INCIDENTAL PRESENTATION OF ADRENAL GANGLIONEUROMA: CASE SERIES AND REVIEW OF LITERATURE

Pathology

Dr. Farhana Zakaria*

M.D. (Pathology) Department of Pathology Srinivasa Institute of Medical Sciences Mukka, Surathkal Mangaluru, Karnataka State, India. *Corresponding Author

Dr. Altaf Khan

M.Ch. (Urology) Department of Urology Yenepoya Medical College Mangaluru, Karnataka State, India

Dr. Rahul Bhargava

M.Ch. (Urology) Department of Urology Yenepoya Medical College Mangaluru, Karnataka State, India

ABSTRACT

Adrenal Ganglioneuromas are uncommon tumours arising from neural crest cells in posterior mediastinum and retroperitoneum. Rarely do they arise from adrenal gland and most of them are incidentally detected and hormonally inactive. Radiologically, they appear as any other adrenal mass, hence histopathological examination and immunohistochemistry plays a major role. With the advent of laparoscopy and robot, outcome of surgical treatment has improved a lot.

KEYWORDS

Adrenal Tumour, Ganglioneuroma, Incidentaloma, Adrenalectomy

INTRODUCTION:

Ganglioneuromas (GN) are rare benign neuroectodermal neoplasm's composed of ganglion and Schwann cells, arising from the neural crest tissue and are most commonly located in the posterior mediastinum and retro peritoneum. They are rarely found in the adrenal gland [1]. These tumors are usually asymptomatic and are detected incidentally in the majority of cases during imaging for other reason. Although the characteristics of adrenal ganglioneuroma on computerized tomography and magnetic resonance imaging have been well described, the exact diagnosis is difficult [2]. Histopathological examination is currently the mainstay of diagnosis. GN's have a very good prognosis with surgical removal and usually don't require any adjuvant therapy. We report seven cases of adrenal ganglioneuroma which were operated over a period of three and half years between March 2016 to October 2019 with review of available literature.

MATERIALS AND METHODS:

Case 1: A 24-year-old male patient admitted with left lower-quadrant pain. He had no significant past medical or surgical history. Physical examination was normal. Abdominal ultrasound was performed which showed a heterogeneous, well-defined mass measuring 5.6×7.3 cm in his left adrenal gland. He underwent abdominal CT, which showing a relatively homogenous left adrenal tumor measuring 5.2×4.3×7.1cm with faint calcification and well-defined edges. Magnetic resonance imaging (MRI) showed a solid mass measuring 5×4×7cm arising from his left adrenal gland. The tumor was slightly hypointense on T1 weighted MRI, whereas it was slightly hyperintense on T2 weighted MRI. After an intravenous injection of gadolinium, the mass showed a progressive, heterogeneous and delayed enhancement. He underwent laparoscopic left adrenalectomy.

Case 2: A 63 year old female patient with no previous co-morbidities was admitted to our hospital with right lower-quadrant pain. She had past medical history of hypertension, well controlled with oral antihypertensive. Physical examination revealed no signs and the results of routine laboratory tests were all found to be within the normal ranges. An abdominal ultrasound was performed which showed a heterogeneous, well-defined mass measuring 15×6cm in the right adrenal gland. She underwent abdominal CT, which showing a relatively homogenous right adrenal tumor measuring 16.5×7.3×3cm with well-defined edges. She underwent open right adrenalectomy.

Case 3: A 55 year old male with DM, on oral hypoglycemics, well controlled, presented to the hospital in a general body checkup camp. General physical examination was normal. Ultrasound suggested a 4x3 cms, well defined mass in the left adrenal gland. He underwent abdominal CT, which showing a relatively homogenous left adrenal tumor measuring 4.4×3×2.5cm with well-defined edges. His underwent laparoscopic left adrenalectomy.

