

INSULIN SECRETING PANCREATIC ADENOMA DEMONSTRATED BY SELECTIVE ANGIOGRAPHY

By D. Singh and S. F. Yu

SYNOPSIS

A case of islet cell adenoma of the pancreas in a 17 year old girl who presented with fits of 6 years duration is described. The tumour was demonstrated by selective angiography and after resection patient made a complete recovery. The values of the various diagnostic procedures for this condition are briefly discussed.

INTRODUCTION

Insulin secreting islet cell tumours of the pancreas are uncommon. Though a few cases have been diagnosed locally, none has been described in the local literature. The clinical manifestations and the diagnostic procedures used are well documented both in textbooks and journals (Miller, D.R., 1965; Whyte, N.G. *et al*, 1966; Bouchier, I.A., 1969; Marks, V. *et al*, 1968). The merits and demerits of the various chemical procedures used are discussed by Marks, V. *et al* (1968).

Selective angiography has not been employed often to diagnose and localize these tumours. They are highly vascular and selective angiography, preferably of the coeliac axis, is of distinct value, especially in the localization of such small tumours (Weissleder, H. *et al*, 1967). However, Pollard and Nebesar (1968) warn against over enthusiasm for making the diagnosis on angiography and they quote that only 20% of these tumours can be diagnosed on the angiogram. This depends largely upon the method of doing pancreatic angiograms. Employing selective angiography, according to Reuter, S.R. and Redman, H.C. (1972) the overall accuracy of angiographic diagnosis is about 60%. Skjoldborg and Madsen (1971) reported 10 consecutive cases of insulinoma; all of them were accurately located before operation by arteriography.

CASE REPORT

A 17 year old female first started having fits at the age of 11 years. She was then investigated and diagnosed as having idiopathic epilepsy and was

Tan Tock Seng Hospital, Singapore.

D. SINGH, M.R.A.C.P., Unit I, Senior Registrar.

S. F. YU, D.M.R.D., Consultant Radiologist, Formerly of ORGH. Now resident in Perth, W.A.

put on Epanutin and Phenobarbitone. Over the years her fits became worse and she was referred to us for further investigations and management.

Patient had given up schooling because of her inability to cope with her studies.

There was no family history of fits or diabetes mellitus.

Clinically she was a cheerful girl though slightly slow mentally. There were no other significant findings on clinical examination. On several occasions the ward staff observed that the patient was either in coma or having an epileptic attack in the early hours of the morning and which responded to intravenous glucose.

Investigations Done

Hb. 13.6 gm.%; TW 3,900; urine FEME: nad, Blood urea 32 mg.%, serum magnesium 2.05 mg.%; serum calcium 8.8 mg.%; L.E. cell test—ve, urine porphyrin—ve; random blood sugar 35 mg.%.
L.P.: C.S.F. clear, under normal pressure, cells 1, chloride 720 mg.%, globulin nil, glucose 25 mg.%, total protein 40 mg.%, C.S.F. VDRL—ve.

Culture: bacteriologically sterile.

Repeat random blood sugar: 36 mg.%.
Blood sugar during fit : 37 mg.%.
. 5 hour fasting G. T. T. :

	Blood Sugar	Urine Sugar
Fasting	40 mg.%	Nil
1st hour	100 mg.%	Nil
2nd hour	80 mg.%	Nil
3rd hour	35 mg.%	Nil
4th hour	35 mg.%	Nil
5th hour	30 mg.%	Nil

Skull and chest X-ray : nad

Selective Coeliac and Mesenteric Arteriogram (Figs. 1 and 2).



Fig. 1.

