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Research Article

SERUM IRON LEVELS IN SIDEROSIS DUE TO HABITUALLY EXCESSIVE IRON INTAKE

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Previous reports from South Africa have drawn attention to the heavy iron intake, and to the high frequency of hemosiderin deposition in the liver and other organs of the indigenous Bantu population (1, 2). In addition, observations in different Bantu population groups have demonstrated elevated levels of serum iron and total iron binding capacity in Bantu adults of both sexes. Saturation is very rarely observed in contrast to findings in idiopathic hemochromatosis (3). In view of these observations it was considered worth while to determine how far serum iron levels reflected the extent of siderosis in a hospitalized population group in this area. Since it is our experience that the severity of hepatic siderosis correlates well with the degree of visceral siderosis elsewhere in the body, the present paper represents our findings in a small series of patients in whom both liver biopsies and serum iron determinations were carried out.

MATERIALS AND METHODS

The liver material for this study came from 26 hospitalized Bantu patients (aged 17 to 66 years) in whom liver biopsies were carried out as necessary adjuncts to diagnosis. Since it was difficult to obtain livers in which siderosis was negligible, one six year old child with minimal siderosis (plus-minus) was added. There were 26 needle biopsies and one surgical biopsy in this series. In Table I, the diseases causing the admission of the patient to hospital are listed. It has been previously shown that there is no association of siderosis to any specific disease (1). The biopsies were examined by routine histopathological methods, but an additional section was stained for hemosiderin by Perl's reaction as described by Lillie (4).

Serum iron levels were determined as previously described (3). Patients in whom a viral hepatitis was suspected clinically were excluded in view of the alterations in serum iron levels known to occur in this condition. In all, a total of 27 subjects (14 males and 13 females) were available for study, but as the data obtained gave significant results it was considered unnecessary to extend the series.

Since these liver biopsies had been obtained for diagnostic purposes it was not possible to determine the degree of siderosis by chemical methods. The degree of hemosiderin deposition was therefore determined subjectively by one observer who was unaware of the serum iron levels. All biopsies were graded when first examined and again at the end of the study after re-staining in order that grading should be as uniform as possible. Siderosis was graded from 0 to 3 plus, according to the degree of hemosiderin deposition in the liver cells (fL) and Kupffer cells (fK), separately, and also according to the total liver deposits (fT). The portal tracts were not considered separately as previous experience indicated that deposits here were variable, being dependent on the degree of portal fibrosis.

RESULTS

The results obtained are summarized in Tables I and II. It will be observed that there is a significant correlation between mean serum iron levels and the presence or absence of siderosis in the liver, especially as determined by the degree of deposition in the Kupffer cells (fK) or in the liver as a whole (fT). The serum iron levels in cases in which the deposits are described as 0 or plus-minus were definitely lower than those in cases with heavily siderotic livers. It was observed, however, that once significant iron deposits were present in the liver no correlation was apparent between the degree of siderosis and mean serum iron levels. For statistical purposes, therefore, the 0 and plus-minus groups were grouped together as were also the 1 plus to 3 plus groups.

In no liver in which hemosiderin was absent (0), of which there were five in the series, did the serum iron levels rise above normal (180 μg. per cent) (Table I). On the other hand, in 3 of the 17 livers in which the iron deposits in the liver were graded 1 plus to 3 plus, the serum iron levels lay below 180 μg. per cent., *i.e.*, Patients 11, 18 and 19 (Table I).

