THE YALE JOURNAL OF BIOLOGY AND MEDICINE 56 (1983), 175-178

Gastrointestinal Manifestations of Diabetic Ketoacidosis

EUGENE J. BARRETT, M.D., Ph.D.,[a] AND ROBERT S. SHERWIN, M.D.[b]

[a]*Assistant Professor of Medicine;* [b]*Associate Professor of Medicine, Yale University School of Medicine, New Haven, Connecticut*

Received April 26, 1983

The evaluation of gastrointestinal symptoms in patients with diabetic acidosis frequently challenges the physician's clinical acumen. Faced with a seriously ill patient, he must judge whether the abdominal pain, nausea, or vomiting are a consequence of the metabolic decompensation, and hence likely to resolve with correction of the ketoacidosis, or if these symptoms signal a serious underlying intra-abdominal process (e.g., cholecystitis, appendicitis, etc.) which may have precipitated the development of ketoacidosis.

The pathogenesis of the reversible gastrointestinal symptoms which frequently accompany diabetic acidosis has not been rigorously defined and may be multifactorial, involving metabolic, humoral, and neural processes. Careful attention to the medical history and abdominal examination greatly facilitates distinguishing patients with intra-abdominal pathology from those with reversible symptoms secondary to ketoacidosis. Similarily, the judicious use of laboratory tests (electrocardiography, blood counts, urinalysis, serum enzyme profile, and abdominal roentgenograms) materially aids in differential diagnosis. Finally, clinical suspicion of an acute abdominal process should prompt early surgical consultation and, if required, surgical intervention as the acidosis is being brought under control.

Gastrointestinal symptoms, including nausea, vomiting, abdominal pain, and distension, are encountered in at least 50–75 percent of patients presenting with diabetic ketoacidosis (DKA) [1,2]. Not uncommonly, these symptoms dominate the clinical picture at the time of initial presentation, leading, in some cases, to a delay in treatment with fluids and insulin. On rare occasions, uncomplicated DKA may be accompanied by physical signs suggestive of an acute surgical abdomen [3]. In some instances, unnecessary hazardous surgical intervention has been undertaken, particularly in the previously undiagnosed diabetic [4]. Since in the vast majority of cases the gastrointestinal manifestations of DKA resolve spontaneously with appropriate treatment of the metabolic disturbance, it is incumbent on the clinician to distinguish gastrointestinal symptoms resulting from DKA per se from those caused by an active intra-abdominal process (e.g., cholecystitis, peritonitis, vascular compromise, or pancreatitis).

In this regard, it should be emphasized that fatalities from DKA most often result from underlying non-diabetic medical and/or surgical emergencies which may go unrecognized due to the severity of the metabolic abnormalities or its depressive effects on mental function [5]. Consequently, it is critical not to overlook a potentially treatable abdominal crisis.

Of common reversible gastrointestinal symptoms associated with ketoacidosis, the nausea and vomiting have been attributed to either a central neurogenic response

Address reprint requests to: Eugene J. Barrett M.D., Ph.D., Endocrinology Section, Department of Medicine, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510

to the ketoacidosis, gastric atony, generalized ileus, gastritis, or pancreatitis [2]. The latter two processes, and rapid expansion of the hepatic capsule, presumably secondary to fatty engorgement of the liver, have been invoked to explain the abdominal pain that so frequently accompanies ketoacidosis [6]. However, largely because these symptoms resolve promptly with fluid and insulin therapy, their pathogenesis remains unclear. It is of interest to note that the entire clinical picture of profound nausea, epigastric pain, and repeated vomiting can be induced in the well-controlled diabetic by withdrawing insulin therapy [7] and reversed with restoration of insulin and fluid replacement. It is possible that the increased circulating levels of glucagon and catecholamines or other hormones accompanying ketoacidosis impede gastrointestinal motility. Even hyperglycemia per se has been implicated in inhibiting gastric emptying [8]. Whether insulin deficiency itself, or the altered metabolic milieu (ketonemia, hyperglycemia, acidosis, and dehydration) associated with insulin deprivation, is responsible for the gastrointestinal symptoms remains unresolved. The awareness that decompensated diabetes may produce episodes of nausea, vomiting, or abdominal pain should lead the physician to evaluate the metabolic control in any known diabetic with these symptoms.

