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DIE ZOLLINGER-ELLISON-SINDROOM

Groot belangstelling is gewek deur die onlangse uitkenning van 'n sindroom bestaande uit hardnekkige maagverswering en grootskaalse oormatige maagsapafskeiding met verwante klierewasse in die eilandjies van Langerhans wat nie insulien afskei nie;¹ die vernaamste kenmerke van hierdie sindroom is verlede jaar in ons briewerubriek bespreek.² In die kort tydjie sedert 1955 toe dit vir die eerste maal beskrywe is, het die omvang van die sindroom uitgebrei—nuwe aspekte word nou as onderdeel daarvan gereken, en by verskeie gevalle het maagverswering glad nie die siektebeeld oorheers nie. Dit is bekend dat diarree soms by hierdie siekte voorkom, maar dit gaan gewoonlik gepaard met tipiese verswering-siektes, hoewel dit ook 'n vroeë simptome kan wees;³ 'n geval is onlangs beskryf waarby onbeheerbare diarree ernstige kaliumtekort veroorsaak het.⁴ By die lykskouing van hierdie pasiënt is 'n alveeskliergewas ontdek wat nie onderskei kon word van die soort wat by hierdie sindroom voorkom nie, maar die enigste tekens van 'n maagsweer was bloeding uit 'n radiologies-bewese akute letsel volgend op behandeling met kortison.

Ook blyk dit dat ander endokriene kliere in baie gevalle aangetas kan word; Donaldson *et al.*³ lewer 'n oorsig van 21 gevalle van hierdie sindroom en het ontdek dat gewasse of oormatige groei van die harsingslymklier, byniere of byskildklier by 6 pasiënte voorgekom het. Hoewel veelvoudige endokrien-klierwoekering 'n familiekwaa kan wees, is daar nog geen bewyse dat oorerflikheid 'n rol speel by die Zollinger-Ellison-sindroom nie. Die aantasting van die ander kliere is veelbetekenend, want by sommige gevalle is die mening uitgespreek dat die afskeidings van hierdie ander kliere aanleiding kan gee tot verswering⁵ en dat die maagdermletsels van hierdie sindroom tot 'n mate daaraan te wyte kan wees. Simptome van die spysverteringstelsel kom dikwels by oormatige byskildklierwerking voor en sommige geneesheren meen dat hulle deur 'n oormaat bloedkalsium veroorsaak word, maar dit blyk dat daar bowendien 'n hoër voorkomsyfer van maagsweere is;⁶ daar is egter selde enigiets wat op die Zollinger-Ellison-sindroom dui by sulke gevalle. Een voorbeeld van hierdie sindroom met endokrien-klierwoekering is reeds beskrywe, waarby die tekens van oormatige byskildklierwerking die ontwikkeling van die maagsweere voorafgegaan het.⁵

Hoewel hipoglisemie die afskeiding van HCl stimuleer, bevat die eilandsêlgewasse nie B-korreltjies nie en skei hulle nie insulien af nie. Dit is moeiliker om te bepaal watter rol glukagon speel; hoewel sommige werkers L-sêlkorreltjies in die gewasse ontdek het,⁷ en biochemiese bewyse dat die serum glukagon of 'n verwante stof bevat,⁵ was daar geen

EDITORIAL

THE ZOLLINGER-ELLISON SYNDROME

Great interest has been aroused by the recent recognition of a syndrome consisting of intractable peptic ulceration and gross gastric hypersecretion in association with non-insulin-secreting adenomata of the islets of Langerhans;¹ its principal features were noted in our correspondence columns a year ago.² During the short time since it was described in 1955, the scope of the syndrome has been expanded—new components have been added, and in several instances peptic ulceration has not dominated the picture. While diarrhoea has been known to occur in this condition, it has usually been in association with typical ulcer-disease, although it may be an early symptom;³ and now a case has been described where intractable diarrhoea produced extreme potassium depletion.⁴ In this patient a pancreatic tumour indistinguishable from those described in this syndrome was found at autopsy, but the only evidence of peptic ulcer was bleeding from a radiologically-shown acute lesion which followed upon cortisone therapy.

