

Cullen's Sign Associated with Metastatic Esophageal Carcinoma

Mark A. Marinella, MD, FACP
Michael Baumann, MD

Department of Internal Medicine, Division of Hematology and Oncology, Wright State University School of Medicine, Dayton, Ohio.

Cullen's sign refers to the presence of periumbilical ecchymosis and is most often recognized as a manifestation of hemorrhagic pancreatitis. However, lesser-appreciated etiologies include ruptured ectopic pregnancy, leaking aortic aneurysm, and intraabdominal malignancy. We report the case of a patient with metastatic adenocarcinoma of the esophagus who developed Cullen's sign shortly before death. Based on this case and previously reported cases, malignancy-associated Cullen's sign portends a dismal prognosis, and may be considered a pre-terminal finding. *Journal of Hospital Medicine* 2008;3:277-278. © 2008 Society of Hospital Medicine.

KEYWORDS: Cullen's sign, metastatic cancer, esophageal carcinoma, ecchymosis, periumbilical.

Examination of the abdomen is an important element of the physical examination, especially in patients with known or suspected cancer. Patients with intraabdominal malignancy occasionally manifest unusual ominous findings on abdominal examination that may portend a poor prognosis: periumbilical adenopathy (Sister Mary Joseph sign),¹ hepatic pulsations,² or a hepatic friction rub or bruit.³ An uncommonly reported, and likely under-appreciated, sign of intraabdominal cancer is periumbilical ecchymosis, also known as Cullen's sign.⁴ Reported below is a case of Cullen's sign associated with metastatic esophageal carcinoma.

CASE REPORT

An 80-year-old man with recently diagnosed esophageal adenocarcinoma presented with fever, cough, lassitude, and abdominal distention. Several weeks earlier, the patient underwent esophagogastroduodenoscopy for dysphagia and weight loss and was found to have a partially obstructing, ulcerated distal esophageal mass. Biopsy revealed poorly differentiated adenocarcinoma. At that time, computed tomography showed mediastinal adenopathy. Subsequently, the patient developed increasing dysphagia with a cough, painful abdominal distention, and profound weight loss and was admitted to the hospital for further evaluation.

The patient was tachycardic and hypotensive. Physical examination revealed muscle wasting, anasarca, and abdominal distention with diffuse tenderness. An area of periumbilical ecchymosis measuring approximately 10 cm in diameter was noted. The patient had not sustained any obvious abdominal trauma or received any injections in the periumbilical area. There were no other significant ecchymoses on the abdominal wall, including the flanks. Computed tomography revealed

pulmonary infiltrates compatible with pneumonia, mediastinal adenopathy, thickening of the distal esophagus, and ascites; there were no obvious liver lesions, pancreatic or retroperitoneal hemorrhage, or evidence of pancreatitis. Liver enzymes, bilirubin, and alkaline phosphatase were normal, but anemia and leukocytosis were noted. Prothombin time and partial thromboplastin time were 20 and 28 seconds, respectively. Platelet count was normal. Broad-spectrum antimicrobials were administered for pneumonia. Because of abdominal discomfort, paracentesis was performed. Approximately 2000 cc of opaque yellow fluid was removed. The ascitic fluid was positive for erythrocytes and adenocarcinoma cells, consistent with his known diagnosis of esophageal carcinoma. The patient developed acute renal failure, and his condition continue to decline. He subsequently was discharged to hospice care and died several days later; an autopsy was not performed.

DISCUSSION

Cullen's sign—ecchymosis surrounding the umbilicus—is classically associated with hemorrhagic pancreatitis, often occurring in conjunction with ecchymosis of the flank (Grey-Turner sign).⁴ Cullen's sign, however, has been reported with other abdominal pathologies such as ruptured ectopic pregnancy, leaking aortic aneurysm, splenic rupture, and retroperitoneal hemorrhage.^{4,5} Hemoperitoneum from any of these processes leads to diffusion of blood along fascial planes, resulting in flank staining (Grey-Turner sign) or periumbilical staining (Cullen's sign). Cullen's sign, however, is traditionally not attributed to malignant disease in standard medical and surgical texts.^{6,7} However, the results of a Medline literature search, which revealed only a handful of case reports, suggests an association between advanced malignancy and Cullen's sign (Table 1). All previous reports occurred in patients with advanced terminal malignancy, although no firm conclusions regarding specific malignancies or other risk factors can be surmised from such a small number of cases.^{5,8,9}

Our patient had stage IV esophageal carcinoma with malignant ascites associated with periumbilical ecchymosis. Unfortunately, serum amylase and lipase were not obtained, but acute pancreatitis-induced Cullen's sign is unlikely because the patient did not have symptoms of pancreatitis and computed tomography did not

TABLE 1
Reported Cases of Malignancy-Associated Cullen's Sign

Reference	Sex	Age	Cancer	Outcome
Present study	M	80	Esophageal	Died
5	M	55	Thyroid	Died
8	M	62	Lymphoma	Died
9	M	32	Hepatoma	Died
9	M	64	Hepatoma	Died

reveal pancreatic inflammation or hemorrhage. It is well known that patients with disseminated visceral adenocarcinoma can develop coagulopathy, and that cannot be excluded in our patient. The likely mechanism of periumbilical blood collection is unclear but could relate to subclinical hemoperitoneum from mesenteric and peritoneal carcinomatosis, abdominal wall trauma, or coagulopathy from cancer and acute renal failure. Nonetheless, it is evident from this and previously reported cases that Cullen's sign complicating cancer has a dismal prognosis and is a premonitory sign. Clinicians should consider occult or metastatic visceral malignancy in patients with unexplained abdominal wall ecchymosis.

Address for correspondence and reprint requests: Mark A. Marinella, MD, FACP, 33 West Rahn Rd., Suite 101, Dayton, OH 45429; Fax: (937) 438-7677; E-mail: Mmarinella@pol.net

Received 7 June 2007; revision received 30 August 2007; accepted 5 October 2007.

REFERENCES

1. Meyerhardt JA, Fuchs CS. Gastric cancer. In: *Clinical Hematology and Oncology: Presentation, Diagnosis, and Treatment*. Philadelphia: Churchill-Livingstone, 2003;887-898.
2. Marinella MA, Klemptner A. Hepatic pulsations in a patient with cholangiocarcinoma. *Arch Intern Med*. 1996;157:133-134.
3. The Abdomen. In: Sapira JD. *The Art and Science of Bedside Diagnosis*. Baltimore, MD: Williams and Wilkins, 1990;371-390.
4. Marinella MA. Cullen's sign. *Hosp Physician*. 1999;35:35-36.
5. Marinella MA. Cullen's sign associated with metastatic thyroid cancer. *N Engl J Med*. 1999;340:149-150.
6. Acute Pancreatitis. In: Silen W. *Cope's Early Diagnosis of the Acute Abdomen*. 18th ed. New York: Oxford University Press; 1991:123-131.
7. Greenberger NJ, Toskes PP. Acute and chronic pancreatitis. In: Braunwald E, Fauci AS, Kasper EL, et al., eds. *Harrison's Principles of Internal Medicine*. 15th ed. New York: McGraw-Hill; 2001:1792-1804.
8. Silvestre JF, Jover R, Betloch I, et al. Cullen's sign secondary to intraabdominal non-Hodgkin's lymphoma. *Am J Gastroenterol*. 1996;91:1040-1041.
9. Mabin TA, Gelfand M. Cullen's sign, a feature in liver disease. *BMJ*. 1974;1:493-494.