

THE SKIN IS, AT TIMES, INDEED THE “WINDOW TO THE SOUL”

(OR UNDERLYING DISEASE)

Jon A. van Heerden, M.D.

QUESTIONS:

1. Is there a specific skin rash that is associated with islet cell tumors of the pancreas?
2. Are glucagonomas benign or malignant?
3. What is the most common presentation of glucagonomas and why?

CLINICAL ASPECTS:

A 78-year-old male from Florida was seen in consultation by a dermatologist. The patient was seeking relief from a skin rash that had been present for 15 years and that was increasingly more troublesome. The patient stated that a host of treatments had been utilized over the years without any success. The rash (Figures 1, 2, 3, 4) was intensively pruritic and tended to get better in one site only to restart in another location. The most troublesome areas were the lower aspects of his legs and his feet, which were so painful that he was unable to walk at all and was no, in fact, wheelchair bound.



Figure 1: Pruritic, erythematous buttock rash.



Figures 2 and 3: Necrotizing, erythematous rash involving both lower limbs.

Figure 4: Painful rash of the toes

The astute dermatologist felt that the rash was a typical example of necrotizing migratory erythema (NME) – a rare rash most often occurring as a cutaneous manifestation of an underlying pancreatic islet cell tumor secreting glucagon (glucagonoma).

Computerized tomographic examination (CT) confirmed the presence of a mass in the head of the pancreas compatible with an islet cell tumor (Figure 5).

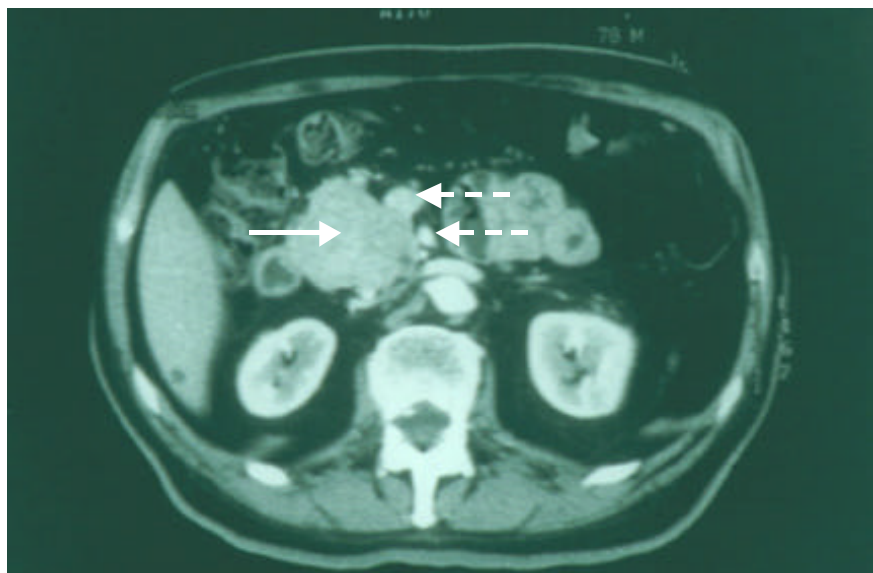


Figure 5: Computerized tomographic examination of the abdomen demonstrating an ~ 5.0 cm mass in the head of the pancreas (solid arrow). The superior mesenteric artery and vein (dotted arrows) are adjacent to this mass but do not appear to be invaded by the mass.

In addition, the CT demonstrated excessive fluid within in the upper gastrointestinal tract with gastric (Figure 6) and jejunal (Figure 7) distention and thickening – radiological findings often found in patients with functioning islet cell tumors.