If, by a combination of clinical and laboratory examination, a diagnosis of ketoacidosis is established in a patient with significant gastrointestinal complaints, the physician must recognize that acute cholecystitis [9], acute pancreatitis [2], and mesenteric vascular insufficiency all occur with increased frequency in the diabetic [2]. Furthermore, development of any severe intra-abdominal process may be sufficient stress to cause decompensation of previously well-controlled diabetes and precipitate an episode of DKA. The need for accurate and timely diagnosis is underlined by the mortality observed when ketoacidosis is complicated by either acute pancreatitis [2] or acute cholecystitis [9]. Fortunately, a combination of careful history, physical examination, and judicious use of laboratory aids can, in most circumstances, lead to appropriate therapy. The nausea, vomiting, and abdominal pain that accompany ketoacidosis are usually acute in onset, beginning after the metabolic abnormality is well established. Therefore, a prior history of polyuria, polydipsia, and nocturia can usually be elicited. Conversely, a history of intermittent abdominal pain or vomiting, occurring over days to weeks prior to presentation, should enhance suspicion of a separate abdominal process. Similarly, a history of fever or significant hematemesis, in patients with DKA and abdominal symptoms, cannot be safely attributed to the ketoacidosis alone and requires full evaluation. Small amounts of hematemesis are not infrequently encountered in ketoacidotic patients, particularly when protracted vomiting has occurred. This may be due to either gastritis or small Mallory-Weiss tears; however, since the bleeding is usually minor, evaluation is not attempted and the etiology remains unknown.

On physical examination the respirations of the acidotic diabetic are often deep and rapid with large excursions of thoracic and abdominal muscles. This contrasts with the rapid, shallow respirations and splinting of the abdominal musculature seen with peritoneal irritation. Bowel sounds, although frequently diminished, are usually present in uncomplicated ketoacidosis and, although gastric atony is common, clinically apparent abdominal distension is unusual. If abdominal tenderness is generalized, if there is no rigidity of the abdominal musculature, and if rebound tenderness is absent, then the likelihood of a localized intra-abdominal process causing the gastrointestinal symptoms is diminished. In the younger child with ketoacidosis and significant abdominal pain and guarding, appendicitis is frequently considered. If localized signs are absent on abdominal and rectal examination, treat-

ment of the ketoacidosis alone will often lead to resolution of symptoms within hours [1].

Laboratory evaluation of the patient with ketoacidosis and abdominal pain should include an electrocardiogram, flat and upright abdominal films, complete blood count, and measurement of serum enzymes (amylase, lipase, alkaline phosphatase, SGOT, SGPT, CPK isoenzymes), in addition to measurements of glucose, pH, electrolytes, and urea nitrogen. This evaluation will help in identifying diabetic patients with abdominal pain secondary to atypical presentation of myocardial infarction, intestinal perforation, gastric atony, generalized ileus, or obstruction. The blood count in uncomplicated DKA usually shows leukocytosis without toxic granulations (probably secondary to the release of "stress" hormones) and evidence of hemoconcentration secondary to dehydration. A hematocrit below 35 percent in these volume-contracted subjects should arouse suspicion that blood loss has occurred.

The evaluation of the serum enzyme pattern in the setting of ketoacidosis and abdominal pain must be approached cautiously. Elevated serum amylase values have been reported in 40 to 79 percent of patients presenting in ketoacidosis [10,11]. The levels of serum amylase can frequently be strikingly elevated (in excess of 1,000 somogyi units/100 ml) in the absence of any symptoms. Furthermore, in several studies there was no relationship between amylase levels and severity of acidosis, or morbidity or mortality during the episode of acidosis [10,11]. Macroamylasemia is not responsible for this increase in serum amylase, and isozyme studies suggest that salivary as well as pancreatic amylase elevations occur in DKA. The renal amylase to creatinine clearance ratio can also be raised during ketoacidosis, in the absence of the clinical picture of acute pancreatitis [8]. In the 21 patients with hyperamylasemia during DKA reported by Knight et al. [10] none had severe back pain or abdominal rigidity, features frequently encountered in patients with acute pancreatitis. These authors further comment that serum lipase activity did not correlate with serum amylase in their patients and was frequently normal or only modestly elevated in the face of striking increases in serum amylase. In summary, it appears that an elevated serum amylase concentration cannot be considered as definitive evidence for clinically significant pancreatic inflammation in the absence of concomitant elevation in serum lipase levels and suggestive physical findings.

