

Clinico-Pathological Patterns of Adrenal Masses among Patients with Adrenal Diseases

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Abstract: Objective, to determine the clinic-pathological patterns of adrenal masses among patients having adrenal diseases in our patients. Methods: This is a retrospective review of 30 patients having adrenal masses at King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia from October 2004 to April 2010. The patient's medical records were reviewed for demographic details, clinical presentations, and histopathological diagnoses and management. Results: Thirty patients were presented with different adrenal lesions. Nine (30%) were Pheochromocytoma (5 males and 4 females) with mean age was 29.5 years (range 14-45 years), and mean tumor size was 6.18 cm. Seven (23.3%) were Incidentaloma (3 males and 4 females) with mean age was 48 years (range 31-65years), and mean tumor size was 9.5 cm. Five (16.7%) were Cushing's disease (4 males and 1 females) with mean age was 33.5 years (range 23-44), and mean tumor size was 8.5 cm. five (16.7%) were Conn's disease (2 male and 3 females) with mean age was 50.5 years (range 36-65), and mean tumor size was 4.1 cm. four (13.3%) were non-functioning adenoma with mean age was 43 years (range 17-69) and mean tumor size was 2.3 cm. Conclusion: Pheochromocytoma is the most common adrenal disease in patients with adrenal lesions in the studied area. It present in younger age group when compared with other adrenal diseases. Testing for pheochromocytoma is recommended for all patients with adrenal masses.

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1. Introduction

The presence, importance, and physiology of the adrenal glands have been described more than 500 years ago. In the 1850s, Addison and Brown-Séquard demonstrated the essential role of these glands in mineral and corticoid function. Adrenal gland autopsies have revealed adrenal masses in at least 2–9% of cases that are above 50 years, and incidental adrenal masses are found in up to 1.3% of computed tomography (CT) scans. About 80% of adrenal masses are non-functional and benign; the remaining are either functional or malignant^[1].

Diseases that affect the adrenal cortex include Conn's disease, Cushing's syndrome, adenoma, adenocarcinoma, Addison's disease, and Incidentaloma. Pheochromocytoma arises from the adrenal medulla^[1]. In present study, we compared the incidence of adrenal diseases in patients presented with adrenal mass in our region, and their demographic details, investigations, and management.

2. Material and Methods

A retrospective cohort study of all patients who presented with adrenal diseases at King Abdulaziz University Hospital, with a capacity of 754 beds, was undertaken. Our hospital is the only university teaching hospital in the western region of Saudi Arabia, and one of four tertiary hospitals in Jeddah. The population in Jeddah approximates three millions and half peoples. Patient's records were reviewed

after we obtained approval from the local ethics committee. Medical records for 47 patients presenting with adrenal diseases between October 2004 and April 2010 were evaluated. Only cases having adrenal mass was proven by radiological and histopathological investigations were included. Patients without adrenal mass were excluded. The information evaluated included patient's age, gender, clinical signs and symptoms, presence of hypertension, presence of diabetes mellitus, results of laboratory tests which included are plasma rennin activity and levels of serum aldosterone measured by a commercially available radioimmunoassay kits (Renin by Riabead; Dainabot, Tokyo, Japan, and aldosterone by Immunotech SA, Marseille, France), cortisol, androgen, free metanephrine, 24-hour urinary catecholamine, metanephrine, and free cortisol levels measured by a commercially available radioimmunoassay kits (IBL, Hamburg, Germany), results of abdominal ultrasounds, CAT scan abdomen, metaiodobenzylguanidine (MIBG) isotope scans, size and side of adrenal mass, and histopathology reports.

Continuous numerical data were tabulated and expressed as mean. Statistical significance was determined when p -value < 0.05 using one way ANOVA test. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17 (SPSS Inc, Chicago, IL, USA).