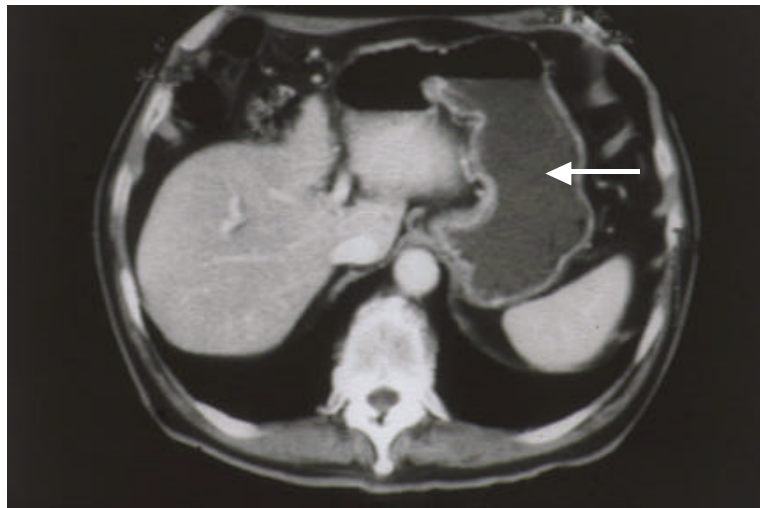


Figure 6: Computerized tomographic scan of the abdomen. Thickening of the gastric wall with excessive fluid in the stomach.



Figure 7: Dilated and thickened loops of jejunum containing a generous amount of fluid.

Biochemical evaluation revealed a serum glucagon level of 2,200 pg/mL (normal, < 60 pg/mL), serum glucose of 109 mg/dL (normal, 70-100 mg/dL), total proteins of 5.3 g/dL (normal, 6.3-7.9 g/dL), and CEA of 3.3 ng/mL (normal, 0.0-5.0 ng/mL).

A radical pancreateoduodenectomy (Whipple procedure) was performed. The gross specimen (Figure 8) and histological findings (Figure 9) were compatible with a benign glucagonoma.

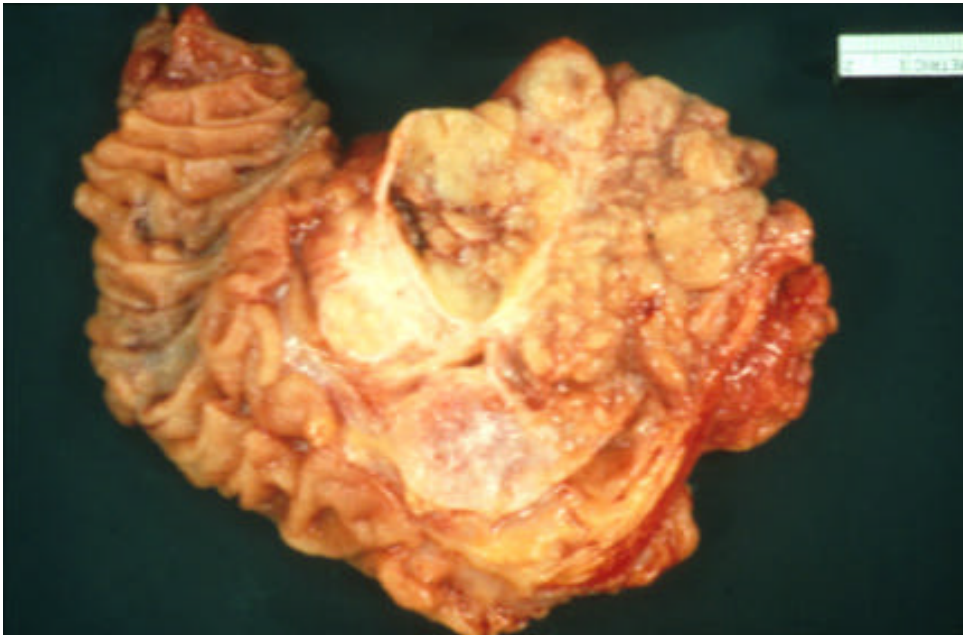


Figure 8: Gross specimen demonstrating multilobular tumor in the head of the pancreas.

