CASE REPORT

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Wischnewski Ulcers and Acute Pancreatitis in Two Hospitalized Patients with Cirrhosis, Portal Vein Thrombosis, and Hypothermia

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ABSTRACT: Accidental hypothermia has been described in the forensic literature but reports of occurrence in hospitalized patients are rare. Associated anatomic lesions include acute hemorrhagic pancreatitis and characteristic acute gastric ulcers termed Wischnewski ulcers. We report here two patients with cirrhosis and ascites; one also had hepatocellular carcinoma. Portal vein thrombosis, acute hemorrhagic pancreatitis and Wischnewski ulcers were present in both. The clinical records documented hypothermia that progressed over several days. Temperature nadirs of 31.0°C (87.8°F) and 32.2°C (90.0°F) were recorded in each patient, respectively, one day before death, although each transiently reached temperatures that did not register on standard monitoring devices. This is the first report that chronicles antemortem body temperatures in hypothermic patients with Wischnewski ulcers and pancreatitis at autopsy. Also, the association of these findings with portal vein thrombosis and cirrhosis has not been previously described. We discuss this constellation of findings with regard to possible mechanistic interrelations.

KEYWORDS: forensic science, forensic pathology, hypothermia, Wischnewski ulcers, hospitalized patients, acute hemorrhagic pancreatitis

Deaths related to accidental hypothermia generally occur because of environmental exposure. Such deaths are usually investigated by forensic pathologists. The literature discusses several anatomic lesions that may be associated with, and serve as markers of, accidental hypothermia. Pulmonary edema may be seen in 27% of these patients and acute hemorrhagic pancreatitis may be present in 18% (1). These findings lack specificity however; for instance, acute hemorrhagic pancreatitis may be seen in a variety of other settings, including chronic alcoholism, cholelithiasis, and in association with certain drugs and infections. Somewhat more specific is a peculiar pattern of acute gastric ulcers termed Wischnewski ulcers. Although not pathognomonic, in the proper circumstances and setting a combination of these abnormalities corroborates the presence and importance of antemortem hypothermia (1).

Wischnewski ulcers are a type of acute gastric lesion that differs from other acute gastric ulcers in a number of respects (2–4). First, the ulcers are multiple and they may occur throughout the gastric mucosa, not limited to fundus or antrum. They characteristically carpet the entire gastric mucosa or a large proportion of the mucosa. Further, they are arranged in a geometrically regular distribution. These ulcers may be found in up to 88% (2) or 93% (3) of hypothermic deaths, although the frequency is variable, depending at least in part on the circumstances of death (ambient temperature, length of time survived, etc.). When stratified according to ambient temperature prevailing at the time of death, the ulcers are more frequent in patients dying from hypothermia when the ambient temperature is >10°C (>50°F) (4). This suggests that a more prolonged period of survival at the decreased temperature is necessary for their development, and may partially explain a lower incidence of this finding in some series.

We report here two hospitalized patients with cirrhosis and portal vein thrombosis who developed progressive hypothermia over the last several days of life and demonstrated acute hemorrhagic pancreatitis and Wischnewski ulcers at autopsy. Well-documented records of body temperature (recorded orally) during these patients' hospitalizations are available. We emphasize also the relationship of hypothermia, Wischnewski ulcers and pancreatitis to abnormalities of the portal vein-hepatic axis in these patients with respect to possible pathogenesis.

Case Histories and Postmortem Findings

Case 1—A 63-year-old man had a history of hepatitis B and C virus infection, with cirrhosis and hepatic encephalopathy. He was abstinent from alcohol. He had chronic obstructive pulmonary disease and had a remote appendectomy and inguinal herniorrhaphy. He was admitted to the University of Texas Medical Branch Hospitals (UTMB) on 22 January 98 for abdominal pain, deteriorating mental status and progressive weakness. On admission, he had ascites, jaundice, and multiple electrolyte abnormalities. He received antibiotics for suspected sepsis, but did not improve. His electrolytes did not normalize, and progressive renal function and men-

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tal deterioration were noted during his 12-day hospital course. His temperature (assessed by oral thermometer) during the initial 6 days of hospitalization was approximately 36°C (96.8°F); his temperature for the remaining 6 hospital days progressively declined (Fig. 1A). A recorded temperature nadir of 31°C (87.8°F) was reached 1 day prior to death, although on the day of his demise his temperature was too low to register.