Other endocrine glands, too, appear to be involved in many cases; Donaldson *et al.*³ reviewed 21 cases of the syndrome and found that tumours or hyperplasia of the pituitary, adrenals or parathyroids had occurred in 6. While multiple endocrine adenomatosis may be familial, there is as yet no evidence of inheritance in the Zollinger-Ellison syndrome. The involvement of the other glands has some significance, for it has been postulated in some cases that their secretions may be ulcerogenic⁵ and that they may be partly to blame for the gastro-intestinal lesions of the syndrome. In hyperparathyroidism, alimentary symptoms are frequently encountered, and are thought to be produced by the hypercalcaemia, but in addition there appears to be a raised incidence of peptic ulcer;⁶ however, there is rarely anything to suggest the Zollinger-Ellison syndrome in these cases. One case of this syndrome with endocrine adenomatosis has been described where the signs of hyperparathyroidism preceded the development of peptic ulceration.⁵

Although hypoglycaemia stimulates the secretion of HCl, the islet-cell tumours do not contain β -granules and do not secrete insulin. The role of glucagon is more difficult to assess; while some workers have found α -cell granules in the tumours^{3,7} and biochemical evidence of the presence of glucagon or a related substance in the serum,⁵ there was no

teken van oormatige afskeiding van hierdie hormoon by die oorspronklike gevalle nie.¹

Op die oomblik kan die sindroom slegs klinies vermoed en by buikopening gediagnoseer word, en daar is gevalle waar die gewasse, selfs by operasie, nie ontdek kan word tensy die alvleesklier verwyder en oopgesny word nie. Waar daar sonder twyfel alvleeskliergewasse bestaan, moet hierdie orgaan verwyder word; dit kos 'n chirurg moed om die liggaam en stert van 'n oënskynlik gesonde alvleesklier uit te sny hopenende dat hy wel gewasse daarin sal vind. By slegs een geval was dit voldoende om die neoplasma van die alvleesklier te verwyder;⁴ die herhalende swere moet ook behandel word en algehele maagverwydering word aanbeveel ten tyde van die pankreatektomie.⁷ Selfs al is daar uitsaaiing, word hierdie soort snykundige ingreep aanbeveel, aangesien die sekondêre neerslae swak mag afskei;⁷ dit blyk dat die gewasse by ongeveer tweederdes van die gevalle kwaadaardig is en dat uitsaaiing by ongeveer die helfte gevalle ontdek is by diagnose (in die lewe of tydens lykskouing).³

Dit lyk onmoontlik dat hierdie vreemde siekte in verband kan staan met die gewone soort maagsweer, want by die Zollinger-Ellison-sindroom is die oormatige afskeiding van maagsappe abnormaal hoog, die swere is geneig om oor en oor te ontwikkel ten spyte van oënskynlik genoegsame snykundige ingreep, en hulle is ook geneig om op sonderlinge plekke te ontwikkel. Miskien is daar 'n anatomiese 'eksokriene'-verduideliking van die herhaalde voorkoms van verswering in die distale dunderm of boonste jejunum: afskeidings van die eilandsêlgewasse kan in die kliersakkies van die pankreas insyfer en dus *via* die hoof- en newebuise van die pankreas in die derm te lande kom.

Hierdie ingewikkelde sindroom sluit dus baie en interessante onderdele in—maagswere wat oënskynlik veroorsaak word deur hormone, neoplasië in 'n swak verstaande deel van die alvleesklier, veelvuldige endokriengewasse, en diarree. As ons eers die Zollinger-Ellison-sindroom verstaan sal 'n hele paar van ons basiese probleme opgelos word.

evidence of hypersecretion of this hormone in the original cases.¹

At present the syndrome can only be suspected clinically and diagnosed at laparotomy, though in some cases even at operation the tumours may not be found unless the pancreas is removed and sectioned. Where there are undoubted pancreatic tumours that organ should be removed; it takes a courageous surgeon to remove the body and tail of an apparently healthy pancreas in the hope that adenomata are present. In only one case has removal of the pancreatic neoplasm sufficed;⁴ in addition, treatment of the recurrent ulcers is needed, and total gastrectomy is recommended at the same time as pancreatectomy.⁷ Even where there are metastases, surgery of this type is advised, as the secondary deposits may secrete poorly;⁷ it appears that the tumours are malignant in about two-thirds of the cases and that metastases have been found in half of them at the time of diagnosis (during life or at autopsy).³

It does not seem possible to relate this strange disease to the ordinary type of peptic ulcer, because in the Zollinger-Ellison syndrome the level of gastric hypersecretion is abnormally high, the ulcers tend to recur in spite of apparently adequate surgery, and the sites tend to be bizarre. Perhaps the frequency of ulceration in the distal duodenum or upper jejunum has an anatomical 'exocrine' explanation: secretions from the islet-cell tumours may leak into the acinar system of the pancreas and thus enter the bowel *via* the main and accessory pancreatic ducts.

Many interesting components are thus entangled in this complex syndrome—apparently hormonally-induced peptic ulcer, neoplasia of an ill-understood part of the pancreas, multiple endocrine adenomatosis, and diarrhoea. When the Zollinger-Ellison syndrome is understood, we should have answers to a number of basic problems.

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