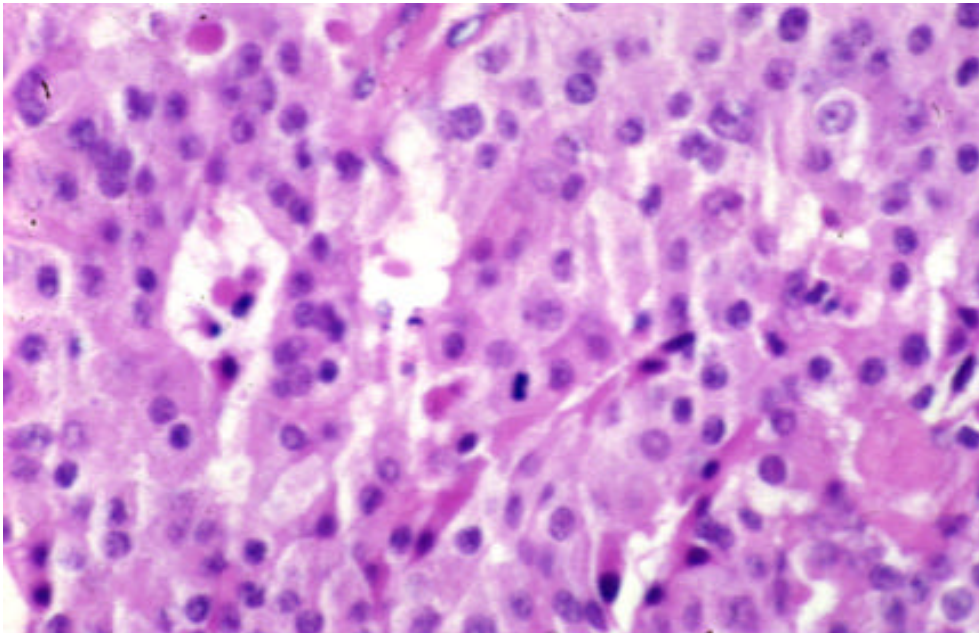


Figure 9: Histology of pancreatic tumor– cords and acinar groups of tumor cells with moderate cytoplasm, uniform nuclei, and a few prominent nucleoli.



The day following resection, all of his intense itching was gone, and within three months, his rash had completely resolved. Five years postoperatively, his serum glucagon level is 32 pg/mL (normal, <60 pg/mL). The patient is symptom free and enjoying a well-deserved retirement (Figure 10).

DATA SUMMARY:

Glucagonomas are very rare islet cell tumors that occur more often in women than men in a ratio of 3:1 and are encountered most commonly in the sixth decade of life. These tumors are most often sporadic in nature, but rarely occur in association with the multiple endocrine neoplasia type I (MEN I) syndrome. The common presenting symptoms are diabetes mellitus (90%), NME with or without stomatitis (64%), weight loss (56%), and hypoaminoacidemia (26%). The latter has been felt to possibly be the imitator of NME since the administration of amino acids may induce a dramatic remission of the rash.

Most glucagonomas are large (range, 3-35 cms), at least 80% are malignant, and ~ 50% already have hepatic metastases at the time of diagnosis.

The only chance for cure is complete surgical excision, which, however, is possible in a minority of these patients. There is a carefully selected role for judicious surgical debulking,

hepatic artery embolization, and, particularly in symptomatic patients, chemotherapeutic agents including long-acting somatostatin, 5-fluorouracil, streptozotocin, adriamycin, and dicarbazine (DTIC).

ANSWERS:

1. NME is a specific marker for pancreatic glucagonomas. It occurs in at least two-thirds of patients. All patients with NME should undergo radiologic evaluation of the pancreas to rule out an islet cell tumor.
2. At least 80% of glucagonomas are malignant with 50% of patients already having hepatic metastases at the time of diagnosis.
3. The most common presentation is adult onset diabetes mellitus. Glucagon is a potent stimulator of gluconeogenesis, glycogenolysis, and ketogenesis – thus the hyperglycemic effects.

REFERENCES:

1. Stacpoole PW. Glucagonoma syndrome: Clinical features, diagnosis, and treatment. *Endocr Rev* 1981; 2:347-361
2. Guillausseau PJ, Guillausseau-Scholer C. Glucagonoma: Clinical presentation, diagnosis, and advances in management. *Front Gastrointest Res* 1995; 23:183
3. Bloom SR, Polak JM. Glucagonoma syndrome. *Am J Med* 1987; 72(5B):25-36

“I’m a great believer in luck. I find the harder I work, the more I have of it.”

Thomas Jefferson