Case 4: A 47 year old female patient was admitted to our hospital with

left lumbar pain. She had no history of hypertension. Physical examination revealed no signs and the results of routine laboratory tests were all found to be within the normal ranges. An abdominal ultrasound was performed which showed a hypoechoic, well-defined mass measuring 35×26mm in the left adrenal gland. She underwent abdominal CT, which showing a relatively homogenous left adrenal tumor measuring 36.5×x 27.3×33mm with well-defined edges. She underwent laparoscopic left adrenalectomy.

Case 5: A 49 year old male patient was admitted to our hospital with right lumbar pain. He was hypertensive, well controlled with two oral antihypertensive. Physical examination revealed no signs and the results of routine laboratory tests were all found to be within the normal ranges. An abdominal ultrasound was performed which showed a heterogeneous, well-defined mass measuring 8×6cm in the right adrenal gland. MRI showed a solid mass measuring 9×7×4cm arising from his right adrenal gland. The tumor was slightly hypointense on T1 weighted images, whereas it was slightly hyperintense on T2 weighted images. After an intravenous injection of gadolinium, the mass showed a progressive, heterogeneous and delayed enhancement. He underwent a robot assisted right adrenalectomy.

Case 6: A 31year old male patient was admitted with history of right flank pain. On examination he had tenderness in right iliac fossa. On ultrasound examination his appendix was found to be inflamed. There was a solid mass lesion arising from left adrenal measuring 31×21mm. On CT abdomen he was found to have appendicitis with left adrenal mass measuring 34×23mm. He underwent laparoscopic appendicectomy and laparoscopic left adrenalectomy in same sitting.

Case 7: A 42 year old asymptomatic male on executive health checkup was found to have a left adrenal tumour on ultrasound examination. His CT abdomen revealed a solid relatively homogenous left adrenal tumor measuring 32.7×x 21.4×23mm with well-defined edges. He underwent a robot assisted left adrenalectomy.

All patients were evaluated with: CBC; RFT; LFT; serum electrolytes; chest x-ray; Ultrasound abdomen; CT abdomen; MRI (wherever possible). An endocrine workup, including urine catecholamine, cortisol levels and a 1mg overnight dexamethasone suppression test was normal in all the cases.

Histopathologically, all lesions were mature adrenal ganglioneuroma with ganglion cells and Schwann cells among a fibrous stroma. All were Vimentin and S100 positive on immunohistochemistry.

All patients are on follow up till date and they don't have any symptoms or recurrence of lesion.

DISCUSSION:

Ganglioneuromas are rare, differentiated and benign tumors arising

from primordial neural crest cells that form the sympathetic nervous system. They occur in all age groups but more commonly before 60 years of age. On histology, they are composed of mature Schwann cells and ganglion cells with fibrous stroma [1]. Ganglioneuroma is a member of a group of neurogenic tumors group that includes ganglioblastoma and neuroblastoma. These tumors are usually non-functional and asymptomatic. They are usually referred to as incidentaloma since they are detected incidentally. By the time they are discovered, they are usually large in size.

Adrenal hyperplasia, adenoma, adrenocortical carcinoma, metastatic deposits, lipoma, myelolipoma, pheochromocytoma and tuberculosis are various differential diagnosis for adrenal lesions [2, 3]. Tumors containing pheochromocytoma together with foci of neuroblastoma, ganglioneuroblastoma, ganglioneuroma or malignant peripheral nerve sheath tumor are called as composite tumors or compound tumor of adrenal medulla [4]. According to literature about 71% of composite pheochromocytoma or paraganglioma coexist with ganglioneuroma. But in our case series of seven patients, we didn't find any composite tumors. Many cases of composite paragangliomas or pheochromocytomas will be functional like normal paragangliomas and pheochromocytomas, with increased levels of catecholamines or corticotropin-releasing hormone [5]. In our case series none of them had increase in level of hormones.

Ganglioneuroma is most commonly found in the posterior mediastinum and retroperitoneum, and the involvement of the adrenal gland is relatively rare (21%). Adrenal ganglioneuroma is usually regarded as having silent hormonal functions and therefore can be asymptomatic [6].