Autopsy revealed cirrhosis, organizing portal vein thrombosis with extension proximally into the splenic vein and acute hemorrhagic pancreatitis. Striking extensive acute ulcers carpeted the gastric mucosa (Fig. 2A) and >1100 cc of bloody fluid (recent hemorrhage) was present in the stomach and proximal small intestine. Other findings included congestive splenomegaly, intestinal mural edema, pulmonary edema, acute pyelonephritis superimposed on chronic tubulointerstitial nephritis, and ischemic changes in the central nervous system. Exsanguination was considered an important component of the mechanism of death.

Microscopy of the gastric ulcers (Fig. 3A) demonstrated sharp demarcation, localized inflammation, and transmucosal necrosis with focal extension into the submucosa. Occasional remnants of necrotic vessels could be recognized in the ulcer beds (Fig. 3B). Blood breakdown pigments stained the luminal surface of the ulcer beds and adjacent mucosa. In the pancreas, large geographic zones of necrosis were surrounded by hemorrhage and neutrophilic infiltrates. Fat necrosis was present in the peripancreatic and interlobular connective tissues.

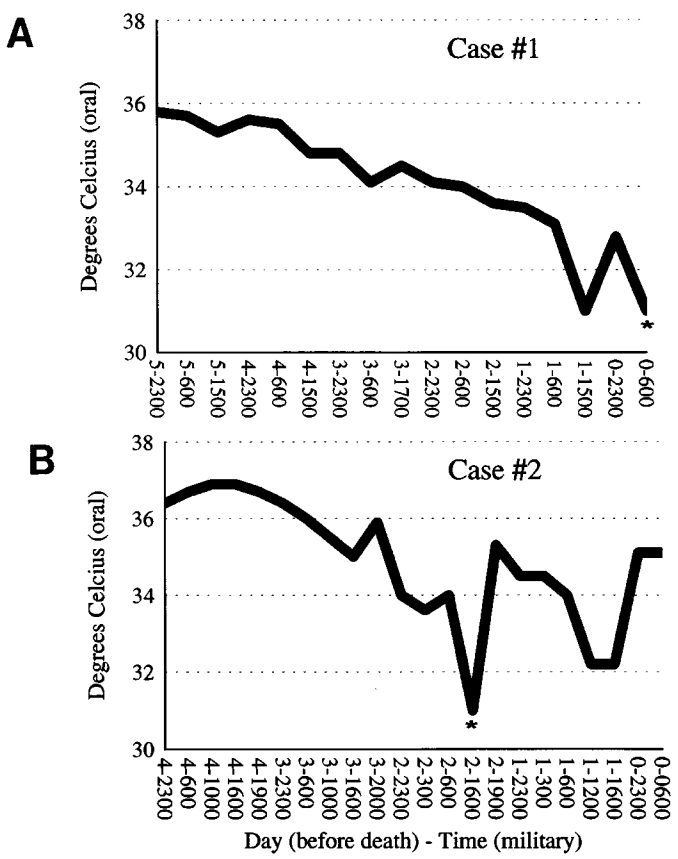

FIG. 1—*Temperature profiles during the terminal hospital courses of Case 1 (panel A) and Case 2 (panel B). The temporal relations are shown along the abscissa as day(s) before death and time during that day. For Case 1, five days are shown (abscissa), and for Case 2, four days are shown. The oral temperatures are plotted along the ordinate.*

Case 2—This 58-year-old lady had a history of hepatitis C infection and cirrhosis. She was abstinent from alcohol. She was admitted to UTMB on 12 March 1998 because of increasing ascites, jaundice, and renal failure. She had an episode of hematemesis several days prior to admission, but no prior history of gastritis or peptic ulcers. A workup demonstrated mass lesions in the liver that were consistent with hepatocellular carcinoma. The diffuse nature of these lesions precluded the possibility of aggressive therapy. Her 3-week hospital course was characterized by progressive deterioration with multiple episodes of hypotension, mental status decline and hypothermia. Her initial oral temperature averaged 36.6°C (97.9°F), but declined over the last four days of life to reach a recorded nadir of 32.2°C (90.0°F). This patient also reached a nonrecordable low temperature two days prior to death (Fig. 1B).

