Glucagonoma without cutaneous manifestations

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Summary: A 63 year old man presented with features of the glucagonoma syndrome, that is thrombo-embolic disease, weight loss, raised sedimentation rate, diabetes mellitus, hypoproteinaemia and reduced plasma amino acid levels, but without necrolytic migratory erythema. The plasma glucagon level was raised and the tumour was demonstrated by abdominal CT scan. Immunofluorescent studies of the resected tumour confirmed the diagnosis. The normal tissue zinc status supports the view that necrolytic migratory erythema is related to zinc deficiency.

Introduction

Necrolytic migratory erythema is the cardinal feature of the glucagonoma syndrome (Mallinson *et al.*, 1974) and is usually what leads to its diagnosis. We report a patient presenting without a skin rash.

Case report

A 63 year old man was admitted with a 2 day history of pleuritic chest pain and the clinical signs of a deep venous thrombosis and pulmonary embolus. He had lost 9.5 kg in weight. Investigations revealed: normal blood film and haemoglobin level, sedimentation rate 64 mm/h, alkaline phosphatase 165 IU/l, (normal 30–155 IU/l), albumin 31 g/l and globulin 26 g/l (both low). A random blood glucose level was 18.8 mmol/l. He was anticoagulated and treated with glibenclamide and diet.

The clinical features suggested a pancreatic neoplasm. Hypotonic duodenography was normal, but an endoscopic retrograde pancreatogram showed a grossly distorted duct in the tail of the pancreas, with stricture and cyst formation, consistent with a tumour. A mass was suggested by ultrasound and confirmed by computed tomographic (CT) scan.

The basal serum glucagon level was 262 pmol/l (normal < 50), gastrin 5 pmol/l, vasoactive intestinal polypeptide 5 pmol/l, pancreatic polypeptide 60 pmol/l and somatostatin 65 pmol/l (all normal). The plasma

zinc level was 1.2 µg/l (normal) and blood leukocyte zinc content 61.7 ng/mg dry weight (normal 50–70). The levels of 21 serum amino acids were uniformly reduced.

A partial pancreatectomy was performed and a 2.0 × 2.5 × 3.0 cm tumour was removed from the tail of the pancreas. The histological appearances were of an islet cell carcinoma with lymph node involvement. Immunofluorescent studies with anti-glucagon antibody confirmed a glucagon-secreting tumour.

He has remained asymptomatic and the diabetes requires dietary treatment alone. Three months after surgery serum glucagon levels, both basal and after a 50 g glucose load, were normal, and the serum amino acid levels had all risen to normal.

Discussion

One hundred and two patients with the glucagonoma syndrome have been reported, but the inclusion of several without skin rashes has been criticized (Holst, 1979). Glucagonomata without the rash often lack other features of the syndrome, have moderate to severe diabetes and large, inoperable tumours (Mallinson & Bloom, 1978). With thrombo-embolic disease, diabetes, weight loss, hypoproteinaemia, an elevated erythrocyte sedimentation rate, and the elevated glucagon levels with low amino acid levels, we believe this to be an example of the glucagonoma syndrome without necrolytic migratory erythema.

The pathogenesis of the rash is not known but is often a late manifestation. It has been associated with amino acid deficiency (Mallinson *et al.*, 1974). Its

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resemblance to acquired zinc deficiency and acrodermatitis enteropathica (Kahan *et al.*, 1977) and, like these conditions, its response to oral zinc supplementations (Mallinson *et al.*, 1978) suggest that the rash is a manifestation of zinc deficiency. The normal tissue zinc status and absence of rash in our patient support this view.

References

- HOLST, J.J. (1979). Possible entries to the diagnosis of a glucagon producing tumour. *Scandinavian Journal of Gastroenterology*, **53**, (suppl.), 53.
- KAHAN, R.S., PEREZ-FIGAREDO, R.A. & NEIMANIS, A. (1977). Necrolytic migratory erythema. *Archives of Dermatology*, **113**, 792.
- MALLINSON, C.N., BLOOM, S.R., WARIN, A.P., SALMON, P.R. & COX, B. (1974). A glucagonoma syndrome. *Lancet*, **ii**, 1.
- MALLINSON, C.N. & BLOOM, S.R. (1978). The hyperglycaemia, cutaneous syndrome. Pancreatic glucagonoma. In *Surgical Endocrinology; Clinical Syndromes*, Friesen, S.R. (ed.), p. 171. Philadelphia: Lippincott.
- MALLINSON, C.N., HANLEY, J., ALLISON, D.J., ADRIAN, T.E. & BLOOM, S.R. (1978). Treatment of malignant pancreatic glucagonoma; effect of zinc on the rash and hepatic embolization on liver metastases. *Gut*, **19**, 448.

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