3. Results

During the study period, a total of 47 patients presented with different adrenal diseases. 30 patients (63.8 %) among them were confirmed to have adrenal mass by Computerized tomography (CT) scan of the abdomen. The others 17 patients (36.2%) were presented with different adrenal diseases without adrenal mass (Addison's disease in 12 patients, Cushing's syndrome secondary to bilateral adrenal hyperplasia in 4 patients, Conn's disease secondary to bilateral adrenal hyperplasia in one patient).

In patients with adrenal mass (30 cases), the mean patient age was 43 years (range 14–72); 15 cases were female and 15 cases were male. Pheochromocytoma was found in nine cases (30%), Incidentaloma in seven cases (23.3%), Cushing's syndrome in five cases (16.7%), Conn's disease in five cases (16.7%), and non-functioning adenoma in four cases (13.3%), (Table 1). Mean age was lowest in patients with pheochromocytoma as 29.5 years (range 14–45 years), followed by Cushing's syndrome as 33.5 years (range 23–44 years), adenoma as 43 years (range 17–69 years), and Incidentaloma as 48 years (range 31–65 years). Mean age was highest in patients with Conn's disease as 50.5 years (range 36–65 years). *P*-value for the age is 0.017 (by one way anova test) which is statistically significant. The male-to-female ratio was 1.3:1 for pheochromocytoma, 1:1.3 for Incidentaloma, 4:1 for Cushing's syndrome, 1:1.5 for Conn's disease, and 1:3 for adenoma.

Mean tumor size was highest in Incidentaloma as 9.5 cm (5.4–15 cm), followed by Cushing's syndrome 8.5 cm (6.6–10.5 cm), pheochromocytoma 6.18 cm (range 3.5–12 cm), and Conn's disease 4.1 cm (range 1.5–4.2 cm). Mean tumor size was lowest in adenoma 2.3 cm (range 2–2.6 cm). Left side adrenal gland involvement was observed in the majority of pheochromocytoma and Cushing's syndrome cases (75% left gland and 25% right gland), and right side adrenal involvement was found in

majority Conn's disease and adenoma cases (75% right gland and 25% left gland). In Incidentaloma, there was equal right and left gland involvement.

Clinical presentations of patients with pheochromocytoma (9 cases) were hypertension in 8 patients (88.8%), diabetes in 4 patients (44.4%). Hypertensions spell (headaches, sweating, palpitations, and paroxysmal hypertension) was present in 2 patients (22.2%). The diagnosis was made by 24-hours urine metanephrines level which was high in all the patients. In Cushing's syndrome (5 cases), hypertension was present in 3 cases (60%), diabetes in 3 cases (60%). All patients have central obesity, moon face, hirsutism, acne, easy brusability and depression. The diagnosis was done by 24-hours urinary free cortisol in 4 patients, and one patient required a low dose dexamethasone suppression test for diagnosis. In patients with Conn's disease (5 cases), hypertension and hypokalemia were present in all cases, and the diagnosis was confirmed by elevated plasma aldosterone concentration and low plasma renin activity in all the patients. In Incidentaloma (7 cases), the diagnosis was made by incidental finding of adrenal mass during CT-Scan examination of the abdomen for others reason. Histopathological analyses of Incidentaloma revealed myelolipoma in four cases, adenoma in two cases, and adrenocortical cancer in one case, (Figure 1).

All the patients (30 cases) underwent surgical resection of the adrenal mass (adrenalectomy), 25 patients (83.3%) by laparoscopy and 5 patients (16.7%) by open surgery. Mean hospital stay in laparoscopic adrenalectomy was 2.4 days (range 1-3 days), and in open adrenalectomy was 4.6 days (range 4-6 days). Complications that we encountered during surgery were one case of bleeding due to splenic injury and one case of injury to the colon in laparoscopic group which was managed accordingly, and 1 case of wound infection in open surgery group. There was no post-operative mortality in our patients.

