Hiroshima Journal of Medical Sciences
Vol.34, No.2, 247~252, June, 1985
HIJM 34-34

Surgical Treatment for Insulinoma: a Study of 6 Cases

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(Received March 25, 1985)

Key words: Insulinoma

ABSTRACT

The authors treated six patients with insulinoma in our department during a period up to 1984, and performed seven operations including one re-operation. In this paper, the results of our study of the clinical symptoms, diagnosis and surgical formula in these cases are presented. Selective angiography and percutaneous transhepatic portal venous sampling (PTPVS) proved useful for pre-operative tumor localization diagnosis. Blood glucose monitoring during operation became a good index for the selection of the surgical formula. In the cases of surfacial and single tumors, enucleation alone was able to obtain satisfactory surgical results. In the cases, however, when re-operative, deep or multiple tumors were suspected, staged distal pancreatectomy under blood glucose monitoring was considered to be indicated. It was therefore thought that the preservation of the pancreas should be made as far as possible.

Since Graham et al[5] reported in 1929 about one case of operation on a single functional β-islet cell adenoma, more than 1450 cases of insulinoma have so far been reported by various researchers. In recent years, the clinical diagnosis of insulinoma can be made rather easily, but several points including the pre-operative and intraoperative tumor localization diagnosis, selection of the surgical formula and complications, still remain unsettled. In the present study, the authors investigated the surgical cases of insulinoma performed in our department regarding their clinical symptoms, diagnoses before and during operation, and surgical formulas.

MATERIALS AND METHODS

The subjects were six patients (seven operations) for whom the operation was performed in our department during the 16-year period up to 1984. Their ages ranged from 35 to 70 years, and the sex ratio was 2 males and 4 females. In these patients, clinical symptoms up to admission, pre-operative clinical diagnosis, provocative test, and rate of correct diagnosis of pre-operative various tumor localization diagnosis were examined, and number of tumors, size, site, surgical formulas for the regions, blood glucose monitoring and surgical results were studied in each individual case.

RESULTS

In all the cases, the main clinical symptoms were unconsciousness, dazed condition, asthenia, lalopathy, and other neuropsychiatric symptoms, and two cases were diagnosed to be psychogenic diseases. In other two patients, gastroenterologic symptoms including upper abdominal pain, nausea and diarrhea were noted. The ailing period extended from 10 months to 15 long years. All patients proved Whipple's triad positive at admission, and the lowest blood glucose level was 3-26mg/dl; (Table I). In all the patients, the ratio of the blood IRI level: blood sugar level (IRI: B.S.) was over 0.3.

In the provocative test, high positive rates, including the prolonged fasting test 5/5 (100%),

Table I. Clinical feature of insulinoma

Case No.	Age.Sex	Principal symptoms	Duration of symptoms	Whipple's triad	Lowest blood glucose level (mg/dl)
1	35•f	Neuropsychiatric & Gastroenterologic symptoms	3yr & 3mo	Present	17
2	69•m	Neuropsychiatric symptoms	10mo	Present	22
3	70•f	Neuropsychiatric symptoms	3yr & 3mo	Present	26
4	69•f	Neuropsychiatric symptoms	1yr	Present	20
5	39•m	Neuropsychiatric & Gastroenterologic symptoms	4yr	Present	26
6-I	58•f	Neuropsychiatric symptoms	15yr	Present	16
6-II	59•f	Neuropsychiatric symptoms	6mo	Present	3

Table II. Diagnosis of insulinoma

Case No.	Age.Sex	Fasting			Provocative tests			
		B.S. mg/dl	IRI μU/ml	IRI/B.S.	Prolonged fasting test	Tolbutamide	Glucagon	Leucine
1	35•f	28	47	0.6	+	N.D.	N.D.	N.D.
2	69•m	22	51	2.3	N.D.	N.D.	+	+
3	70•f	38	15	0.4	N.D.	+	—	+
4	69•f	45	121	2.7	+	+	N.D.	N.D.
5	39•m	27	31	1.1	+	+	+	+
6-I	58•f	44	24	0.5	+	N.D.	N.D.	+
6-II	59•f	59	49	0.8	+	N.D.	+	N.D.
Positive rate (%)					5/5 (100)	3/3 (100)	3/4 (75)	4/4 (100)