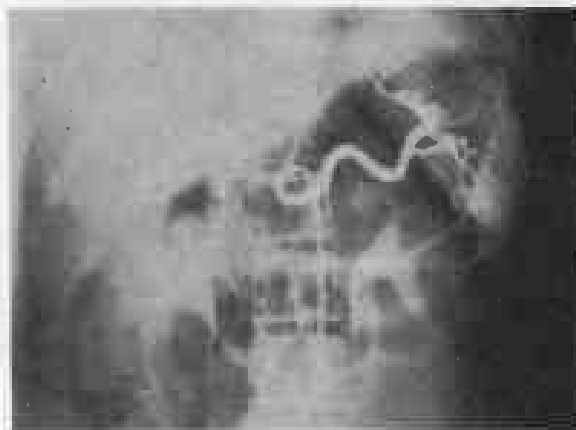


Fig. 2.

Figs. 1 and 2. Tumour arrowed.

Both the coeliac and mesenteric trunks were separately catheterised and injected through the right femoral puncture.

An insulinoma of about 1.5 cm. in diameter was seen in the body of the pancreas. It was lying lateral to the body of the first lumbar vertebra. It was superimposed over the left first transverse process and upper pole of the left kidney. It was vascular and was supplied by the pancreatic branches of the splenic artery. It showed a persistent stain.

Following resection of the tumour, the blood glucose levels rose and symptoms of epilepsy disappeared suggesting that all the tumour tissue was removed.

Patient has remained well on follow up for 2 years.

Histology

Benign islet cell tumour of the Pancreas.

DISCUSSION

Any case of hypoglycaemia should be thoroughly investigated to exclude a surgically treatable cause. Tumours of the islets of Langerhans are clinically the most important cause of hypoglycaemia and the majority of these (85%) are benign adenomas (Marks, V. and Rose, R. C., 1965). Howland and his colleagues in 1929 for the first time reported cure of hypoglycaemia by excision of a benign islet cell tumour.

In insulin secreting adenomas cerebral symptoms predominate over symptoms due to hyperadrenalinism. They are usually repetitive in the same patient and as expected occur most often in the early morning or after fasting. Both features are well illustrated by our patient. There was no family history of diabetes mellitus in our patient though a family history of diabetes has been reported in about 25-30% of patients with functioning islet cell tumours (Principles of Internal Medicine—Harrison's—1970).

Several investigations are available to confirm the diagnosis of an insulin secreting islet cell tumour. The oral glucose tolerance test and the prolonged fast test, with or without exercise, are unreliable. Whipple's triad is indicative, but is non-specific (Marks, V. *et al*, 1968). Our patient in a way fulfilled Whipple's triad: namely symptoms in the morning before breakfast, blood sugars <50 mgm. % and relief of symptoms after intravenous glucose. Intravenous Tolbutamide test (Fajan's, S. S. *et al*, 1961) is useful. It is suggestive but not pathognomonic. A more specific test is the estimation of plasma insulin and blood glucose levels simultaneously following intravenous Tolbutamide (Beason, S. A. and Yalow, R. S., 1961; Samols, E. and Marks, V. 1963). This test usually innocuous is not completely without danger (Davidson, P. C., 1965). The intra-muscular glucagon test which has not been widely used in the diagnosis of insulinoma appears to be safe and useful. False negatives are uncommon and false positives are rare (Mark, V. *et al*, 1968). We were unable to assay the plasma insulin and because of the very low blood glucose levels, we decided not to do the intravenous Tolbutamide test.

There are two procedures available to confirm and localize these tumours. Pancreatic scan has so far proved to be disappointing, whereas selective angiography has been more rewarding. It is proving to be of great value in the diagnosis of pancreatic tumours. The majority of islet-cell tumours are readily detectable angiographically because of their abundant neo-vascularity and dense capillary staining. Tumours as small as 1 cm. in diameter may be demonstrated (Reuter, S. R., Redman H. C.,

1972). Angiographic visualization of the pancreas is achieved by separate successive injection into the coeliac and superior mesenteric arteries, often combined with super selective catheterization of the hepatic, gastro-duodenal, splenic and dorsal pancreatic arteries. No specific complications are associated with this procedure apart from those that can be encountered in per-cutaneous trans-femoral arteriography performed for any purpose (Ferrucci JT *et al*, 1973). To confirm and localize the tumour, we did selective angiography.

