Prolonged and Massive Administration of Iron-Dextran Complex Resulting in Selective Glomerular Iron Deposition in the Kidneys

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Hemosiderin deposition in the kidney tubules is a frequent finding in many different entities associated with intravascular hemolysis.1,2 In primary hemochromatosis, relatively minimal iron deposition is observed in the convoluted tubules.3 The discovery of iron positive granules in the glomerular capillary tufts, with absence of iron positive granules in the kidney tubular epithelium is rare. Reports of this finding are found only in animal experimentation with iron-dextran.4,5

This communication concerns a patient who, because of gastrointestinal hereditary telangiectasia, suffered repeated episodes of blood loss, resulting in iron deficiency anemia. The patient was treated with large amounts of iron-dextran parenterally over a prolonged period of time, resulting in widespread organ hemosiderosis with the unusual finding of striking glomerular iron deposition.

CASE REPORT

This 54 year old Negro male, (J. G. B.), was first seen at Highland General Hospital in 1951 seeking treatment for a 20 year history of spontaneous nosebleeds. Easy bruising or bleeding following dental extractions was denied. Family history was significant in that the patient’s father, brother, and sister died of nosebleeds. Another younger brother also suffered from frequent spontaneous nosebleeds. On physical examination, multiple telangiectases of the lips, tongue and both sides of the nasal septum were noted. C.I. series and barium enema revealed no lesions visible to explain the repeated guaiac positive stool findings. The initial laboratory values were: MCV 80, MCH 21, MCHC 26, Hb 2.2, Hct 8.4, Reticulocyte count 0.7. Bone marrow aspiration showed erythroid hyperplasia with absent iron granules on Prussian blue stain. The serum iron was 12 micrograms per cent, total iron binding capacity was 383 micrograms per cent. Over the ensuing years, Mr. B. has required numerous blood transfusions (198 units) because of repeated epistaxis. In an attempt to decrease the frequency of blood transfusions, Mr. B. was given approximately 30 ml. Imferon,* I.V., weekly since 1960 (6.240 ml. total was administered from 1960 to 1966). In August, 1960, the patient began to develop evidence of left ventricular failure. Concomitantly, the liver became palpable. He subsequently developed progressively severe cardiac failure, hepatosplenomegaly and ascites. On May 30, 1966, Mr. B. was admitted to Highland General Hospital following a sudden and severe episode of epistaxis. At the time

*Imferon distributed by Lakeside Laboratories, Inc.
Fig. 1.—(× 52) Hematoxilin-Eosin. Thin walled tortuous ectatic blood vessels are seen in the lamina propria of the gastric mucosa, extending to the lumen.

Of admission, the patient was hypotensive (BP 60/00) and semicomatose. There was evidence of severe congestive heart failure and ascites. Hematocrit was 9 per cent. Despite emergency blood transfusion, the patient expired.

Pertinent autopsy findings: Severe hemosiderosis was found in the liver, spleen, bone marrow, lymph nodes, skin, endo- and pericardium, adrenal capsule and sinusoids, renal
Fig. 2.—(× 52) Hematoxilin-Eosin. Ectatic thin walled blood vessels are seen in the submucosa.

glomeruli, but not in renal tubular epithelial cells. The gastric and intestinal sections showed multiple foci of ectatic thin walled blood vessels localized in the lamina propria of gastric mucosa (Fig. 1), and submucosa (Fig. 2). The gastrointestinal hemorrhages may have originated from one of the very superficial telangiectases which are seen to protrude into the lumen (Fig. 1). Each kidney weighed 200 gm. and had a smooth, nongranular cortex and a
ADMINISTRATION OF IRON-DEXTARN COMPLEX

Deep purple color. The microscopic examination of the kidneys reveals a generalized slight basement membrane thickening of the glomerular capillaries without a nodular hyalinization. Only moderate glomerular-capillary congestion is observed. In the prominent glomerular lining cell cytoplasm, a fine golden brown pigment deposition is seen on hematoxilin-eosin stain, which with Prussian blue technique, proved to be iron positive (Fig. 3, 4, 5). No "blue" granules are seen in any part of the tubular system of either kidney.

DISCUSSION

Iron-dextran administered i.v. is considered a safe therapeutic agent, especially if the patient with the iron deficiency needs iron-dextran therapy and has a small muscle mass. Foye and Feichmeir's case showed a similar underlying ailment and necessitated iron-dextran therapy. In their case, total iron-dextran administered was 1 liter, given intramuscularly over a period of 3½ years. Our case received slightly over 6 liters of iron-dextran intravenously over a period of approximately 6 years. Iron-dextran is a sterile, aqueous solution of a complex of ferric hydroxide and a dextran of low molecular weight, each milliliter containing 50 mg. of iron and 200 mg. of dextran. Iron-dextran complex possesses a considerable intrinsic stability. Iron-dextran in concentrations as high as 5 per cent of iron does not precipitate plasma proteins (including fibrinogen) from solution. Clotting time does not seem to be affected. Dextrans of various molecular weights have various effects on red blood cell aggregation. High molecular dextran increases the aggregation (D150,D500). Low molecular dextran (D40) can disagggregate aggregated human erythrocytes in vitro. The dextran in the iron-dextran retains its antigenic nature, but the clinical significance of this fact is doubtful since allergy to iron-dextran is very rare.

Rabbits who received intravenous saccharated iron oxide showed iron containing precipitates in glomerular capillary lumina a few minutes after the injection. If rebiopsied 5-7 days following the injection, the precipitates diminished in amount. Proteinuria was noted, probably as an expression of capillary wall damage since pyknosis of endothelial cell nuclei was seen. Later a hyalin change of the glomeruli was observed followed by scarring. Rabbits injected intramuscularly with iron showed iron accumulation in the glomeruli often with thrombosis. Albuminuria was noted later. Rats injected with iron-dextran showed deposits of hemosiderin in the glomeruli. The tubules were found free. Dogs injected with ferrivenin showed iron positive granules in the endothelial cells of the kidney glomerular tufts.

The paucity of human case reports following massive and long-standing iron-dextran therapy makes comparison with our case unfeasible. Morphologically, our case showed iron particles in the glomerular lining cells of the

Fig. 3.—(× 275) Prussian blue stain for iron. The glomerulus shows slight basement membrane thickening with iron positive blue granules present in the glomerular lining cells.

Figs. 4 and 5.—(× 1000 [oil]) Better visualization of a kidney glomerulus illustrating the thickened basement membrane and the iron granules in the cytoplasm of glomerular lining cells.
tufts. Clinically, however, there was no albuminuria. Through personal communication with Dr. Foye, we find that the patient of their case report is still alive and well, without any clinical symptoms referable to the kidneys. He has received 3 liters of iron-dextran to date. The difference in iron-dextran administration between their case and ours consists of the fact that in our case Mr. J. G. B. had 30 ml. of iron-dextran I.V. weekly regardless of his hematological status. Dr. Foye’s patient, however, is permitted to lose blood through his periodic spontaneous G.I. hemorrhages and only then is iron-dextran administered. It would appear that the latter is the more desirable mode of therapy.

SUMMARY

A case with massive long-standing iron-dextran administration is reported. Selective glomerular iron deposition is the outstanding feature of the generalized hemosiderosis. Similar glomerular iron deposits have been described in experimental animals.

SUMMARIO IN INTERLINGUA

Es reportate un caso de massive perdurative administrationes de ferro-dextrano. Le selective deposition glomerular de ferro es le aspecto le plus prominent de del hemosiderosis generalisate. Simile depositiones de ferro ha essite descripte in animales experimental.

REFERENCES

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