Ganglioneuromas are usually detected incidentally while evaluating for different symptoms or during a health check up [7]. Ultrasonography reveals a well-circumscribed, homogenous, hypo-echoic lesion [8]. On CT abdomen the adrenal ganglioneuromas are seen as encapsulated, solid well circumscribed masses [9]. They are either iso or hypo attenuating to muscle. In about 20% the masses may demonstrate calcifications which are usually speckled and fine but sometimes may be coarse [10, 11]. On MRI, the lesions are well circumscribed. T1 weighted images have homogeneously low or intermediate signal. T2 weighted have heterogeneously intermediate or high signal. ADC values are usually higher than that of neuroblastoma [8, 12]. The 18F-labeled fluoro-2-deoxy-glucose positron emission tomography (FDG-PET) may help distinguish between adrenal carcinoma and ganglioneuroma, based on the lowest standardized uptake value (SUV), when compared to adrenal carcinoma [4, 13].

The macroscopic characteristics (Figure a) of adrenal ganglioneuroma are an encapsulated mass with a firm consistency and a solid, homogeneous, grayish-white cut surface. Histopathological examination shows mature ganglion cells and Schwann cells among a fibrous stroma. Microscopically (Figure b and c) they can be classified in two main groups: "mature type" and "maturing type". The mature type is composed of mature Schwann cells, ganglion cells and perineurial cells within a fibrous stroma while completely lacking neuroblasts and mitotic figures [14]. The maturing type consists of cells with different maturation levels, ranging from mature cells to neuroblasts with a similar stroma. Detection of neuroblasts is indicative of ganglioneuroblastomas or neuroblastomas. According to immunohistochemical analysis, ganglioneuroma are characterized by reactivity for S-100, vimentin, synaptophysin and neuronal markers [15]. In our case series all the seven tumors were reactive for Vimentin and S100.

Adrenal ganglioneuroma is described as a well-circumscribed tumor with lobular shape and low attenuation [13]. Tumors of size larger than 6cm should be considered malignant until proved otherwise. There is no medical treatment for such tumors. Ganglioneuroma, although benign, can grow aggressively. Patients treated surgically for a benign neurogenic tumor have an excellent prognosis.

There are different options for removal of adrenal tumour; from open surgery, laparoscopic to robotic. The reduced hospital stay and morbidity have resulted in laparoscopic adrenalectomy becoming the gold standard procedure for the surgical removal of a vast majority of small sized (<6cm) adrenal lesions [16]. With increased experience in laparoscopic techniques, tumors larger than 6cm can also be now safely operated by laparoscopy [17].

With the advent of robot, more and more adrenal surgeries are now carried out with robot assistance as it is safe with similar clinical outcomes as laparoscopic procedure [18]. In our case series two patients underwent removal of tumour by robot assistance.

The prognosis for an adrenal ganglioneuroma following surgical resection is good without the need for additional treatment [1, 2]. None of the seven cases in our series had any recurrence.

CONCLUSION:

Adrenal ganglioneuromas are rare, hormonally silent benign tumors. They are usually detected incidentally. Some large tumors can mimic adrenal malignancies. Hormonal evaluation before surgery is a must for all incidentally detected adrenal tumors. Definitive diagnosis can be done by histopathology and immunohistochemistry. With advent of minimally invasive procedures like Laparoscopy and Robotic surgery, outcome of surgeries is better.

Acknowledgement: Nil

Conflict of Interest: Nil

FIGURES

(a) Macroscopic appearance of adrenal ganglioneuroma

(b) Low power view (10x) showing admixture of ganglion cells and Schwann cells in H&E.

(c) Mature ganglion cells with intervening stroma (H&E, X400).