+: Positive, —: Negative, N.D.: Not done

Table III. Results with preoperative examinations

Case No.	No, Size(cm), Site	Angio.	PTPVS	U.S.	CT	Scinti.	ERCP
1	Single adenoma, 3.5×3×3, tail	−	N.D.	N.D.	N.D.	−	N.D.
2	Single adenoma, 3×2.5×1.5, tail	+	N.D.	N.D.	N.D.	−	N.D.
3	Single adenoma, 1.5×1×1, body	−	N.D.	N.D.	N.D.	−	−
4	Single adenoma, 1×1×1, body	+	N.D.	N.D.	N.D.	−	−
5	Single adenoma, 0.8×0.8, head	−	+	−	−	−	−
6-I	Single adenoma, 1.5×1×1, head	−	+	−	−	−	−
6-II	Multiple adenomas, 0.1~1.7×1.5×1, head~tail	+	− • +	+	−	−	−
Positive rate (%)		3/7 (43)	3/4 (75)	1/3 (33)	0/3 (0)	0/7 (0)	0/4 (0)

PTPVS: Percutaneous transhepatic portal venous sampling.
+: Positive, −: Negative, N.D.: Not done

Table IV. Surgical treatment and results

Case No.	No. Size(cm), Site	Type of operation	Glucose monitoring	Results	Long term follow-up
1	Single adenoma, 3.5×3×3, tail	Enucleation	+	Cure	Died at 2yr due to duodenal perforation
2	Single adenoma, 3×2.5×1.5, tail	Enucleation	+	Cure	Healthy at 12 yr
3	Single adenoma, 1.5×1×1, body	Enucleation	+	Cure	Healthy at 8yr & 9mo
4	Single adenoma, 1×1×1, body	Enucleation	+	Cure	Died at 1yr & 10mo due to hepatic failure
5	Single adenoma, 0.8×0.8, head	80% distal resection	+	Cure	Healthy at 3yr & 11mo, I.G.T.
6-I	Single adenoma, 1.5×1×1, head	Enucleation	−	Cure	Recurrence of hypoglycemic attack at 7mo
6-II	Multiple adenomas, 0.1~1.7×1.5×1, head~tail	80% distal resection	+	Cure	No symptom according to hyperinsulisms, I.G.T.

+: Positive responce, −: Negative responce, I.G.T. : Impaired glucose tolerance.

tolbutamide tolerance test 3/3 (100%), glucagon test 3/4 (75%) and L-leucine tolerance test 4/4 (100%) were observed (Table II). The rates of correct diagnosis of the pre-operative various tumor localization diagnosis proved to be angiography 3/7 (43%), PTPVS 3/4 (75%) and ultrasonography 1/3 (33%) (Table III).

The cases 1, 2, 3, 4, 5 and 6-I had single adenoma, and the diameter of the tumors ranged from 0.8 cm to 3.5 cm, and the sites included 2 cases at the head, 2 cases at the body and 2 cases at the tail. The case 6-II was a case of re-operation, being multiple adenomas, and the tumors in the sizes of 0.1 cm to 1.7 cm were observed over the whole pancreas.

Since the cases 1, 2, 3 and 4 were surfacial tumors, enucleation was given, whereas case 5 was a re-laparotomized case, and the tumor was not easy to discover, so that staged distal pancreatectomy was performed (Table IV). In the above five cases, hyperglycemic rebound was found by blood glucose monitoring during the operation (Fig. I). In case 6, enucleation was given at the first operation (6-I), but hyperglycemic rebound was not shown. In the re-operation (6-II) performed in about 7 months, it was found to be a multiple tumor, and 80% distal pancreatectomy was given, and hyperglycemic rebound was shown (Fig. II).

