Adrenal Disorders, Presentations and Ways of Investigations

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ABSTRACT:

BACKGROUND:

Adrenal disorders in surgical practice are presented either as hyperfunctional disorders or non functional disorders (incidentalomas). Functionally, medullary tumors (pheochromocytoma) result in excess secretion of catecholamines[1], on the other hand, functioning adrenocortical tumors could secrete excess of cortisol (Cushing syndrome), aldosterone (Conn's syndrome) or sex hormones (virilizing syndromes).[2] . Aim of our study was to identify the most common types of adrenal tumors, its presentation and outlining the best diagnostic work up and to show our experiences in dealing with adrenal disorders in Iraq.

METHODS:

This is a prospective study of 20 cases diagnosed as having adrenal disorders, admitted and evaluated in Baghdad Teaching Hospital-Medical City from January 2002 to December 2004. The collected data including; age, gender, presentations, methods of investigations and histopathological records.

RESULTS:

Their assessment revealed that adrenal disorders were most commonly encountered in the (30-39) years age group (9/20, 45%). The mean age was 40 years with a female preponderance and female: male ratio of 2: 1. Obesity was noted in (7/20, 35%). Headache was manifested in (5/20, 25%), palpitation in (4/20, 20%) and uncontrolled hypertension in (4/20, 20%). Plasma cortisol was elevated and its diurnal rhythm was lost in (8/20, 40%), 24-urinary VMA was elevated in (6/20, 30%). 24-urniary 17-ketosteroid was elevated in (1/20, 5%). The most commonly encountered clinical type of adrenal disorders was hypercortisonism in the form of Cushing disease and syndrome (8/20, 40%).

CONCLUSION:

Adrenal disorders mostly affect young age group patients with a female preponderance. Functioning adrenal disorders have presented earlier than non functioning ones owing to the symptoms they had caused. U/S, CT scan, MRI and IVP are very important in visualization, localization, assessment of distant metastases and finally discrimination of benign from malignant disorders.

KEY WARDS: Adrenal Disorders, Presentations, Investigations.

INTRODUCTION:

Historically, in 1552, the Roman anatomist Barthoomaeas Eustachius first described the adrenal glands referring to there as "glandular renibus incumbetes" (gland lying on the kidneys[3]) Pathologically, hyperplastic and neoplastic conditions affecting the adrenal gland my be associated with excess secretions of various hormones producing a wide variety of clinical syndromes.[4, 5] The absence of evidence of hormonal excess in the presence of an enlarged adrenal gland usually indicates that the tumor is an incidental finding (incidnetaloma) and not the functionally adenoma[6] .

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Adrenal disorders in surgical practice are presented either as hyperfunctional disorders or non functional disorders (incidentalomas).

Functionally, medullary tumors (pheochromocytoma) result in excess secretion of catecholamines[1], on the other hand, functioning adrenocortical tumors could secrete excess of cortisol (Cushing syndrome), aldosterone (Conn's syndrome) or sex hormones (virilizing syndromes).[2] The management of adrenal disorders includes multiple steps. First step is by history and physical examination which should lead to the suspicion of an adrenal disorder [7, 8].

The second step is by laboratory tests to diagnose functional tumor. [8] Localization studies is the 3rd step in the management. The initial localizing procedure of choice is a contrast enhanced CT scan because it can detect virtually all adrenal masses that are large enough to cause a syndrome [1].

MRI adds more accuracy to the localization procedure and even small lesions can be accurately identified.[8] Step four; all patients are prepared preoperatively to correct their blood pressure, D.M., hypovolemia, electrolyte imbalance, and alkalosis if any is present.

Aim of our study was to identify the most common types of adrenal tumors, its presentation and outlining the best diagnostic work up.

PATIENTS AND METHODS:

This is a prospective study of 20 patients of adrenal disorders were collected at the Baghdad Teaching Hospital-Medical City during the period from January 2002 to December 2004. The patients were assessed clinically and investigated by certain hormonal studies to determine the adrenal function. The adrenal masses were also evaluated radiologically to determine the site and the extent of the disease. Data were collected regarding the association between adrenal disorders and certain varieties namely, age (patients were grouped in 10 years cohort), sex, presenting symptoms and signs, duration of illness, biochemical, radiological investigations and histopathological results.