REFERENCES:

1. Geoerger B, Hero B, Harms D, Grebe J, Scheidhauer K, Berthold F: Metabolic activity and clinical features of primary ganglioneuromas. *Cancer*. 2001, 91: 1905-1913.
2. Erem C, Ucuncu O, Nuhoglu I, Cinel A, Cobanoglu U, Demirel A, Koc E, Kocak M, Guvendi GF: Adrenal ganglioneuroma: report of a new case. *Endocrine*. 2009, 35: 293-296.
3. Yamaguchi K, Hara I, Takeda M: Two cases of ganglioneuroma. *Urology*. 2006, 67: 622.
4. Rhondeau G, Nolet S, Latour M, Braschi S, Gaboury L, Lacroix A, Panzini B, Arjane P, Cohade C, Bourdeau I: Clinical and biochemical features of seven adult adrenal ganglioneuromas. *J Clin Endocrinol Metab*. 2010, 95: 3118-3125.
5. Shahani S, Nudelman RJ, Nalini R, Kim HS, Samson SL: Ectopic corticotropin-releasing hormone (CRH) syndrome from metastatic small cell carcinoma: a case report and review of the literature. *Diagn Pathol*. 2010, 8: 56.
6. Jain M, Shubha BS, Sethi S, Banga V, Bagga D: Retroperitoneal ganglioneuroma: report of a case diagnosed by fine-needle aspiration cytology, with review of the literature. *Diagn Cytopathol*. 1999, 21: 194-196.
7. Lee JH, Chai YJ, Kim TH, Choi JY, Lee KE, Kim HY, Yoon YS, Kim HH.

- Clinicopathological Features of Ganglioneuroma Originating From the Adrenal Glands. *World J Surg.* 2016; 40:2970–2975.
8. Loneragan GJ, Schwab CM, Suarez ES, Carlson CL. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma: radiologic-pathologic correlation. *Radiographics.* 2002; 22:911–934.
 9. Ichikawa T, Ohtomo K, Araki T et-al. Ganglioneuroma: computed tomography and magnetic resonance features. *Br J Radiol.* 1996;69 (818): 114-21.
 10. Duffy S, Jhaveri M, Scudierre J et-al. MR imaging of a posterior mediastinal ganglioneuroma: fat as a useful diagnostic sign. *Am J Neuroradiol.* 26 (10): 2658-62.
 11. Johnson GL, Hruban RH, Marshall FF et-al. Primary adrenal ganglioneuroma: CT findings in four patients. *Am J Roentgenol.* 1997; 169 (1): 169-71.
 12. Gahr N, Darge K, Hahn G et-al. Diffusion-weighted MRI for differentiation of neuroblastoma and ganglioneuroblastoma/ganglioneuroma. *Eur J Radiol* 2011;79(3):443-6.
 13. Mackie GC, Shulkin BL, Riberio RC, Worden FP, Gauger PG, Mody RJ, Connolly LP, Kunter G, Rodriguez-Galindo C, Wallis JW, Hurwitz CA, Scheingart DE: Use of [18]F-fluoro-deoxyglucose positron emission tomography in evaluating locally recurrent and metastatic adrenocortical carcinoma. *J Clin Endocrinol Metab.* 2006, 91: 2665-2671.
 14. Allende DS, Hansel DE, MacLennan GT. Ganglioneuroma of the adrenal gland. *J Urol.* 2009; 182:714–715.
 15. Sasaki SI, Yasuda T, Kaneto H, Otsuki M, Tabuchi Y, Fujita Y, Kubo F, Tsuji M, Fujisawa K, Kasami R, Kitamura T, Miyatsuka T, Katakami N, Kawamori D, Matsuoka TA, Imagawa A, Shimomura I. Large adrenal ganglioneuroma. *Intern Med.* 2012, 51: 2365-2370.
 16. C.D. Smith, C.J. Weber, J.R. Amerson. Laparoscopic adrenalectomy: new gold standard. *World J. Surg.*, 23 (1999), pp. 389-396
 17. A. Agrusa, G. Romano, G. Frazzetta, D. Chianetta, V. Sorce, G. Di Buono, et al. Laparoscopic adrenalectomy for large adrenal masses: single team experience *Int. J. Surg.*, 12(Suppl. 1)(2014), pp. S72-S74
 18. Economopoulos KP, Mylonas KS, Stamou AA, Theocharidis V, Sergentanis TN, Psaltopoulou T, Richards ML. Laparoscopic versus robotic adrenalectomy: A comprehensive meta-analysis. *Int J Surg.* 2017; 38:95–104.