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Original Research

Adrenal ganglioneuroma: The Padua Endocrine Surgery Unit experience

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HIGHLIGHTS

- Adrenal ganglioneuromas (AGN) are benign, and rare tumors.
- The preoperative diagnosis is challenging and cannot be achieved by imaging techniques.
- AGN are hormonally silent and asymptomatic in most cases.
- Laparoscopic adrenalectomy may achieve a definitive cure.

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ABSTRACT

Background: Adrenal ganglioneuroma (AGN) is a rare tumor that originates from the gangliar cells of the sympathetic nervous system. It represents less than 5% of all adrenal masses. AGN occurs as a large mass, with benign behavior and no relevant symptoms and hormonal secretion, but it is often misdiagnosed because the preoperative radiological diagnosis is generally challenging. The aim of the present paper is to report the experience of a tertiary referral academic center regarding the management of AGN and review the relevant literature.

Methods: The demographic, diagnostic, surgical, and pathological findings of 666 consecutive patients who were adrenalectomized at the Padua Endocrine Surgery Unit between 1990 and 2015 were retrospectively reviewed in order to focus on AGN.

Results: The pathology confirmed AGN in 10 patients (1.5% of cases; median age 35 years, range 19–73). The diagnosis was incidental and never available before surgery. Eight patients were asymptomatic, two presented lower back and abdominal pain. The mass was non-secreting in all cases. Preoperative imaging techniques were inconclusive about the nature of the mass in all cases. The median size of the tumor was 55 mm (range 30–80). The laparoscopic approach was performed in 60% of cases. No recurrences occurred after surgery at a median follow-up of 10 years (range 1.7–18.2).

Conclusion: The diagnosis of AGN may be challenging and most often occurs after surgery, since it is frequently confirmed by histological examination. Radical excision may be achieved by laparoscopic adrenalectomy, with a subsequent definitive cure and excellent prognosis at long term follow up.

1. Introduction

Ganglioneuromas are benign neoplasms originating from the neural crest and composed of gangliar cells, mature Schwann cells and nerve fibers. The adrenal gland represents the most frequently involved site (30% of cases), followed by sympathetic ganglia in mediastinum (21.8%), retroperitoneum (20.8%) and neck (10.9%) [1]. However, adrenal ganglioneuromas (AGN) are rare, representing less than 5% of adrenal tumors [2]; they are usually sporadic, but can also be associated with some hereditary endocrine diseases (Neurofibromatosis type 1 and Multiple Endocrine Neoplasia type 2) [2,3]. AGN may be present with symptoms related to mass effect (abdominal pain); most often they are asymptomatic and

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Table 1
Patients (n = 666) undergoing adrenal surgery at Padua Endocrine Surgery Unit (1990–2015).

Adrenal diseases	Patients (n)
Aldosterone-producing tumor (Conn disease)	182
Adrenocorticotrophin-dependent or independent hypercortisolism (Cushing's disease/syndrome)	154
Androgen secreting adenoma	5
Pheochromocytoma/Paraganglioma	114
Primary and secondary adrenal malignancies	87
Non-secreting benign adrenal tumors	124

discovered incidentally at imaging techniques [3]. The preoperative diagnosis of AGN is often difficult and very challenging due to the lack of biochemical markers and specific hormonal release, and because imaging techniques do not allow preoperative differential diagnosis. Therefore, AGN are often misdiagnosed [4], and a definitive diagnosis can be achieved only by histopathology [5]. Because of its rarity, only a few case-reports and some limited case-series are available in literature; therefore, information regarding the diagnosis and the management of AGN are limited.

The aim of the present paper is to review the experience of a tertiary referral academic center regarding diagnostic and therapeutic management of AGN; it also includes a review of the literature, in order to provide clinicians with information concerning this uncommon tumor.

2. Materials and methods

The present retrospective study focused on patients who underwent adrenalectomy for histologically confirmed AGN, selected among 666 surgically treated patients with adrenal disease at the Endocrine Surgery Unit, University of Padua, Italy, between 1990 and 2015 (Table 1).

Inpatient and outpatient medical records were reviewed to gather the relevant demographic, clinical and laboratory hormonal assessment (including adrenocorticotrophin (ACTH), urinary daily free cortisol levels, aldosterone/renin ratio, daily urinary cathecolamines/metanephrines levels), the results of the preoperative imaging studies, the operative approach, and pathology finding. Outcomes and postoperative follow-up data were also assessed according to the last available medical record, and further verified by phone interview with each available patient.

The study was conducted according to the PROCESS criteria [6].

Results are expressed as absolute numbers, percentages, mean, median and range. No further statistical elaborations were performed because of the scarcity of cases.

3. Results

Final pathology revealed AGN in 10 patients (6 women and 4 men; median age at diagnosis 35 years, range 19–73), who underwent laparotomic adrenalectomy in 4 cases and laparoscopic transperitoneal adrenalectomy via lateral approach in 6 cases (Table 2). The right adrenal gland was most frequently involved (80% of cases).

In 8 patients the diagnosis was incidental, since no relevant symptoms directly related to the mass were present; in two patients relevant lower back or abdominal pain was present which referred to the mass since it disappeared after adrenalectomy. None of the patients had clinical symptoms of adrenal hyperfunction, or presented elevation of cathecolamines, aldosterone/renin ratio or abnormal corticosteroid secretion, except one patient who exhibited moderately increased levels of urinary cortisol excretion associated with permanently suppressed ACTH levels.

Four patients underwent a preoperative computed tomography (CT) scan and magnetic resonance imaging (MRI), one patient underwent only MRI and five patients only a CT scan. The CT scan described a homogenous, hypodense and well circumscribed mass, with a mean density of >10 HU, without any changes on the

Table 2
Main features of 10 patients undergoing surgery for adrenal ganglioneuroma.

Age	Sex	Symptoms	Adrenal hormonal secretion	Tumor size (mm)	Therapy	Imaging techniques	Follow-up (months) and outcome
35	M	none	normal	40	R laparotomic adrenalectomy	CT scan + MIBG scintigraphy	Not available
73	M	none	normal	80	R laparotomic adrenalectomy	CT scan + MIBG scintigraphy	Not available
19	F	none	normal	62	R laparotomic adrenalectomy	CT scan	Not available
45	F	none	normal	60	R laparotomic adrenalectomy	CT scan	218 no recurrence
31	F	none	normal	50	R laparoscopic adrenalectomy	CT + MRI	186 no recurrence
23	M	lower back pain	normal	70	L laparoscopic adrenalectomy	CT + MRI + MIBG scintigraphy + 18-FDG-PET	125 no recurrence
35	F	none	normal	40	L laparoscopic adrenalectomy	CT scan	114 no recurrence
43	F	none	high levels of urinary cortisol; suppressed ACTH	30[a]	R laparoscopic adrenalectomy	MRI	111 no recurrence
35	F	abdominal pain	normal	70	R laparoscopic adrenalectomy	CT + MRI+ 18-FDG-PET	48 no recurrence
39	M	none	normal	50	R laparoscopic adrenalectomy	CT + MRI+ 18-FDG-PET	20 no recurrence

M male; F female; R Right; L Left; CT computed tomography; MRI magnetic resonance imaging; 18-FDG-PET Positron Emission Tomography with F-18 Fluorodeoxyglucose; MIBG metaiodobenzylguanidine scan.

[a] An additional 17 mm cortical adenoma responsible for a subclinical hypercortisolism was present.