These data were analyzed and the results shown in the form of tables.

RESULTS:

Table (1) shows the distribution of patients according to their age and sex. The most affected age group was (30-39 years) (9/20, 45%).The mean age was 40 years old, and there was a female preponderance with ♀:♂ ratio of 2:1. The mean age for Cushing patients was 35 years and that of pheochromocytoma patients was 40 years. Concerning the main symptoms and signs, table (2) clarifies that obesity was noted in (7/20, 35%) of patients who were proved later to have hypercortisonism. On the other hand, headache was found in (5/20, 25%), hypertension in (4/20, 20%) and palpitation in (4/20, 20%) of patients; all found later on to have pheochromocytoma, on of them had buccal mucosal neuroma (1/20, 5%).

It was noticed that (5/20, 25%) of patients were incidentally found during a diagnostic procedure done for another suspicion. Table (3) entails the different ways used to investigate our patients with adrenal disorders. Plasma cortisol and its diurnal rhythm was done in (13/20, 65%) of patients.

Serum cortisol was elevated and the diurnal rhythm was lost in (8/20, 40%) of patients, and it was found to be elevated (> 7mg/24 hr) in 6 of them (6/20, 30%). The low dose dexamethasone suppression test was done in the 8 suspected Cushing patients (8/20, 40%) and it showed no response in all of them.

The high dose dexamethasone suppression test was also performed in the 8 suspected Cushing patients showing positive response in 4 of them while the other 4 expressed a negative response.

Serum electrolytes were investigated in all of the patients (20/20, 100%) and have shown hypokalemia in three out of the 8 patients with hypercortisonism (3/8, 37.5%). High levels of urinary 17-ketosteroid was found in 1 patient (1/20, 5%).

Regarding the imaging technique, spine X-ray was done in 8 Cushing patients (8/20, 40%) and showed osteoporotic changes in (6/8, 75%) of them. Ultrasound was performed in all of the 20 patients and it showed right sided lesions in (8/20, 40%), left sided lesions in (7/20, 35%) and bilateral lesions in (5/20, 25%) of patients. The size was more than 5cm in (3/20, 15%) of patients proved later on to have adrenal carcinoma. CT scan was done in (15/20, 75%) of cases and in addition to ultrasound findings it showed more detailed information regarding the structure of the lesions being for example solid with cystic changes in (3/20, 15%) of patients who had adrenocortical carcinoma. Also CT scan showed the presence of paraaortic lymphadenopathy in one case (1/20, 5%) proved to be stage III adrenocortical carcinoma. Moreover, brain CT scan was performed in 4 patients who responded to the high dose dexamethasone suppression test and it showed pituitary adenoma, their abdominal CT scan demonstrated bilateral adrenal enlargement.

MRI was employed in 4 patients (4/20, 20%) and it showed in the T_2 weighted image a dark lesion in (2/20, 10%) of cases which were adrenal adenomas, a bright lesion in (1/20, 5%) of patients which was adrenocortical carcinoma and a very bright lesion in another patient (1/20, 5%) who had pheochromocytoma. IVP was performed in 9 patients (9/20, 45%) and it showed bilateral normal kidney function in all of them but with a mass effect and displacement of the pelvicalyceal system in 3 patients (3/20, 15%) who had large adrenal tumors.

In respect to the clinical types of adrenal disorders, table (4) shows that hypercortisonism in the form of Cushing disease and Cushing syndrome was found in (8/20, 40%) of patients, pheochromocytoma was manifested in 6 patients (6/20, 30%), one patient (1/20, 5%) had presented with a virilizing tumor and 5 patients (5/20, 25%) were incidentally diagnosed as having an adrenal mass.

Table1: Distribution of patients according to age and sex.

