INSULINOMA: A MULTICENTER AND RETROSPECTIVE ANALYSIS OF THE SPANISH EXPERIENCE DURING THREE DECADES

Endocrine tumors
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INTRODUCTION

Insulinoma (annual incidence, 4 cases per million inhabitants) is the most common functioning pancreatic neuroendocrine tumor. The series of insulinoma reported in Spain are scarce and have been usually performed in a small number of patients (<10) from a single hospital.

OBJECTIVE

The aim of our study has been to retrospectively review a series of patients with insulinoma from our area studied and followed over the past 30 years.

PATIENTS AND METHODS

Retrospective study of all insulinomas diagnosed at the departments of Endocrinology in four Spanish hospitals: Ramón y Cajal (Madrid), Virgen de la Concha (Zamora), Nuestra Señora de Sonsoles (Avila) and Hospital General (Segovia).

Inclusion criteria were histological demonstration of tumor and/or the presence of biochemical and morphological criteria compatible with insulinoma. In each patient clinical, hormonal, diagnostic and therapeutic data were registered.

RESULTS

Demographic data

The distribution of patients according to study hospitals were: Hospital Ramón y Cajal, Madrid (n = 19, 9 of them belonging to the health area and 10 from other hospitals); Hospital Virgen de la Concha, Zamora (n = 5); hospital Nuestra Señora de Sonsoles, Avila (n= 3); and Hospital General Segovia (n = 2). A positive correlation between the number of insulinomas diagnosed in each hospital and the number of inhabitants for the health area of each center was found (Figure 1).

Figure 1. Correlation between number of cases of insulinoma diagnosed in the last 30 years and population per hospital health area (r=0,967; p=0,033).

Clinical data

Twenty nine patients [23 women (79.3%); mean age 48.7 ± 17.4 years (range, 16-74), body mass index 28.5 ± 5.6 kg / m2 (range, 22.9 to 45.8)] were studied. Most of them (41.4%) were diagnosed at 50-70 years (Figure 2A).

The majority (n=18, 62.1%) of patients showed fasting hypoglycemia, about a third (31%) both fasting hypoglycemia and postprandial, and 6.9% only postprandial hypoglycemia (Figure 2B).

The tumor was sporadic in 26 (89.7%) patients and in 3 (all women) associated to MEN 1. Three patients (10.3%, 2 women) had multiple insulinomas and 2 (6.9%) patients (2 women of 48 and 65, respectively) had malignant insulinomas, both sporadic.

Hormonal and localizing study

Blood glucose, insulin and C-peptide are shown in Table 1. Glucagon test for glucose after fasting was performed in 4 patients (Figure 3).

Localizing study located the insulinoma in all patients except one (n = 28, 96.5%) with MEN. Abdominal CT detected 21 cases (71.4%; sensitivity 95.4%). The rest was discovered by endoscopic ultrasonography (n = 3), MRI (n=1), 68Ga-DOTA-exendin-4 PET/CT (n=1), intraarterial injection of calcium (n=1) and intraoperative ultrasonography (n=1). The diagnostic sensitivity for echo-endoscopy, abdominal ultrasonography and intraoperative MRI in our study was 85%, 75% and 40%, respectively.

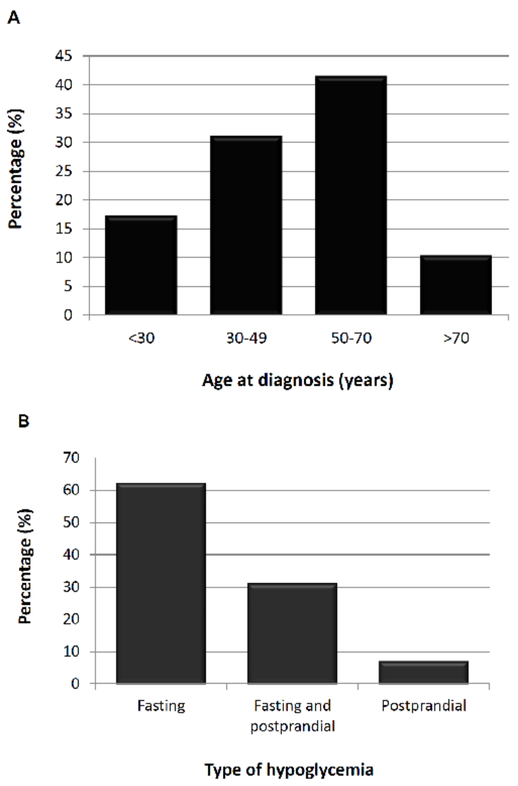

Figure 2. Percentage distribution of 29 patients with insulinoma according to age at diagnosis (A) and type of hypoglycemia (B).

