Gastrointestinal Manifestations of Amyloidosis

Review of the Problem with Report of a Representative Case

ROBERT S. MERRILL, M.D.

Amyloidosis is a disease of uncertain cause, characterized by the deposition and accumulation of an amorphous, homogeneous material, "amyloid," around small blood vessels, in connective tissue stroma, and encroaching upon parenchymal cells in many body tissues and organs. Amyloid is an abnormal acidophilic scleroprotein, formed at the periphery of histiocytes, and composed of at least 2 separate protein fractions. It is identified by its staining affinity for Congo red, iodine and sulfuric acid, and methyl violet.

Since the original report by Wild in 1886, many attempts have been made to classify the various forms of amyloidosis in an orderly fashion, on the basis of organ involvement, staining characteristics, the presence of predisposing chronic inflammatory disease, association with multiple myeloma, and the presence of certain familial characteristics. Among the various forms of amyloidosis, there is much overlapping with regard to organ involvement, and the classification most generally accepted is that proposed by Briggs: (1) primary systemic amyloidosis; (2) secondary amyloidosis, associated with predisposing disease; (3) senile cardiac amyloidosis; (4) amyloidosis associated with multiple myeloma; (5) tumor-forming amyloidosis. The familial form of amyloidosis, with its characteristic involvement of the eye, nervous system, and heart, is generally grouped with primary systemic amyloidosis.

The diagnosis of amyloidosis had formerly seldom been made antemortem, but with the increased use of biopsy in addition to the Congo red test, more frequent antemortem diagnoses are now being made. Biopsy sites include the tongue, mucous membranes, skin, muscle, lymph nodes, kidney, liver, small bowel, and rectum. The frequency of involvement and the high percentage of positive findings in biopsies have made the liver and rectum the sites of choice, the rectum being the most convenient and safest.

With the exception of some cases of secondary amyloidosis, where regression of the amyloid has been noted following cure or control of the predisposing condition, amyloidosis is fatal; renal and cardiac failure are the most frequent causes of death. Although the gastrointestinal tract is frequently involved, symptoms are rare, and seldom are pathologic changes in the digestive tract detected by X-ray technics. A proved case of pri-
mary systemic amyloidosis with some unusual and rarely reported gastrointestinal features is presented.

CASE REPORT

A 67-year-old white male carpenter was first seen in November 1960 for evaluation of epigastric pain, weight loss, and anorexia of 5 or 6 months' duration. He had been hospitalized in August 1960 for similar complaints, at which time the physical examination and upper gastrointestinal X-rays were reported as "normal." Because of progressive weight loss, continued epigastric pain, and anorexia, the patient was referred for further study.

Except for a duodenal ulcer diagnosed in 1954, without subsequent exacerbation, the patient's past history was entirely normal. Abnormalities found on physical examination were a chronically ill appearance, epigastric tenderness, pallor, and a readily palpable liver, which was smooth, firm, and nontender. The liver occupied the entire right upper quadrant and epigastrium, extending approximately 6 cm. below the right costal margin. The patient was hospitalized for further studies.

First Hospital Admission Laboratory data revealed hemoglobin values of 9.8-10.8 gm./100 ml. consistently; 1-2+ albuminuria with granular casts, white cells, and red cells; and stools positive for occult blood. Alkaline phosphatase values were < 2, 8.0, and 7.2 U. (normal, 2.2-8.6 S-J [Shinowara-Jones] U.; amylase, 46, 30, and 26 mg./100 ml. (normal, 40-100); bilirubin, 0.33, 0.5, and 0.5 mg.; SGOT, 36, 29, and 17 U.; thymol turbidity, 4.5, 3.0, and 2.7 U.; serum cholesterol, 330 mg./100 ml.; total protein, 5.6 gm. %, with a 1.7:1 A/G ratio. BSP tests revealed 20% retention in 45 min. Cephalin cholesterol flocculation was 2+ in 48 hr. Serum electrolytes and EKG were normal. The BUN varied from 18 to 20 mg./100 ml. Chest X-ray was normal except for moderate generalized cardiomegaly. Upper gastrointestinal X-rays demonstrated an active ulcer in the first portion of the duodenum and posterior displacement of the stomach. Barium enema was normal. The patient was treated with diet, antacids, and atropine, with a good subjective response. Repeat gastrointestinal X-rays in approximately 2 weeks revealed an ulcer in the region of the pyloric canal, which was believed to represent the same defect seen previously, and the possibility of malignancy was entertained.

After 2 additional weeks of ulcer therapy, follow-up X-rays revealed 2 active ulcers, 1 in the base of the bulb and 1 in the pyloric canal. A gastric analysis revealed free hydrochloric acid with normal response to histamine. Surgical exploration was recommended but refused. After a total of 6 weeks of ulcer management, the patient was subjectively improved, and at his own insistence was released from the hospital in mid-December of 1960, agreeing to readmission a month later.

Second Admission Upon readmission of the patient, it was found that the liver had enlarged and extended to the level of the umbilicus, occupying the entire right upper quadrant and epigastrium. The liver was smooth and nontender. There had been an additional 6-lb. weight loss. Laboratory studies revealed an amylase of 40 mg./100 ml.; bilirubin, 0.5 mg.; thymol turbidity, 2.7 U.; cephalin cholesterol flocculation, negative in 48 hr.; alkaline phosphatase, 7.2 S-J U.; SGOT, 36 U.; hemoglobin 9.8 gm./100 ml.; and occult blood in the stool. Serum proteins were 5.6 gm. %, with a 1:1 ratio. Repeat X-rays of the upper gastrointestinal tract demonstrated improvement in the general appearance, with no evidence of ulceration of the pyloric canal but a small, shallow crater at the base of the duodenal bulb. In view of the subjective and objective improvement and the essentially normal liver-function tests despite the progressive hepatomegaly and weight loss, the patient was discharged.

Third Admission One week after discharge, the patient experienced a sudden episode of periumbilical pain without nausea or vomiting, but with marked weakness and sweating, and was readmitted as an emergency with a suspected perforation of the duodenal ulcer. Within