Islet cell tumours are usually small (1 - 2 cm.) and difficult to locate at laparotomy. They are distributed equally in the head, body and tail. In Miller's series (1965) of 13 patients, 10 had lesions in the head and neck. To do a distal pancreatectomy when a tumour is not located often fails to cure the hypoglycaemia. Miller, D.R. (1965) advises against a distal pancreatectomy when an adenoma is suspected but not found. On the other hand Whyte, N.G. *et al*, 1966 advocated that hemi-pancreatectomy should be done even if a solitary adenoma is found at laparotomy because multiple tumours are not uncommon. Such drastic surgery does not appear justifiable since only 5-10% of cases have multiple adenomas, which could be distributed anywhere in the pancreas. Skjoldborg & Madsen (71) prefer the most simple surgical procedure viz. resection of the tumour: if the patient is not fully cured, a new angiography and re-exploration would be preferable to extensive dissection at the time of the original operation. We feel that if selective angiography was employed more often with some of the other tests mentioned, then it might help to avoid a difficult and often fruitless exploration and more important, an unnecessary and often useless hemi-pancreatectomy with its resultant morbidity and mortality.

CONCLUSION

A 17 year old girl with fits due to an insulinoma is described. Selective angiography confirmed and

localized the tumour. Resection of the tumour resulted in complete cure. The values of some of the tests used are discussed.

ACKNOWLEDGEMENT

We wish to thank Dr. W. Chan, Sr. Chest Physician and head of Unit I, and Dr. J. Supramaniam, M.S., T.T.S.H. for allowing us to publish this case.

REFERENCES

1. Bouchier, I.A.: "Hormone-secreting tumours of the pancreas." *British J. Clin. Practice.*, 23, 265-69, 1969.
2. Berson, S.A., and Yalow, R.S.: "Plasma insulin in health and diseases." *Amer. J. Med.*, 31, 874, 1961.
3. Davidson, P.C.: *Lancet, Correspondence*. "Insulin secretion and Glucagon." 2, 954, 1965.
4. Fajans, S.S., Schneider, J.M., Schteingart, D.E. and Conn, J.W.: "The diagnostic value of sodium tolbutamide in hypoglycaemic states." *J. Clin. Endo.*, 31, 371-86, 1961.
5. Ferrucci, J.T. and Eaton, S.B.: "Radiology of the Pancreas." *New Eng. J. Med.*, 288, 506-510, 1973.
6. *Harrison's Principles of Internal Medicine*. 6th Edition. McGraw Hill Book Co., p. 543, 1970.
7. Marks, V. and Rose, F.C.: "Hypoglycaemia." Philadelphia: F.A. Davis Co., pp. 86-87, 1965.
8. Marks, V. and Samols, E.: "Glucagon test for insulinoma: a chemical study in 25 cases." *J. Clin. Path.*, 21, 346-52, 1968.
9. Miller, D.R.: "Adenomas of pancreas." *Arch. Surg.*, (Chicago) 90, 509-520, 1965.
10. Pollard, J.J. and Nebesar, R.A.: *New Eng. J. Med.*, 279, 1035, 1968.
11. Reuter, S.R. and Redman, H.C.: "Gastrointestinal Angiography." Philadelphia: WB Saunders Co., 1972.
12. Samols, E. and Mark V.: "Insulin Assay in Insulinomas." *B.M.J.* 1, 507, 1963.
13. Skjoldborg, H. and Madsen, B.: "Selective angiography in surgical management of pancreatic insulinomas." *Acta. Chir. Scand.*, 137, 169-174, 1971.
14. Whyte, N.G. and Jackson, I.M.D.: "Insulin—Secreting adenoma of the pancreas." *Scot. Med. J.*, 11, 7-13, 1966.
15. Weissleder, H., Radiker, U., Niemann, H. and Emmrick, J.: "Pancreas Diagnosis with selective angiography." *Rontgenblatter*, 20, 501-511, 1967. (In German).