Age groups (years)	Males	Females	Total	
			No.	%
1-9	1	1	2	10%
10-19	1	1	2	10%
20-29	1	1	2	10%
30-39	1	8	9	45%
40-49	1	2	3	15%
50-59	0	1	1	5%
60-69	1	0	1	5%
Total	7	14	20	100%

Table2: Main symptoms and signs.

Symptoms & signs	Hypercortisonism		Pheochromocytoma		Virilizing tumor		Incidentaloma	
	No.	%	No.	%	No.	%	No.	%
Obesity	7	35%						
Headache			5	25%				
Uncontrolled hypertension			4	20%				
Palpitation			4	20%				
Recurrent loin pain							4	20%
Diabetes mellitus	2	10%						
Hirsutism	1	5%			1	5%		
Myopathy	1	5%						
Sweating			1	5%				
Oral mucosal neuromas			1	5%				
No symptoms							1	5%

Table3: Diagnostic modalities.

Investigation	No.	%
Plasma cortisol and its diurnal rhythm	13	65%
Dexamethasone suppression test	8	40%
24 hours urinary excretion of VMA	11	55%
24 hours urinary excretion of 17-ketosteriod	1	5%

Serum electrolytes	20	100%
Spine X-ray	8	40%
Ultrasound	20	100%
CT scan	15	75%
MRI	4	20%
IVP	9	45%

VMA= Venyl Mandelic acid.

Table 4: Clinical Types of Adrenal Disorders.

Type	No.	%
Cushing disease	4	20%
Cushing syndrome	4	20%
Pheochromocytoma	6	30%
Virilizing syndrome	1	5%
Incidentoma	5	25%
Total	20	100%

DISCUSSION:

The mean age was 40 years and there was a 2:1 female preponderance; this result concedes with that of: Suresh KN [9]: who found a ♀:♂ ratio of 2.3:1 and the mean age of 38.6 years. Pheochromocytoma mean age was 40 years and that of Cushing was 35 years, this is in accord with that of: Bjorn Edwin et al: [10] who found a mean age of 40 years in pheochromocytoma patients. Maad M.A. Rahman & Usama Al Abid (13): who conducted a mean age of 35 years in Cushing patients. Concerning the clinical features by which our patients have presented, obesity was the most common manifestation in Cushing patients (7/8, 87%), it was a central obesity (face, dorsal neck, trunk). This result is in accordance with that of:

Maad M. A. Rahman and Usama Al Abid[11]: who found that central obesity was the most common presenting feature in Cushing patients (84%). Patients with pheochromocytoma were most commonly presented with headache (5/6, 83.3%), palpitation and hypertension (4/6, 67%) in each of the former and the latter. The least commonly presenting feature was sweating (1/6, 16.7%). These results concede with that of: Couldwell WT et al[12]: who stated that the most common presenting clinical features of pheochromocytoma were headache 80%, uncontrolled hypertension (65%) and palpitation (60%). Harrison BJ[13]: who elaborated that in descending order of frequency:

Headache, palpitation and sweating are the most common clinical manifestations of pheochromocytoma. In regard to investigations of our patients, plasma cortisol and its diurnal rhythm was done in (13/20, 5%) 8 of them were suspected Cushing patients and 5 incidentalomas (as part of the screening), this is in accord with: Melvin MG et al [14]: who estimated that all patients with incidentally found adrenal masses should be screened for cortisol and urinary VMA. Serum cortisol was elevated and the normal diurnal rhythm with its maximum level at 8:00 was lost in Cushing patients. This concedes with: Wheeler MH and Sadler GP [3]: who found that loss of diurnal variation is frequently exhibited in Cushing patients. Regarding the dexamethasone suppression tests, the low dose test was done in the suspected Cushing patients and it showed no response (thus confirmed the diagnosis of hypercortisonism). The high dose test performed in the 8 Cushing patients and manifested a positive response in 4 of them and the other four were non responders (the former proved later to have bilateral adrenal hyperplasia secondary to a pituitary adenoma and the latter to have a primary adrenal tumor).