Table 1. Blood glucose, insulin and C-peptide at baseline at diagnosis, at the end of the prolonged fasting (72h) test and in the latest clinical visit.

	Baseline at diagnosis	Fasting test (72 h)	Baseline at last clinical visit[a]
Glucose (mg/dl)	64,1 ± 22,3	37,3 ± 6,5***	102,8 ± 26,0***
Insulin (μU/ml)	24,4 ± 24,5	25 ± 20,3	10,2 ± 15,3**
C-peptide (ng/ml)	3,17 ± 1,86	3,17 ± 1,54	1,74 ± 1,30*
Nadir time (h)		9,0 ± 4,4	

*p<0,05; **p<0,01;***p<0,001 frente al valor basal al diagnóstico
[a]Time to last clinical visit: median, 53 months; range 1-378.
Normal range: Glycemia 80-120 mg/dl; insulinemia 5-25 μU/ml; and C-peptide 0,5 a 2,0 ng/ml

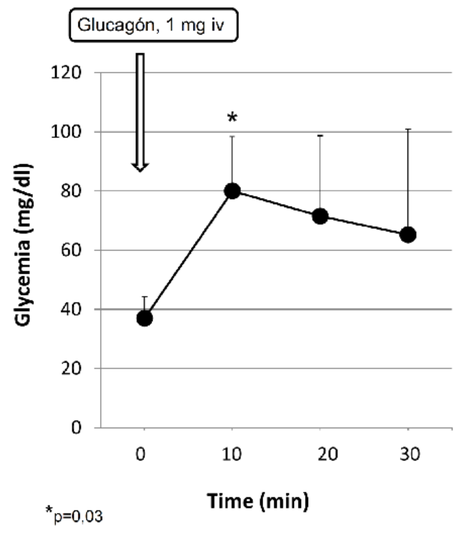

Figure 3. Serum glucose response to glucagon (1 mg iv) after fasting in 4 patients with insulinoma.

Table 2. Data related to the tumor.

		Number	Percentage (%)
Localization	Head	11	37,9
	Body	13	44,8
	Tale	4	13,8
	Ectópic	1	3,4
Multifocality	Single	26	89,7
	Multiple	3	10,3
Malignant	No	27	93,1
	Yes	2	10,3
TNM staging	IA	23	88,5
	IB	2	7,7
	IV	1	3,8
Classification (OMS, 2010)	G1	21	77,8
	G2	4	15,4
	G3	1	3,8
Size, mean ± SD (cm)		1,70 ± 0,71 (range, 1-4)	

Table 3. Data related to therapeutic results and clinical outcome.

	Number	Percentage (%)
Surgical intervention	27	93,1
Curative surgery	24	88,9
Reintervención	3	11,1
Liver transplantation	1	3,5
Tumor-related mortality	1	3,5
Time of follow-up, mean ± SD (months)	76,7 ± 86,2 (range, 1-378)	

Therapy

Most patients (n=27, 93.1%) underwent surgery (median time from diagnosis to surgery, 4 months, interquartile range 2-7 months). Data related to the tumor and therapeutic results are shown in tables 2 and 3.

Clinical follow-up

Clinical follow-up was performed in 25 patients (86.2%) for 76.7 ± 86.2 months (median, 53 months; range, 1-378). Data related to the clinical outcome are shown in table 3.

CONCLUSION

This is the larger series of insulinoma reported in Spanish patients. Insulinoma is a very rare tumor, usually benign, small and solitary, affecting women more frequently between 45-50 years which is habitually located with abdominal CT. Surgery by enucleation is the most commonly used surgical technique achieving a high cure rate.

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