Table 1 Characteristics of patients with adrenal masses

Disease	Sex	No. of patients	Mean age (+_ SD) (Years)	p value	Confident interval for mean	Mean tumor size
Pheochromocytoma	M	5	29.5 (+_ 3.25)	0.017	22.46 – 43.54	6.18 cm (3.5-12)
	F	4				
	Total	9				
Incidentaloma	M	3	48 (+_ 2.89)	0.56	42.39 – 58.18	9.5 cm (5.4-15)
	F	4				
	Total	7				
Cushing's disease	M	4	33.5 (+_ 4.20)	0.066	23.90 – 45.30	8.5 cm (6.6-10.5)
	F	1				
	Total	5				
Conn's disease	M	2	50.5 (+_ 2.94)	0.025	33.63 – 67.96	4.1 cm (1.5-4.2)
	F	3				
	Total	5				
Non-functioning adenoma	M	1	43 (+_ 3.57)	0.247	7.51 – 77.49	2.3 cm (2-2.6)
	F	3				
	Total	4				
Total		30	----	----	36.02 – 47.05	----

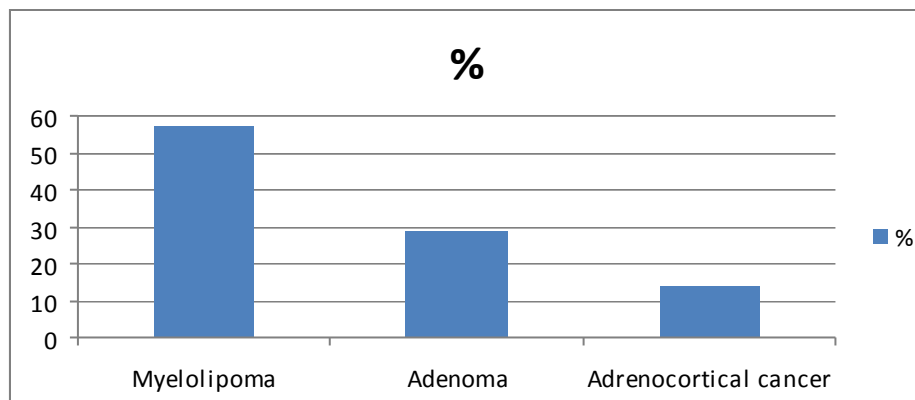


Figure 1 Histopathology of Incidentiloma

4. Discussion

Adrenal masses raise challenging questions for physicians and their patients. While several different algorithms and methods for determining the optimal treatment of these lesions have been published, most physicians would agree that patient evaluation should begin with a careful history analysis, a physical examination, and diagnostic studies focusing on whether the mass is hyper-functional or malignant^[2].

Pheochromocytoma is a tumor that arises from chromaffin and sustentacular cells of the adrenal and extra-adrenal paraganglia^[3]. Its incidence is approximately 2–8 cases per million persons per year and it is responsible for a curable form of hypertension in 0.1–1.0% of all hypertensive patients^[4]. Unfortunately, some patients die from complications associated with unsuspected pheochromocytoma during or shortly after operative procedures, baby delivery, or minor operations^[5]. International figures showed that the age at presentations peak in the fourth and fifth decades with males and females being equally affected^[6]. Traditionally, pheochromocytoma has been referred to as the “10% tumor” with 10% of cases being bilateral, 10% malignant, 10% extra-adrenal, 10% hereditary, and 10% occurring in children^[7]. Our study showed that pheochromocytoma is the most common adrenal disease in patients with adrenal masses in the study area. In addition, mean patient age was lower in pheochromocytoma (29.5 years) when compared with other adrenal diseases. Mean patient age was reported as 44 years by **Humphrey et al.**, in 2008^[6,8] and 54 years by **Mathew et al.**, in 2008^[8,9]. In the present analysis, it affected more males than females (male-to-female ratio 1.3:1). Others have reported it to be more common in females^[9,10]. In the present work, it involved the left adrenal gland (75%) more often than the right one. There were no cases of pheochromocytoma with family history of the disease, bilateral disease, or

extra-adrenal or malignant growth. Thus, the 10% rule is not applied to our group of patients. Hypertension was present in 88.8% of our patients, comparable to the values reported by **Kent et al.**, in 2005 (83.7%)^[11] and **Richard et al.**, in 1999 (82%)^[11,12].