Autopsy confirmed the presence of hepatocellular carcinoma, which was widely disseminated in the liver. The tumor also invaded the inferior vena cava and the portal vein. Both intrahepatic segments of the portal vein, the extrahepatic portal vein and the splenic vein were occluded by tumor invasion and by thrombus which was propagated proximally from the intravascular tumor. Striking acute ulcers carpeted the entire gastric mucosa (Fig. 2B); the duodenal mucosa was hemorrhagic. Acute hemorrhagic pancreatitis was present, and consisted of fat necrosis and hemorrhage distributed evenly throughout the pancreas. Superficial hemorrhagic necrosis was present in the cecum and ascending colon. Additional findings included a diffluent spleen and pulmonary edema.

Microscopy of the gastric lesions in Case 2 was similar as in Case 1, and consisted of well-demarcated ulcers with inflammation, necrosis and blood breakdown pigments. The duodenal mucosa was diffusely ulcerated; the duodenal ulcer bed was similar in microscopic appearance to the gastric mucosal lesions. Sections of the pancreas revealed extensive necrosis, acute inflammation and hemorrhage. Congestion and abundant neutrophils were present in the spleen (acute splenitis).

Discussion

The cases we have presented here are unusual in a number of respects. Hypothermia developed in these individuals during hospitalization. This is unusual of itself, and suggests that hypothermia was based on metabolic, physiologic, or neurologic derangements, rather than exposure per se (since the ambient temperature was not below the mid-70°F range). In one of these patients, Case 2, the problem of hypothermia was addressed antemortem by the provision of additional blankets and sheets, but the patient refused, stating that she was "hot." This is consistent with the well-known phenomenon of "paradoxical undressing" during hypothermia (5). The extensive nature of the gastric ulcers in these cases is also unusual. Wischnewski ulcers, acute "stress" ulcers occurring in the setting of hypothermia, are often fairly extensive. However, hemorrhage from these ulcers leading to exsanguination and consequently death has not been previously reported.

The term gastric "stress ulcer" encompasses several forms of acute lesions in the stomach, including mucosal hemorrhages, erosions, and ulcers. These lesions occur in a variety of settings, are located in the more proximal parts of the stomach and only rarely extend as far distally as the antrum. Acute gastric mucosal injury has been reported as a consequence of a myriad of different condi-