In the long-term follow-up, one patient was found to be dead due to perforation by duodenal ulcer, and the other died of hepatic failure. In two patients out of the remaining four, impaired glucose tolerance at 75g-OGTT was noted.

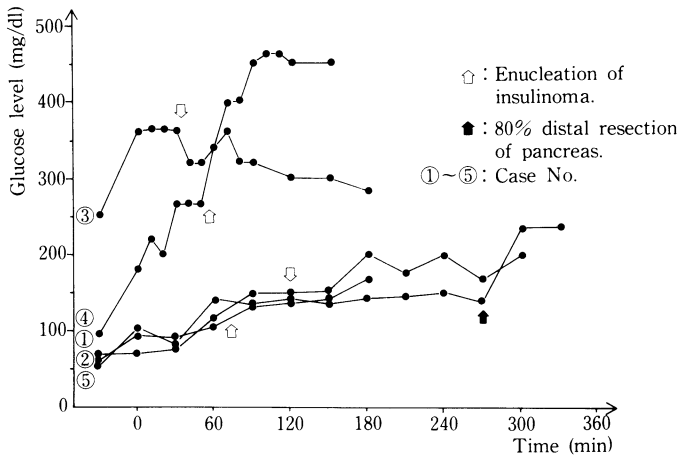

Fig. I. Blood glucose monitoring during operation

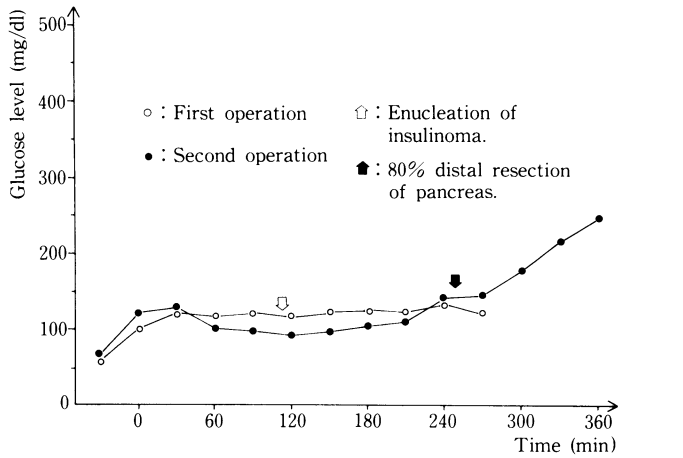

Fig. II. Blood glucose monitoring during operation of case 6

DISCUSSION

According to the summation made by Stefanini et al[11] (1973), among 951 patients with insulinoma, 84% were benign tumors, while 16% were malignant tumors, and 83% were single-onset and 13% were multiple, the remaining 4% being multiple endocrine adenomatosis (MEN)[1,7]. They added that malignant tumors contained 10% of multiple ones. In the cases of the authors' own, cases 1, 2, 3 and 4 were easily recognizable to be surfacial and single-onset tumors, and blood glucose monitoring after enucleation noted hyperglycemic rebound. The prognosis was satisfactory.

According to Stefanini et al[11], the mortality was 6.7% after the first operation and 18% after the second operation, so that the risk after the second operation was trebled. As has been explained so far, the majority of insulinoma can be regarded as a disease with good prognosis, provided that the enucleation of the tumor can be made without fail. In the cases of re-operations, as well as deep-rooted tumors and multiple tumors, however, operations should be performed quite cautiously.

Among the cases treated by the authors, in case 5 at re-operation, the tumor was deep-rooted, so that staged distal pancreatectomy was performed under blood glucose monitoring. As a result the tumor was resected by 80% distal resection. On the other hand, in case 6 at the initial operation (6—I), we were able to discover the surfacial and single-onset tumor quite easily, and enucleation was given. However, blood glucose monitoring failed to discover hyperglycemic rebound. Although the post-operative blood glucose level remained normal, hypoglycemic episodes occurred in about 7 months, and the second operation detected multiple tumors over the whole pancreas, so that 80% distal pancreatectomy was given and hyperglycemic rebound was noted. Although the prognosis of this case has been good, careful observation of the further progress has to be made in view of the fact that it has been multiple tumors.