Incidentiloma are adrenal tumors discovered in imaging tests that are performed for non-adrenal-related conditions^[12]. The frequent use of imaging techniques, particularly CT scans, which consistently detect adrenal lesions larger than 1 cm, has resulted in the detection of Incidentiloma in 0.35–5% of studies^[13]. The majority of Incidentiloma are biochemically nonfunctional and benign. However, in approximately 10% of cases, incidental adrenal masses are functional^[13]. Incidentiloma was found to be the second common adrenal mass in our patients: Histopathological examination are reviewed and revealed myelolipoma in 57.1% of cases, adenoma in 28.6%, and adrenocortical cancer in 14.3% of cases^[14]. **Young et al.**, in 2000^[15] reported that 82% of adrenal masses were non-functional adenomas, 5% were subclinical Cushing’s syndrome, 5% were pheochromocytomas, 5% were adrenocortical cancers, 2.5% were metastases, and 1% were aldosterone-producing adenomas, whereas **Giovanni et al.**, reported adenoma in 45.2%, cancer in 3.2%, Cushing’s disease in 10.8%, pheochromocytoma in 19.2%, Conn’s disease in 5.6%, angiomyolipoma in 7.2%, and metastasis in 4.8% of patients^[15].

Primary aldosteronism is characterized by the overproduction of the mineralocorticoid hormone aldosterone by the adrenal glands^[15,16]. It is among the most common causes of secondary hypertension^[17]. Primary hyperaldosteronism has many causes, including adrenal hyperplasia, adenoma and carcinoma. When it occurs due to a solitary aldosterone-secreting adrenal adenoma, it is known as Conn’s syndrome^[18]. Cushing’s syndrome is a hormone disorder caused by high levels of cortisol in

the blood ^[19, 20]. This can be caused by taking glucocorticoid drugs, or by tumors that produce cortisol or adrenocorticotropic hormone in pituitary or adrenal gland ^[20,21]. In our study Cushing's syndrome and Conn's disease were found to be the third most common presentations, with non-functional adenoma being the least cause.

Despite the small sample size of our study, it provides initial evidence about the patterns of adrenal mass in Saudi Arabia, as we have a limited study in our area regarding adrenal disease. We think that we have a different disease patterns among our patients in comparing to international studies, and for that reason we recommend other physicians in different regions in Saudi Arabia to conduct more studies about adrenal mass to have a better understanding of those diseases.

Conclusions

We conclude that pheochromocytoma is the most common adrenal disease in patients having adrenal lesions in the study area. It is present in the younger age group when compared with other adrenal diseases. Testing is recommended for all patients with adrenal masses.

Disclosure of Benefit:

The authors have no conflicting interests, and are not supported/funded by any drug company.

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References:

