Adrenal Ganglioneuromas: Experience from a Retrospective Study in a Chinese Population

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Purpose: Ganglioneuromas (GNs) are benign neoplasms of combined neural crest, schwannian, and connective tissue origin, occurring rarely in the adrenal glands. The present study is to share our experience regarding diagnostic and therapeutic management of these tumors.

Materials and Methods: Adrenal GNs of 15 patients were found incidentally with ultrasonography and were evaluated subsequently with computed tomography (CT) scan. Clinical data as well as follow-up data were collected retrospectively. All the patients received operative resection.

Results: The mean age of the patients was 38.4 years (range, 25-52 years; male to female ratio, 2:1). Of study subjects 11 patients had unilateral GN on the right side, and the remaining 4 on the left side. All but 1 patient were asymptomatic. No hormonal secretion was apparent. Mean size of the tumors in CT scan was 6.27 cm (range, 2.5-14 cm), while 10 were larger than 5 cm. Eight patients underwent open adrenalectomy and the remaining 7 underwent laparoscopic anterior adrenalectomy. Histologically, all 15 neoplasms were completely differentiated, mature GN. We had no mortality or significant morbidity. Mean duration of hospitalization was 5.5 days (range, 3-7 days). There was no recurrence, during a mean follow-up of 5.4 years (range, 1-10 years).

Conclusion: Pre-operative diagnosis of adrenal GNs remains difficult merely according to physical examination. Therefore, we recommend complete operative resection once malignancy cannot be excluded by pre-operative analyses. Laparoscopic adrenalectomy is a reasonable option, at least for tumors ≤ 5 cm.

Keywords: adrenal gland neoplasms; ganglioneuroma; pathology; diagnosis; humans.

INTRODUCTION

Ganglioneuromas (GNs) are benign neoplasms mainly originating from retroperitoneum and posterior mediastinum and less frequently in the adrenals, and are considered to occur more frequently in children or young adults.[1-6] Clinically, adrenal ganglioneuromas, usually hormonally non-secreting, may be often incidentally found in radiologic finding without any symptoms or present secondary to pressure effects on adjacent structures. Therefore, the size of adrenal GNs is larger than those of their more common counterparts in the posterior mediastinum.[7-9] The aim of this study is to share our experience regarding delineate the clinical course, diagnostic imaging, and operative treatment of primary adrenal ganglioneuromas in adults in China.

MATERIALS AND METHODS

Between June 1997 and June 2011, a total of 15 patients with histologically proven adrenal incidentalomas were admitted to Department of Urology in Huashan Hospital and its Nanhui Branch of Fudan University, Shanghai, China (Table). Their clinical data were collected retrospectively, as well as follow-up data. All the patients were found with ultrasonography and were evaluated subsequently with computed tomography (CT) scan. To evaluate the functional status of the adrenal tumors, biochemical and hormonal screening was carried out in all patients. The study protocol involving human materials were approved by the Institutional Ethic Committee of Huashan Hospital and its Nanhui Branch.

RESULTS

Clinical Findings

The mean age of the patients was 38.4 years (range, 25-52 years; male to female ratio, 2:1). All but 1 patient were asymptomatic. As shown in the Table, patient 4 had complaints of atypical upper abdominal pain and a 14-cm adrenal mass was found during ultrasonographic investigation. No hormonal secretion was apparent. Hormonal evaluation revealed that catecholamine level was within the normal range in all cases. All the 15 cases in our series had normokalemia.

Imaging Findings

All neoplasms were reported as unilateral adrenal lesions and seven of ten were right sided in CT scan. Mean size was 6.27 cm (range, 2.5-14 cm), while 10 were larger than 5 cm (Table). All cases had a solid appearance and low unenhanced attenuation value, up to 30 Hounsfield units (HU). Contrast enhanced CT scan showed increased attenuation of 40 HU in 1. Masses surround but not infiltrate main aortas and/or vein in CT scan and arteriography (patient 4; Figures 1, A, B, C and D). None was shown with calcification. Arteriography in this patient showed that the mass did not invade the kidney artery. The remaining neoplasms were homogeneous. CT scan showed evidences neither of surrounding tissue infiltration nor regional lymph node enlargement.

Treatment

All patients underwent complete resections, 8 open and 7 laparoscopic adrenalectomies. Mean operative time of open procedures was 90 min (range, 65-150 min). All laparoscopies were completed without conversion. Mean laparoscopic operative time was 104 min (range, 70-200 min).