In only one case in the current series was anemia

TABLE I

Serum iron levels, degree of hepatic siderosis, and primary disease causing admission of patient to hospital

Subject	Sex	Age	Disease	Serum iron μg. %	Degree of liver siderosis		
					fL	fK	fT*
1	F	34	Hypochromic anemia	64	0	0	0
2	F	22	Amoebiasis	88	0	0	0
3	M	28	Splenic vein thrombosis	136	0	0	0
4	F	30	Undiagnosed	149	0	0	0
5	M	21	Tuberculosis of spine	176	0	0	0
6	F	6	Malnutrition	60	+	±	±
7	M	36	Hilar lymphadenopathy	125	+	±	±
8	F	23	Chiari's syndrome	167	±	±	±
9	F	22	Pellagra and malnutrition	244	±	0	±
10	F	30	Gonococcal arthritis	264	+	±	±
11	M	47	Hepatic carcinoma	160	+	+	+
12	F	40	Obesity	201	+	+	+
13	F	60	Diabetes mellitus	274	+	++	+
14	F	18	Pellagra and malnutrition	444	+	+	+
15	M	48	Cirrhosis	243	++	++	++
16	F	34	Pellagra and malnutrition	304	+++	+	++
17	M	40	Pellagra and malnutrition	324	+	+++	++
18	M	64	Carcinoma of pancreas	120	++	+++	+++
19	F	43	Pellagra and malnutrition	123	+++	+++	+++
20	M	48	Cirrhosis	201	+++	+++	+++
21	M	31	Tuberculous peritonitis	250	+++	+++	+++
22	M	52	Pellagra and malnutrition	250	++	+++	+++
23	M	42	Diabetes mellitus	250	++	++	+++
24	M	35	Pellagra and cirrhosis	274	+++	+++	+++
25	M	43	Hypertension	385	+++	+++	+++
26	M	44	Pellagra and malnutrition	434	+++	+++	+++
27	F	55	Congestive cardiac failure	490	+++	+++	+++

* The discrepancy which sometimes exists between fT, fL, and fK is due to the fact that fT also takes into consideration the hemosiderin deposits in the portal triads.

TABLE II

Correlation of mean serum iron levels and degree of hepatic siderosis

Degree of siderosis*	Number of subjects	Serum iron, μg./100 ml.			"t"†
		Mean	Range	Standard deviation of mean	
A. In liver cells (fL)					
0 and ±	7	146.3	64–244	22.4	3.29
+ to +++	20	258.8	60–490	25.9	
B. In Kupffer cells (fK)					
0 and ±	10	147.3	60–264	21.8	3.82
+ to +++	17	278.1	123–490	26.4	
C. In total liver (fT)					
0 and ±	10	147.3	60–264	21.8	3.82
+ to +++	17	278.1	123–490	26.4	

* 0 = No hemosiderin deposits present. ± = Minimal hemosiderin deposits. + to +++ = Mild to severe hemosiderin deposits.

† Significance of difference between means calculated according to Hald (6).

of the iron deficiency type present. In this subject the serum iron level was 64 μg. initially at the time of the biopsy and hemosiderin was not demonstrated in the liver. When the degree of siderosis was doubtful (plus-minus), the serum iron levels were variable.

CONCLUSIONS

These findings indicate that high serum iron levels in hospital practice in this region are indicative of increased hemosiderin deposition in the liver of patients who are not suffering from disorders liable to cause elevation of the serum iron levels such as hepatitis, hemolytic anemia, and pernicious anemia in relapse. Occasionally, however, normal serum iron levels may be observed in cases with well marked siderosis. In two of the three siderotic cases with normal serum iron levels in the present series, the patients were seriously ill with advanced neoplastic disease. In view of the findings by Finch and Finch (5) that serum iron levels may fall in patients with hemochromatosis who develop liver carcinoma or severe infection, the probability that the normal serum iron levels in these two patients may be due to concomitant neoplasia must be considered.

The data are insufficient to permit any conclusions regarding the probability of a low serum iron level being found in a siderotic liver.

SUMMARY

Serum iron levels and the severity of siderosis as determined by liver biopsy were correlated in a series of 26 South African Bantu adults and one child derived from a population known to be habituated to an excessively high iron intake. The correlation between mean serum iron levels and the degree of siderosis was highly significant if the patients were divided into groups with and without significant hepatic deposits. There was, however, no correlation between the serum iron levels and the severity of siderosis once significant iron deposition was present in the liver.

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