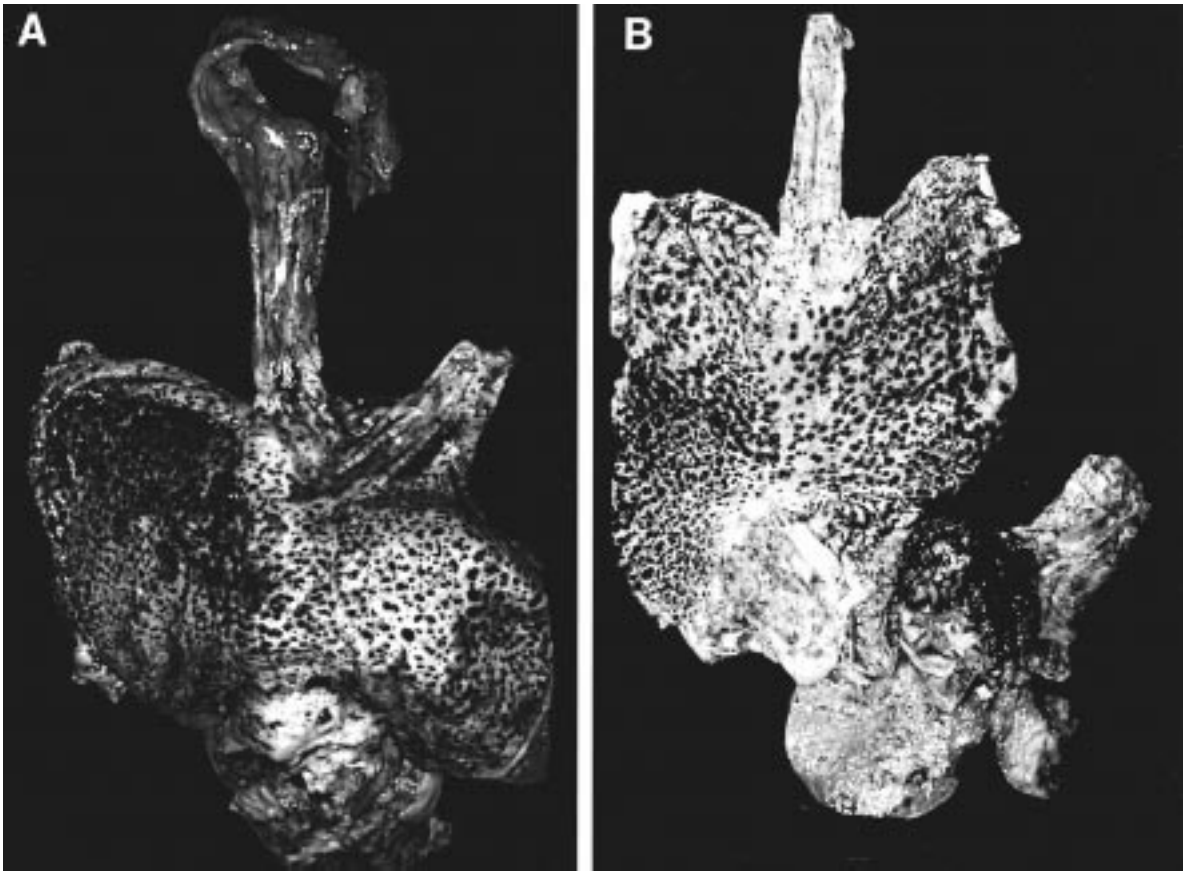

FIG. 2—*A: Case 1; gross view of the gastric mucosa. The stomach has been opened along the greater curvature; the esophagus is at the top of the figure. Acute ulcers (black to gray) carpet the mucosal surface of the stomach. B: Case 2; gross view of the gastric mucosa. Similar orientation and appearance as in panel A. The duodenal mucosa is diffusely ulcerated. C: Case 1; detail of gastric mucosal ulcers, remarkable regularity of distribution.*