There was no mortality, minor morbidity or complications in our patients. No patient needed blood transfusion. Mean duration of hospitalization was 5.5 days (range, 3-7 days). There was no recurrence, during a mean follow-up of 5.4 years (range, 1-10 years). The abdominal pain of patient 4 was relieved after the adrenalectomy. In the procedure of patient 4, the tumor was found to conglutinate with posterior wall of inferior vena cava, upper pole of right kidney, right erector spinae and part of the liver. After complete resection of the mass, regional lymph node between inferior vena cava and aorta was found to be enlargement and gather into a mass. It was impossible to completely separate the lymph node from the vein. Therefore, one lymph node was removed to histopathology. No blood pressure fluctuation was found in all the surgery procedures.

Histopathology

Mean tumor size on pathologic examination was 6.93 cm (range, 3-15 cm) on maximum diameter, while the mean radiologic preoperative size of 6.27 cm. All tumors were nodular and well encapsulated. The cut surface was stramineous in 6 cases and tan-white in 9 cases. Eight tumors were hard as rubber; the remaining two tumors were soft. Microscopically, all neoplasms consisted of fascicles of Schwann-like cells and dispersed mature ganglion cells (Figure 2). No neoplasm showed immature neuroblastic cells or areas of pheochromocytoma. No calcifications were found.

In patient 4, the neoplasm macroscopically seemed to destruct the surrounding gland (Figure 3). One lymph node was removed from that patient and the histopathology showed mature gangli-

Table. Clinical and imaging features of the series.

Patient	Gender	Age (years)	Symptom	CT Size	Pre Contrast HU	Post Contrast HU	Functiona Status	Surgical Technique	Histological Size (cm)
1	F	45	None	(cm)	<30	<30	None	Laparoscopic	3
2	M	30	None	2.5	<30	<30	None	Laparoscopic	5
3	M	33	None	5	30	30	None	Open anterior	14
4	M	25	Abdominal pain	12	<30	40	None	Open anterior	15
5	F	41	None	14	<30	<30	None	Laparoscopic	3
6	F	44	None	3	<30	<30	None	Open anterior	8
7	M	49	None	7	<30	<30	None	Open anterior	7
8	F	52	None	6.5	30	30	None	Open anterior	8
9	M	29	None	8	<30	<30	None	Laparoscopic	5
10	M	38	None	4.5	<30	<30	None	Open anterior	5
11	M	31	None	5	<30	<30	None	Laparoscopic	4
12	F	33	None	4	<30	<30	None	Laparoscopic	4
13	M	45	None	3.5	<30	<30	None	Laparoscopic	5
14	M	40	None	4	<30	<30	None	Open anterior	9
15	M	41	None	8	<30	<30	None	Open anterior	9

Keys: M, male; F, female; CT, computerized tomography; HU, Hounsfield Unit.

on cells. Immunohistochemistry was employed in patients 3 and 4, showing positive staining of ganglion cells for neuron-specific enolase (NSE) (Figure 4), synaptophysin and positive staining of Schwann cell-specific marker (S100) (Figure 5).

DISSCUSSION

Neoplasms of ganglion cell origin include neuroblastomas, ganglioneuroblastomas, and GNS, among which GNs are benign neoplasms of combined neural crest, schwannian, and connective tissue origin. GNs are considered to occur more frequently in children or young adults. The largest series of primary GNs came from the Enzinger and colleagues, where 42% of their patients were less than 20 years old in a series of 88 GN patients.[1] Other studies also had similar results.[2-6] However, only 20% (3/15) were ≤ 30 years old (mean, 38.4 years) in our series, which is concordant with other studies where the mean age at diagnosis to be around 39 to 50 years.[8-10] In fact, this adrenal pathology can affect all age groups, including older patients, because GN patients are usually asymptomatic and without physical examinations it is difficult to find GNs for other medical problems. Occasionally GNs may produce nonspecific, mass-related symptoms, as in patient 4. GNs may secrete catecholamine often in pediatric ganglioneuromas and neuroblastomas,[4,11] but rarely in mature GNs,[8-10,12] which is consistent with our findings.

Radiologic diagnosis of adrenal GN on CT scan have been well described that low attenuated (non-enhanced attenuation below 40 HU), homogeneous masses which demonstrate slight to moderate enhancement,[5,6,10] and often surround but not infiltrate main aortas and/or vein. Our series also showed this feature even in arteriography. Approximate 2.4 to 60% of GN cases with calcifications have been reported in the literatures.[13-15] In our series, there was no calcification.

