jelliffe, D. B., and Stuart, K. L.: Veno-occlusive disease of liver with nonportal type of cirrhosis, occurring in Jamaica, Arch Path. 57: 285, 1954.
3. Wurm, M.: Vena-occlusive disease, Klin. Wschr. 18: 1527, 1939.
4. Hashem, M.: Etiology and pathology of types of liver cirrhosis in Egyptian children. Journal of the Eogyptian Medical Association 22: 319, 1939.

5. Selzer, G., Parker, R. G. F.: Senecio poisoning exhibiting as Chiari's syndrome: Report on 12 cases, Amer. J. Path. 27: 885-907, 1951.
6. Bras, G., and Hill, K. R.: Veno-occlusive of liver: Essential pathology. Lancet, 2: 161-163, 1956.
7. Jelliffe, P. B., Bras, G., and Mucherjee, K. L.: Arch. Dis. Childhood. 32: 369, 1957.
8. Safouh, M. and Sheta, A. H.: Hepatic vein occlusive disease of Egyptian children. J. Pediat. 67:415-422, 1965.
9. Tınaztepe, B., Tınaztepe, K., Uzunalimoğlu, B.: Veno-occlusive disease of the liver. Turkish J. of Pediatrics. 9: 49, 1967.
10. Al-Hasany M. and Mohamed A. S. :Veno-occlusive disease of the liver in Iraq. Nine cases occurring in three Bedouin families, Arch. Dis. Childhood. 45: 722, 1970.
11. Gore, D. O., Stuart, K. L. and Bras, G.: Veno-occlusive disease of the liver: Surgical aspects, Surgery 49: 334, 1961.
12. McFarlene, A. L., Brandy, W. J.: Hepatic enlargement with ascites in children. Brit. M. J. 1: 838, 1945.
13. Asprey, G. F. and Thornton, P.: W. Indian Med. J. 2: 233, 1953.
14. Bras, G., Berry, D. M., Györgi, P.: Plants as aetiological factor in veno-occlusive disease of the liver, Lancet. 1: 960, 1957.
15. McLean, E., Bras, G., and Györgi, P.: Veno-occlusive lesions in livers of rats fed Crotalaria fulva, Brit. J. Exp. Path. 45: 242, 1964.
16. Prince, A. M.: An antigen detected in the blood during the incubation period of serum hepatitis, Proc. Nat. Acad. Sci. 6: 814, 1968.