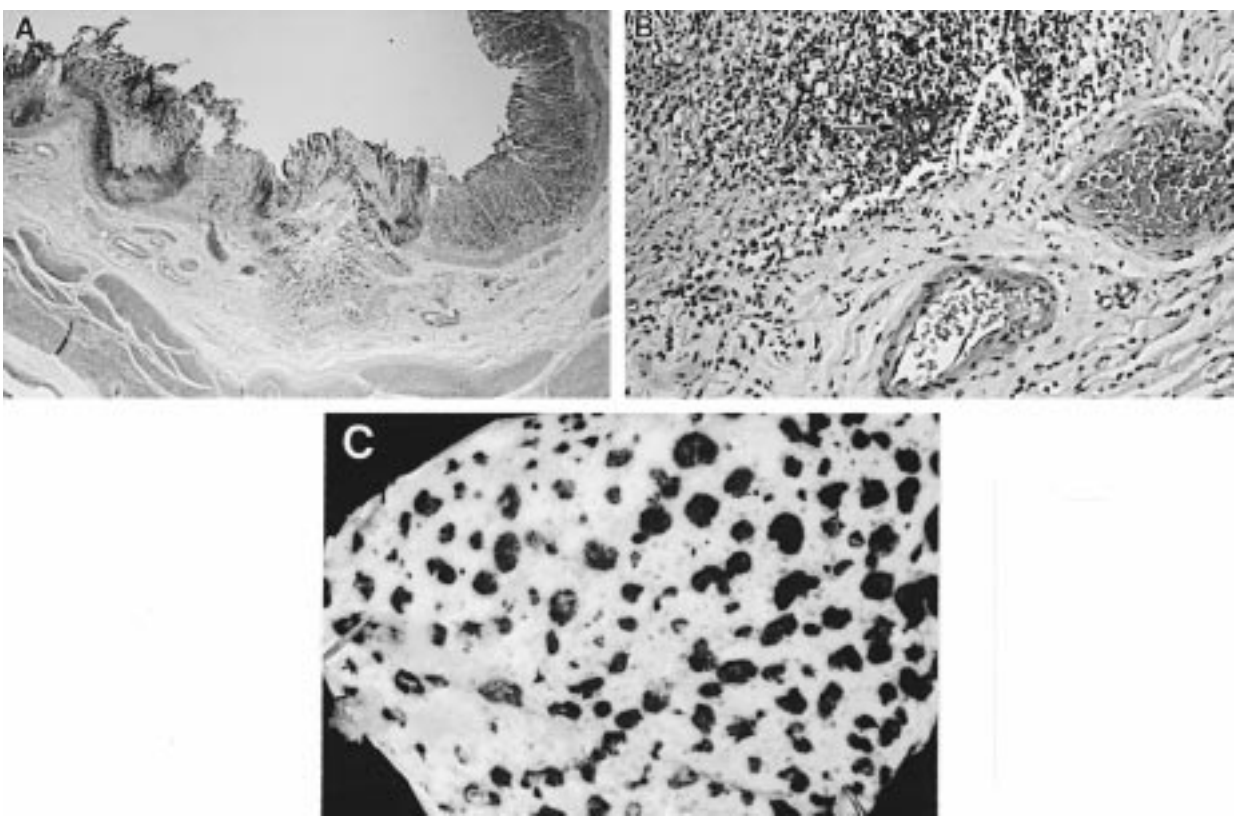

FIG. 3—*A: Photomicrograph of Wischnewski ulcers. Sharp demarcation and variable depth of penetration. The ulcer at left extends to, but not through the muscularis mucosa while the ulcer in center extends into the submucosa (hematoxylin-eosin; original magnification ×40). B: Microscopic detail of the base of a Wischnewski ulcer. Inflammatory cells and necrotic remnants of gastric mucosa surround a necrotic vascular profile (arrow) in the upper part of the figure. The larger vessels below are in the submucosa (hematoxylin-eosin; original magnification ×400).*

tions, including shock, sepsis, trauma, renal failure, and others. Stress ulcers occurring in the setting of several specific stressors are referred to by eponymic names: Cushing's ulcers in the setting of brain injury, and Curling's ulcers in cutaneous thermal burns. The cases reported here illustrate a form of stress ulceration occurring in the setting of systemic hypothermia, Wischnewski ulcers. The lesions reported here occurred in the setting of documented hypothermia (and in association with acute hemorrhagic pancreatitis); however, the role, if any, of any of the complicating medical conditions in formation of these lesions in these patients is unknown. Although attempts have been made to separate acute ulcers on basis of etiology and/ or morphology (6–8), more recent texts (9) favor a unifying approach. Nevertheless, the lesions reported here were more widespread and had a more regular distribution than ulcers referred to in the literature as Cushing's ulcers, Curling's ulcers or otherwise unspecified "stress ulcers." In addition, inflammatory infiltrates as seen here are not usually a component of other types of acute gastric ulcers, at least in the acute phase.

The mechanism of formation of acute stress ulcers is unknown. The histologic characteristics (2) of the ulcers, and experimental data (6,7) suggest an ischemic—reperfusion etiology. It has been theorized that in the setting of hypothermic stress, direct sympathetic and parasympathetic stimulation, increased circulating catecholamines, and histamine and serotonin secretion by gastric mucosal mast cells lead to mucosal ischemia. The eventual collapse of central thermoregulatory mechanisms, exhaustion of catecholamines, and loss of vascular smooth muscle constriction lead to mucosal reperfusion and to hemorrhagic ulceration (2). Our two cases were noteworthy also because of the particular combination of findings. The constellation of hypothermia, Wischnewski ulcers, portal vein thrombosis, and hemorrhagic pancreatitis has not been previously reported. The striking similarity of findings in these two cases suggests this combination of lesions may have mechanistic importance. The entire venous drainage of the stomach is through the portal venous system. Therefore, blockage of this conduit would be expected to alter gastric blood flow. Indeed, Vigneri et al. 1992 (10) reported that cirrhosis and portal hypertension alter the state of gastric mucosal microcirculation and produce a situation in which the gastric mucosa is more susceptible to stressors leading to acute ulceration. These two cases support this idea and suggest an important role for altered gastric microcirculation in the genesis of Wischnewski ulcers.

The forensic literature details ambient temperatures prevailing at the time that hypothermic deaths were presumed to have occurred (4). The two cases reported here offer a unique insight into antemortem body temperatures and temporal relationships in patients who die after developing these lesions. As seen from the temperature profiles (Fig. 1), the lowest recorded temperature in each case was 31.0°C (87.8°F) and 32.2°C (90.0°F). In each, the temperature fell below a recordable level, but this was only transient (Case 2) or terminal (Case 1). Although oral temperatures are generally considered not as accurate as true core temperatures (e.g., rectal), the error is probably toward an underestimation of temperature (that is, oral temperature is probably usually equal to or lower than the core temperature). Therefore, the minimum body temperature required for development of these lesions is 31–32°C (87.8–90.0°F). Further, the amount of time that these patients were significantly hypothermic (<34°C (<93.2°F)) was on the order of 1 to 2 days. Nevertheless, as mentioned above, these patients each had multiple complicating medical conditions that may have contributed significantly to formation of these lesions, and therefore also may have affected parameters such as temperature or time required for their formation.

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