

**\*\* no patient handout**

## **Glucagonoma syndrome - Skin**

### **Synopsis**

Glucagon-producing tumors of the pancreas have been associated with a distinctive eruption called necrolytic migratory erythema (NME) that often clears with surgical resection of the glucagonoma. Some patients with NME have normal glucagon levels, and at least 15 patients with NME have been described without glucagonoma. Weight loss, abdominal pain, diarrhea, and fever may accompany the glucagonoma. Pruritus and burning of the skin have been reported. Pancreatitis and celiac sprue have been associated with NME. Most patients with glucagonoma have mild diabetes mellitus. Ascites and other signs of cirrhosis / hepatic dysfunction such as gastrointestinal bleeding or hepatic encephalopathy may be present. There is a waxing and waning course. Lesions may improve spontaneously and reappear after some months. Clinical improvement or resolution of cutaneous lesions is expected after surgical excision or surgical debulking of the pancreatic lesion.

### **Codes**

ICD10CM:

D37.8 – Neoplasm of uncertain behavior of other specified digestive organs

SNOMEDCT:

16424000 – Glucagonoma syndrome

### **Look For**

Erythematous papules that coalesce and spread. Central vesiculation progresses to postinflammatory healing while the periphery remains erythematous and becomes scaly. Lesions may appear eczematous. Erosive lesions may also be present. NME may have a distinctive scalloped border. Peripheral expansion and central clearing results in a serpiginous or arcuate morphology. The intertriginous areas, particularly the perineal and intergluteal cleft, are most frequently involved. Flexural areas, as well as the abdomen, breasts, lateral neck, central face, and extremities may be affected. Glossitis and angular cheilitis can be present.

### **Diagnostic Pearls**

Zinc deficiency has similar intertriginous lesions and should be excluded with a plasma or serum zinc determination.

### **Differential Diagnosis & Pitfalls**

- Immunobullous diseases such as **pemphigus vulgaris**, **bullous pemphigoid**, and **paraneoplastic pemphigus** should be considered, but in glucagonoma, there are no immunoreactants.
- **Subacute cutaneous lupus erythematosus**
- **Acquired acrodermatitis enteropathica**

- **Drug eruption**

## **Best Tests**

Glucagon levels after overnight fast: elevated levels (700-7,000 pg/mL), normal (40-150 pg/mL, depending on the laboratory), and especially elevated immunoreactive glucagon may be seen. Anemia, elevated glucose levels or abnormal glucose tolerance test, hypoaminoacidemia, elevated sedimentation rate, elevated liver function tests, hypoalbuminemia, hypozincemia, elevated prothrombin time, and other hepatic abnormalities are often present. Glucose tolerance test, and CT scans of abdomen if glucagon levels elevated. Abdominal CT scan may show a pancreatic or hepatic lesion.

A biopsy of the eruption is helpful in narrowing the differential diagnosis, especially if blood tests and imaging are not initially performed.

## **Histopathology Findings:**

Common features

- Pale, vacuolated keratinocytes replace the stratum granulosum and upper stratum spinosum
- Scattered dyskeratotic keratinocytes in the upper epidermis
- Partial or confluent necrosis of the upper epidermis
- Mild to moderate superficial perivascular lymphocytic infiltrate with some neutrophils

Occasional features

- Psoriasiform epidermal hyperplasia with neutrophilic spongiosis
- Subcorneal pustules
- Subcorneal or intraepidermal cleft formation
- Acantholytic cells within the clefts

## **Management Pearls**

If the diagnosis is suspected, there should be careful work-up to find the lesion as outlined above.

## **Therapy**

Resection of the glucagonoma has resulted in clearance of the eruption. Streptozocin (a nitrosourea compound) has been beneficial in patients with hepatic metastases (approximately 50% of patient at the time of diagnosis). Treatment of the eruption with potassium permanganate

baths, topical corticosteroid, and antifungal preparations may be beneficial. Somatostatin has been shown to decrease glucagon levels and may also suppress skin lesions.