It is reported that radiologic findings are apt to underestimate tumor size. In our series, the mean radiologic size was 6.27 cm, while the mean histologic size was 6.93 cm. Tumor size > 5 cm, heterogeneity, and calcifications are considered to be radiologic signs indicating malignant adrenal tumor. The largest tumor of our series was measured 14 cm, and resected by open, transabdominal adrenalectomy due to the suspicion of cancer.[16-19] However, many aggressive tumors share these features. Pre-

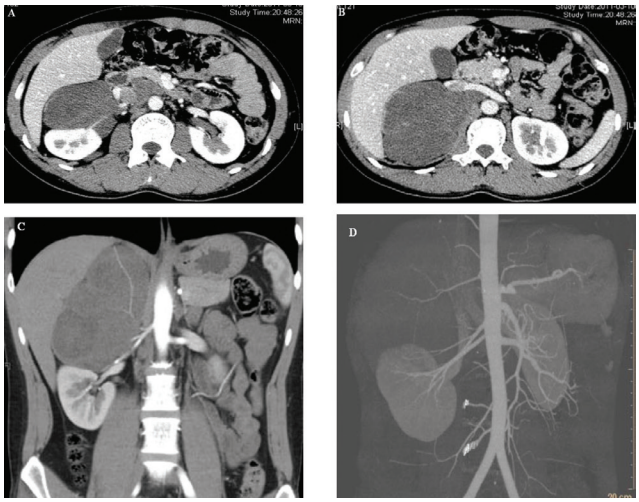

Figure 1. (A) Computed tomography scan showing a right adrenal ganglioneuroma with postcontrast enhancement of 40 Hounsfield and surround the renal artery, (B) a right adrenal ganglioneuroma pushing forward inferior vena cava, conglutinating with posterior wall of inferior vena cava and surrounding tissues, (C) the coronal computed tomography scan reconstruction showing a right kidney pushed downward and a vasa vasorum from abdominal aorta to tumor and (D) renal arteriography showing a vasa vasorum from abdominal aorta to tumor.

operative diagnosis of adrenal GNs remains difficult. The final diagnosis depended on histopathology. Macroscopically, most GNs are large, encapsulated masses of firm consistency with a solid, homogenous, grayish-white cut surface. Microscopically, GNs mainly consist of mature and maturing ganglions and

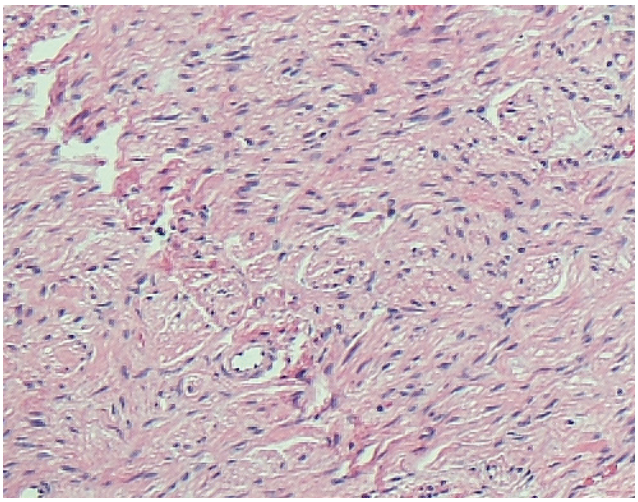

Figure 2. Mixture of large mature ganglion cells and spindle-shaped Schwann like cells. Hematoxylin and eosin staining ×100, original magnification.

Schwann cells in our series. Our immunohistochemical analysis showed that they were characterized by reactivity with S100 and neuronal markers such as NSE.[1,9,15]

Fine needle aspiration biopsy (FNAB) in the diagnosis of adrenal lesions has a long history,[20] however, insufficient material for diagnosis and its complications restrict its application.[21-24] It is only suggested in doubted metastatic adrenal carcinoma.[25-27] No patient of our series was undergone FNAB.