Abnormal values for SGOT, SGPT, LDH, and other liver enzymes have been reported to occur frequently in patients admitted in ketoacidosis. Knight has reported mild to marked elevations of hepatic enzymes in 33 percent of 36 episodes of ketoacidosis [12]. In approximately half of these cases, some underlying disease of the hepato-biliary tree was sufficient to explain the abnormal serum enzyme pattern, while in the remaining patients no specific cause for the abnormal liver enzyme pattern could be identified. As with amylase, no significant correlation existed between the serum levels of hepatic enzymes and the presence or severity of abdominal symptoms. It has been suggested that in these cases reversible hepatocellular damage, sufficient to allow release of cytosolic enzymes, occurs during the development of ketoacidosis. Fatty infiltration of the liver and reduced hepatic perfusion may contribute to this process.

This discussion of the difficulties involved in the laboratory diagnosis of abdominal pathology in ketoacidotic patients with gastrointestinal symptoms serves to underline again the importance of history and physical examination in the evaluation of these patients. When the duration of severity of gastrointestinal symptoms or the physical findings lead the physician to suspect an intra-abdominal inflammatory

process, early surgical consultation and further diagnostic evaluation should be undertaken as dictated by the clinical situation (e.g., paracentesis, endoscopy, etc.). The abdominal pain, nausea, and vomiting which occur secondary to diabetic acidosis alone resolve with improvement of the metabolic picture. Thus, when the gastrointestinal symptoms persist beyond the first 12 to 24 hours after beginning treatment of DKA, additional etiologies should be actively sought. Finally, it should be emphasized that the presence of DKA should not lead to unnecessary delays when immediate surgical intervention is indicated. As soon as fluid deficits are for the most part replaced and acidosis is corrected (usually within four to six hours) the required surgical procedures may be undertaken. Frequent assessment of serum glucose and electrolytes and of fluid balance must continue through the operative and post-operative period. This information will allow appropriate insulin and fluid replacement and avoid the complications of hypoglycemia, hypokalemia, or recrudescence of acidosis.

REFERENCES

1. Katz LA, Spiro HM: Gastrointestinal manifestations of diabetes. New Eng J Med 275: 1350–1361, 1966
2. Marble A, White P, Bradley RF, et al: Joslin's Diabetes Mellitus. 11th edition. Philadelphia, Lea and Febiger, 1971
3. Valerio D: Acute diabetic abdomen in childhood. Lancet i: 66–67, 1976
4. McKittrick LS: Abdominal symptoms with or without abdominal lesions in diabetic acidosis. New Eng J Med 209: 1033–1036, 1933
5. Beigelman PM: Severe diabetic ketoacidosis (Diabetic coma). Diabetes 20: 490–500, 1971
6. Campbell IW, Duncan LJP, Innes JA, et al: Abdominal pain in diabetic metabolic decompensation: Clinical significance. JAMA 233: 166–168, 1975
7. Atchley DW, Loeb RF, Richards DW, et al: On diabetic acidosis. J Clin Invest 12: 297–329, 1933
8. MacGregor IL, Gueller R, Watts HD, et al: The effect of acute hyperglycemia on gastric emptying in man. Gastroenterology 70: 190–196, 1976
9. Mundth ED: Cholecystitis and diabetes mellitus. New Eng J Med 267: 642–645, 1962
10. Knight AH, Williams DN, Ellis G, et al: Significance of hyperamylasaemia and abdominal pain in diabetic ketoacidosis. Br Med J 3: 128–131, 1973
11. Vinicor F, Lehrner LM, Karn RC, et al: Hyperamylasemia in diabetic ketoacidosis: sources and significance. Ann Int Med 91: 200–204, 1979
12. Knight AH, Williams DW, Spooner RJ, et al: Serum enzyme changes in diabetic ketoacidosis. Diabetes 23: 126–131, 1974