- [1] Mansmann G, Lau J, Balk E, Rothberg M, Miyachi Y, Bornstein SR. The clinically inapparent adrenal mass: update in diagnosis and management. *Endocr Rev.*, 2004 Apr;25 [2]:309-40.
- [2] Grumbach M M, Biller BM, Braunstein GD, Campbell KK, Carney JA, Godley PA and *et al.*; Management of clinically inapparent adrenal mass. *Ann. Intern. Med.*, 2003 Mar 4;138 [5] 424-429.
- [3] Chavez-Rodriguez J, Pasieka JL. Adrenal lesions assessed in the era of laparoscopic adrenalectomy: a modern day series. *Am J Surg.*, 2005 May; 189 [5]:581-6.
- [4] Gill IS. The case for laparoscopic adrenalectomy. *J Urol.*, 2001 Aug; 166 [2]:429-436.
- [5] Kim AW, Quiros RM, Maxhimer JB, El-Ganzouri AR, Prinz RA. Outcome of laparoscopic adrenalectomy for pheochromocytomas vs aldosteronomas. *Arch Surg.*, 2004 May; 139 [5]:526-531.
- [6] Humphrey R, Gray D, Paulter S, Davies. Laparoscopic comparison with open adrenalectomy for resection of pheochromocytoma; A review of 47 cases, *Can J Surg.*, 2008 Aug;51 [4]:276-80
- [7] Kercher KW, Novitsky YW, Park A, Mathew BD, Litwin DE, Heniford BT; Laparoscopic curative resection of pheochromocytoma, *Ann. Surg.*, 2005 Jun;241[6]:919-928.
- [8] Kim AW, Quiros RM, Maxhimer JB, EL Ganzouri AR, Prinz RA; Outcome of laparoscopic adrenalectomy for pheochromocytoma versus aldosteronomas, *Arch Surg.*, 2004 May ;139[5];526-529.
- [9] Mathew J M, Chandaran P, Sundaram, Laparoscopic adrenalectomy for pheochromocytoma versus other surgical indications, *JLS2000*;12[4]:338-384.
- [10] Thompson GB, Young WF, Adrenal Incidentaloma. *Curr Opin Oncol.*, 2003 Jan; 15 [1]:84-90.
- [11] Shen WT, Sturgeon C, Duh QY. From Incidentaloma to adrenocortical carcinoma: the surgical management of adrenal tumors. *J Surg Oncol.*, 2005 Mar 1; 89 [3]:186-92.
- [12] Conzo G, Tricarico A, Belli G, Candela S, Corcione F, Del Genio G, and *et al.*; Adrenal Incidentaloma in laparoscopic era and role of correct surgical indications; Observation from 255 consecutive adrenalectomies in an Italian series. *Can J Surg.*, 2009; Dec; 52 [6]; 281 -286.
- [13] Dackiw AP, Lee JE, Gagel RF, Evans DB. Adrenal cortical carcinoma. *World J Surg.*, 2001 Jul; 25 [7]: 914-26.
- [14] Mulatero P, Dluhy RG, Giacchetti G, Boscaro M, Veglio F, Stewart PM. Diagnosis of primary aldosteronism: from screening to subtype differentiation. *Trends in Endocrinol Metab.*, 2005 Apr, 16 [3]: 114-9.
- [15] Schirpenbach C, Segmiller F, Diederich S, Hahner S, Lorenz R, Rump LC, and *et al.* Diagnosis and treatment of primary hyperaldosteronism in Germany, *Dtsch, Arztebl int.*, 2009 May;106 [18] 305-311.
- [16] Kim RM, Lee J, Soh EY; Predictors of resolution of hypertension after adrenalectomy in patients with aldosteronism producing adenoma, *J. Korean Med Sci.*, 2010 Jul; 25[7]; 1041-1044.
- [17] Amar L, Plouin PF, Steichen O; Aldosterone producing adenoma and other surgically correctable form of aldosteronism, *Orphanet J Rare Dis.*, 2010 May;19:5-9 Review.
- [18] Arnaldi G, Angeli A, Atkinson AB, Diagnosis and complications of Cushing's syndrome: A consensus statement. *J Clin Endocrinol Metab.*, 2003; Dec88 (12): 5593-5602.
- [19] Magiakou MA, Chrousos GP. Cushing syndrome in children and adolescents: Current diagnosis and therapeutic strategies. *J Endocrinol Invest.*, 2002 Feb; 25 [2]:181-194.
- [20] Ding XF, Li Han Z, Yan WG, Gao Y, Li XQ, Role of adrenalectomy in recurrent Cushing's disease, *Chinese Medical Journal*, 2010;123 [13] 1658-1662.
- [21] Thompson KS, Hayman AV, Ludlam WH, Devenag CW, Lorianx DL, Sheppard BC. Improved quality of life after bilateral laparoscopic adrenalectomy for Cushing disease, a ten year experience. *Ann Surg.*, 2007 May; 245 [5]; 790-795.

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