When adrenal incidentalomas are found, complete resection is

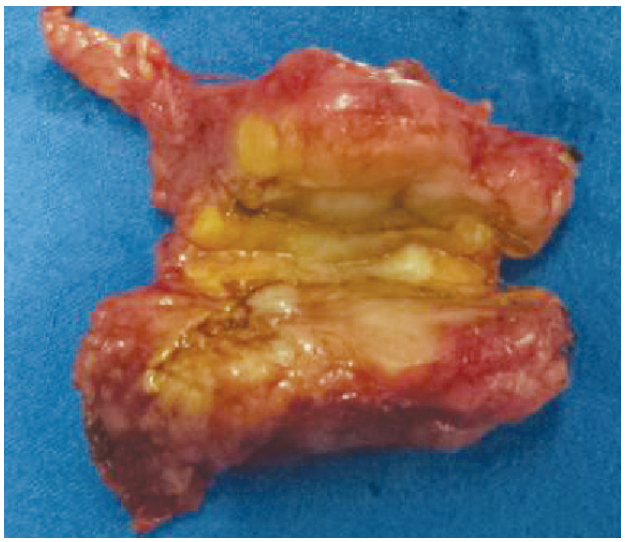

Figure 3. The neoplasm macroscopically seemed to destruct the surrounding gland.

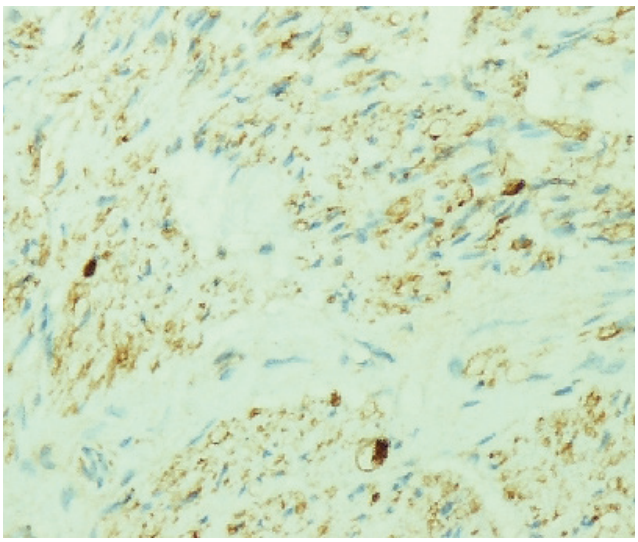

Figure 4. Neuron-specific enolase positive ganglion cells, stained brown. Schwann-like cells are also weakly positive, while adrenal cortical cells are negative.

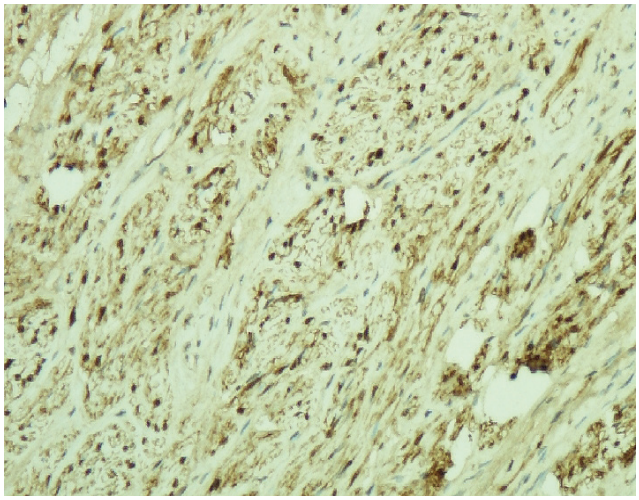

Figure 5. Schwann cell-specific marker (S100) positive cells stained brown.

suggested if the size is more than 4 cm.[28-30] In our series, 3 patients strongly requested to resect the tumors even when the size was less than 4 cm. Prognosis of mature adrenal ganglioneuromas after surgery is terrific. All surgeries were carried out with no mortality and minimal morbidity despite the large size of the neoplasms. After a mean follow-up of 5.4 years (range, 1-10 years), no recurrence was observed. In the procedure, complete resection is recommended in case of malignant transformation of adrenal GN.[31-33]

As the laparoscopic approach develops, almost all adrenal masses could be resected laparoscopically regardless of the size. Recently, Zografoset and colleagues have succeeded to resect large adrenal GN with the size up to 13 cm by transabdominal laparoscope.[7]

CONCLUSION

Pre-operative diagnosis of adrenal GNs remains difficult; therefore, we recommend complete operative resection once malignancy cannot be excluded by pre-operative investigations. To weigh the pros and cons according to our experience, laparoscopic adrenalectomy is a reasonable option, at least for tumors ≤ 5 cm.

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Liping Li and Jialiang Shao contributed equally in this work.

CONFLICT OF INTEREST

None declared.

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