Diarrhea Associated with Pancreatic Islet-Cell Tumors

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In 1955, Zollinger and Ellison described a syndrome characterized by extreme gastric hypersecretion, intractable ulcer disease, and the presence of a non-beta islet-cell tumor of the pancreas. Review of the earlier literature disclosed other examples of the same entity, and many more cases have since been recognized and reported. Zollinger and Ellison postulated that a humoral factor released from the tumor, was responsible for the clinical manifestations. The demonstration by Gregory et al. of a gastrin-like substance in extracts obtained from primary or secondary tumors verified their hypothesis. Some instances of complete reversal of the clinical picture after surgical removal of the tumor provided further substantiation.

One of the 2 patients described in Zollinger and Ellison's original report had severe diarrhea, but no particular significance was attached to this symptom at the time. As more cases were recognized, it became apparent that diarrhea frequently occurred, often preceding the appearance of ulcers and, at times, remaining the only manifestation of an islet-cell tumor. The relief of the diarrhea in a number of these patients after excision of the tumor again suggested a causal relationship, the nature of which has not been completely elucidated.

It is the purpose of this paper to (1) report 2 cases of pancreatic islet-cell tumors, manifested only by severe diarrhea; (2) review similar cases reported in the literature; and (3) consider the possible mechanisms in the development of diarrhea in these patients.

CASE REPORTS

Case 1

J. M., a 32-year-old male, was admitted to the hospital on Nov. 15, 1961, for evaluation of an increasingly severe diarrhea of 18 months' duration. The patient then had

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an average of six bowel movements a day, with some fecal incontinence. The stools were soft, fatty in appearance, and often covered with a layer of oil. Dietary measures and a number of medications had given no relief, and the patient's weight had decreased from 74 kg. to 54 kg. Other symptoms included bouts of epigastric pain radiating to the back, unrelated to meals, but relieved by vomiting copious amounts of clear, acid-tasting fluid. Past personal history, familial history, and review of systems were noncontributory. The positive physical findings were limited to the abdomen, which was distended, tympanic, and tender in the epigastric region. Bowel sounds were exaggerated.

Hemoglobin, blood counts; erythrocyte sedimentation rate; serum Na, K, Cl, CO₂, Ca, P, and alkaline phosphatase; serum proteins and electrophoresis; serum bilirubin; BSP; thymol turbidity; serum amylase; oral glucose-tolerance test; urinalysis; BUN; PSP test; creatinine clearance; chest X-ray; ECG; stool cultures; urinary 5H-IAA; cholecystogram; barium enema; and proctoscopy gave normal results. Examination of stools showed undigested food and the presence of fat; benzidine reaction was positive on three occasions. On a calculated intake of 55 gm. fat per day, the mean fecal fat excretion was 30 gm., with 80% neutral fats. The pH of the feces varied between 7.6 and 7.8. Nocturnal gastric aspiration gave a 12-hr. volume of 2,698 ml., with an acid output of 273 mEq. The hourly basal acid output of 22.7 mEq. increased only to 30.5 mEq. after "maximal" histamine stimulation. Barium meal X-ray study revealed hypertrophic gastric rugae and hypersecretion. The duodenum was dilated. There was coarsening of the mucosal folds, and segmental dilation of the small bowel. In a few areas, a cobweb-like appearance, as described by Weber et al., was visible. The transit

Fig. 1. Microphotograph of tumor of Case 1. (Masson’s trichrome, × 500)