This result is consistent with that of: Maad M. A. Rahman & Usama Al Abid [11]: who conducted that none of the suspected Cushing patients responded to the low dose dexamethasone suppression test, however patients with hypercortisonism due to bilateral adrenal hyperplasia secondary to pituitary adenoma had responded to the high dose dexamethasone suppression test. Urinary VMA was performed in 11 patients, six with pheochromocytoma and 5 with adrenal incidentalomas also as part of screening.

This result is in accord with: Harrison BJ [13]: patients with pheochromocytoma usually excretes VMA in urine in excess of 7mg/24 hh. Serum electrolytes were investigated in all of the patients and have shown hypokalemia in 3 out of the 8 patients with hypercortisonism. (3/8, 37.5%) .This result goes with that of: Couldwell WT et al [12]: who demonstrated hypokalemia in 40% of Cushing patients. Concerning the imaging technique, spine X-ray was done in the 8 Cushing patients (8/20, 40%) and it showed osteoporotic changes in 6 of them (6/8, 75%). This result is in accord with that of: Wheeler MH and Sadler GP [3]: who found osteoporosis in 70% of Cushing patients. Maad M. A. Rahman and Usama Al Abid [11]: who conducted osteoporotic changes in 77% of Cushing patients.

Including abdominal ultrasound, CT scan, MRI and IVP and their value in the investigation of our patients. They have enriched our preoperative knowledge about the underlying adrenal pathology regarding: its site, size, its relation to the surrounding structure, documenting any local invasion or distal metastasis and discrimination between benign and malignant adrenal tumor.

Couldwell WT et al [12]: who conducted that in case of suspected adrenal malignancy and resection of the ipsilateral kidney may be needed, IVP or CT scan with IV contrast is important to verify the function in contraleteral kidney.Doppman JL et al [15]: who found that adrenal adenoma, adrenal cancer and pheochromocytoma can be differentiated according to their brightness on MRI T2-weighted image. Considering the clinical types of adrenal disorders, hypercortisonism was found in (8/20, 40%) next to it was pheochromocytoma in (6/20, 30%), incidentaloma was found in (5/20, 20%) and virilizing syndrome in (1/20, 5%). This result concedes with that of:

Suresh KN et al [9]: who found that in descending order of frequency, Cushing disease and syndrome, pheochromocytoma, incidentaloma, and virilizing tumor are the most common presenting clinical syndromes of adrenal disorders.

Regarding the histopathological study of the resected adrenal samples, the diagnosis of malignancy was established mainly according to the weight and size of the tumor (weight > 100gm and size > 5cm) even if the tumor had an intact capsule, in addition other features such as nuclear atypia, tumor necrosis and vascular invasion also have suggested malignancy. This concedes with: Medeiros LJ [16]; who conducted that accurate weight of the adrenal neoplasm is very important, as tumors weighing less than 50 gm are almost always benign, while the weight of malignant lesions is usually greater than 100gm. Page DL[17]; who estimated that severe nuclear atypia, vascular invasion and tumor necrosis may in combination support the diagnosis of adrenocortical cancer over adrenal adenoma. Malignancy in the form of adrenocortical cancer was present in 3 cases.

Two of them were in the early stages (I, II) and they were functioning adrenocortical tumors.

The other one was in the late stage III and it was a non functioning incidentally found adrenocortical cancer. This result is in accord with: Isao Hara et al[18]; who found that functioning adrenocortical tumors cause various symptoms that lead to earlier presentation than the non functioning lesions.

While the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) have no published TNM staging system for malignancy of the adrenal gland, the staging system which was proposed by Mcferlone[19] and modified by Sullivan et al[20] and Henley et al[21] is the most commonly used for adrenocortical cancer. According to the results of histopathological study, malignancy was documented in the form of adrenocortical cancer and non of the medullary lesions “pheochromocytoma” had demonstrated malignancy. This result may be attributed to the earlier presentation of pheochromocytoma patients owing for symptoms of headache and palpitation. The patient with the virilizing tumor was proved by histopathological study to have a benign adenoma, this result disagree with: Couldwell WT et al[14] who conducted that virilization secondary to an adrenal neoplasm usually indicates an adrenocortical cancer. This disagreement may be attributed to the small patient sample in our study.

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