What is important for surgical treatment of insulinoma is how to perform radical resection of the tumor, rather than how the technique should be. In other words, the important point is whether accurate tumor localization diagnosis before and during operation is given, and whether the tumor is resected without fail.

In the reports[2-4,6,8-10] made by various researchers concerning various graphic diagnostic methods, the rate of accurate diagnosis with angiograhy achieved the best record of 60-70%, followed by PTPVS. In the patients treated by the authors, the rate of accurate diagnosis of angiography was 43% (3/7), while PTPVS was given to 2 patients out of 4 who proved negative, and the rate of accurate diagnosis was 75% (3/4) in them, providing us with influential information for tumor localization diagnosis.

As an auxiliary method for the evaluation whether the tumor is resected or not during operation, we have blood glucose monitoring. According to Tutt et al[13], 23% of their patients did not show hyperglycemic rebound during operation. However, since the majority of these patients showed the normalization of their blood glucose levels after operation, they were regarded as false negative cases. In our own cases, the positive rate of blood glucose monitoring was 86% (6/7), and this inspection system can be considered to be useful. In 1981 Teichmann et al[12] gave a monitoring to their patients on the rapid determination method of IRI during operation, and found it effective, so that the usefulness of monitoring may henceforth be considered more highly.

REFERENCE

1. **Brunt, L.M. and Wells, S.A.Jr.** 1983. The multiple endocrine neoplasia syndrome. Ann. Chir. Gynaeco. **72:** 153-159.
2. **Dunn, D.C.** 1971. Diabetes after removal of insulin tumor of pancreas; A long-term follow-up survey of 11 patients. Br. Med. J. **2:** 84-87.
3. **Fajans, S.S. and Floyd, J.C.Jr.** 1975. Differential diagnosis of spontaneous hyperglycemia, P.453-478. *In* L.T. Kryston (ed.), In endocrinology and Diabetes. Grune and Statton, New York.
4. **Galbut, D.L. and Markowitz, A.M.** 1980. Insulinoma; Diagnosis, surgical management and long-term follow-up. Am. J. Surg. **139:** 682-687.
5. **Howland, G. and Campbell, W.R.** 1929. Dysinsulinism; convulsions and coma due to islet cell tumor of pancreas, with operation and cure. JAMA **93:** 674-680.
6. **Glickman, M.H., Hart, M.J. and White, T.T.** 1980. Insulinoma in Siattle; 39 cases in 30 years. Am. J. Surg. **140:** 119-126.
7. **Hashizume, K. and Yamada, T.** 1983. Multiple endocrine neoplasia MEN-type I. Nippon Rinsho

41: 1279-1285.

8. **Ingemansson, S. and Lunderquist, A.** 1975. Portal and pancreatic vein catheterization with radioimmunologic determination of insulin. Surg. Gynecol. Obstet. **141:** 705-711.
9. **Ohashi, M. and Maruge, K.** 1983. Insulinoma diagnosed by percutaneous portal vein catheterization. Horumon To Rinsho **31:** 158-160.
10. **Rayfield, E.J. and Goldberge, K.** 1983. Transportal blood sampling for pre-operative localization of insulinoma. Mt. Sinai J. Med. **50:** 258-262.
11. **Stefanini, P. and Carboni, M.** 1974. Beta-islet cell tumors of pancreas; Results of a study on 1067 cases. Surgery **75:** 597-609.
12. **Teichmann, R.K. and Spelsberg, F.** 1982. Intraoperative biochemical localization of insulinomas by quick radioimmunoassay. Am. J. Surg. **143:** 113-115.
13. **Tutt, G.O., Edis, A.J. and Service, F.J.** 1980. Plasma glucose monitoring during operation for insulinoma; a critical reappraisal. Surgery **88:** 351-356.