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Original Article

Demographic and Clinicopthologic Properties of Patients Operated for Adrenal Masses

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Abstract

Background: The prevalence of adrenal incidentaloma is nearly 4 to 10% and increases with age. Most adrenal masses are nonfunctioning adrenocortical adenomas and found as an adrenal incidentaloma in 80% of cases, but also be conditions requiring therapeutic intervention. We presented our patients with adrenal masses and their management.

Patients and methods: We documented age and gender of patients, and also size, clinical and histopathologic diagnoses of the adrenal masses; diagnostic dilemmas and preferred operation techniques in case series between 01 January; 2015 and 31 December; 2019.

Results: We performed 59 operations on 41 women and 18 men patients with median age of 52.67 years; 25 open and 34 laparoscopic adrenalectomies. Histopathologic analysis revealed 28 adrenocortical adenoma, 5 pheochromocytoma, 7 myelolipoma and one pseudocyst, endothelial cyst and adrenal medullar hemorrhage. Malign ones are 5 adrenocortical carcinoma, 5 metastases from non-squamous lung cancer, 2 from renal cell carcinomas and one from colon adenocarcinoma metastases, and one follicular dendritic cell sarcoma and one lymphoma. Two of non-squamous lung cancer metastases were rarely seen poorly differentiated carcinoma showing enteric differentiation and pleomorphic carcinoma. In addition, one renal cell carcinoma was metastases to contralateral adrenal. One of adrenal mass was operated with a miss diagnosis of adrenocortical carcinoma but reported as a follicular dentritic cell sarcoma after histopathologic analysis.

Discussion: Atypical sarcomas, unexpected tumor metastases and also skip to other adrenal site metastases can be found as an adrenal mass. Adrenalectomy should be performed if hormonal activity or malignancy present. Laparoscopic surgery is feasible in benign lesions and also in some malignant lesions.

Keywords

Adrenal mass, Adrenal incidentaloma, Adrenal cancer, Adrenalectomy

Introduction

The incidence of adrenal masses (AM) increases with widely use of diagnostic radiologic devices and most of time we found them as an adrenal incidentaloma (AI). AI is an asymptomatic AM detected on imaging studies performed for another medical situation. With progress on imaging technology, the prevalence of AI has become up to 4 to 10% and increases with age [1]. The prevalence of AI increases approximately 5% on abdominal computed tomography reports, and even as high as 32% on post-mortem examinations [2].

AIs are nonfunctioning adrenocortical adenomas in 80% cases, but may also represent conditions requiring therapeutic intervention; for instance, hormone producing masses and/or adrenocortical carcinoma (ACC). Their incidences are

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reported up to 23.0% and 12.0%, respectively. Cysts, ganglioneuroma, myelolipoma, hematoma and metastases from lung, breast and renal cancer, malign melanoma, and lymphoma could also present as an AM [3].

The guidelines of the European Society of Endocrinology collaborated with the European Network for the Study of Adrenal Tumors, the American Association of Clinical Endocrinologists collaborated with the American Association of Endocrine Surgeons and Korean Endocrine Society and some reviews discussed and reported the management of AMs [2,4,5]. We presented our patients operated for AMs and their clinical and histopathologic remarkable points and preferred surgical techniques.

Patients and Methods

Clinical evaluation

We assessed any AM clinically for adrenal hormone over activity. We performed other diagnostic work-ups if lesion is more than one cm or lesions that are less than 1 cm but, clinical signs and symptoms are suggestive of adrenal hormone excess. We preferred adrenalectomy (ADX) for unilateral AMs if significant hormone excess present. Hormonal evaluation for cortisol excess; 8.00 a.m. cortisol, DHEA-S, ACTH and in hypertensive patients for evaluation of hyperaldosteronism; plasma renin activity, and serum aldosterone were evaluated. Urinary normetanephrine, and metanephrine were measured. Overnight one mg dexamethasone suppression test was performed in all of the cases. We performed hormonal evaluation 6 months after the initial visit and annually in subsequent visits for non hormone secreting AMs.

We used non-contrast CT in first line radiological diagnostic modality and diagnosed the AM as a benign lesion if measured Hounsfield units is low or equal the 10, homogeneous character and smaller than 4 cm. We did not use any further imaging modalities in these circumstances. On the other hand, if the AM is indeterminate and do not have significant hormone excess, we used other imaging modalities or interval imagings like non-contrast CT or MRI in 6-12 months. We performed ADX if lesion increased in size by more than 20% or 5 mm in maximum diameter. If any lesions consisted of heterogeneity and invasive components with suspicious of malignancy, we used other diagnostic modalities, especially MRI to plan the extent of operation.

Management of the adrenal masses

We generally performed laparoscopic ADX for unilateral AM if less than 6 cm in diameter and without any evidences of local invasion was present, but preferred open ADX if lesions were more than 6 cm in diameter and/or any evidences of local invasion present obeying the advices of guidelines and some reviews [2,4,5]. In time, with the increase in the skill of surgery, we also operated some malignant masses or lesions larger than 6 cm as we performed all operations trans-abdominally.

Patients

We documented age, gender and also size and clinical and histopathologic diagnoses of the AMs; diagnostic dilemmas and preferred operation techniques in case series between 01 January; 2015 and 31 December; 2019 at Haydarpasa Numune Education and Research Hospital. We especially documented and highlighted the differences in the diagnoses of the masses before surgery as a clinical diagnosis and after

Table 1: Clinical and histopahologic analyses and demographic properties of patients operated due to adrenal masses.

		Total Patients	Clinical Diagnosis		Histopthalogic Diagnosis	
			Benign Suspected	Malign Suspected	Benign Reported	Malign Reported
Total Patients		59	41	18	44	15
Median Age Of Patients (Min-Max) Years		52.67 (17-82)	50.36 (17-74)	58.23 (40-82)	51 (17-74)	50.07 (35-82)
40 years	**<**	8 (13.5%)	8	0	7	1
	≥	51 (85.5%)	33	18	37	14
Gender	**Man**	18 (30.5%)	8	10	8	10
	Woman	41 (69.4%)	33	8	36	5
Site of the Mass	**Right**	27 (45.7%)	18	9	21	6
	Left	32 (54.3%)	23	9	23	9
Radiologic Size (mm)		51.89 (14-200)	44.5 (14-200)	69.29 (15- 140)	46.2 (16-200)	69.21 (14-140)
40 mm	**<**	24 (40.6%)	22	2	21	3
	≥	35 (58.3%)	20	15	23	12
60 mm	**≤**	42 (71.18)	35	7	35	7
	>	17 (28.58%)	7	10	9	8
Size after Histopathologic Analysis (mm)		62.27 (10-190)	52.17 (10-160)	86.64 (14-190)	52.5 (10-160)	93 (14-190)
Surgical Technique	**Open**	25 (42.3%)	10	15	11	14
	Laparoscopic	34 (57.6%)	31	3	33	1

surgery as a histopathologic diagnosis. The ethical approval number is 771/12/2019-18 and taken from SBU Haydarpasa Numune Education and Research Hospital.

Results

Results of clinical and histopathologic evaluations

We performed 59 operations on 41 (69%) women and 18 (21%) men patients and 86% were older than 40 years with median age of 52.67 years. Thirty two (nearly 54%) of AMs was located on the left site. Radiological median size of the AMs is 51.89 mm but histopathologic analysis revealed the median size of the tumors was 62.27 mm. Malign lesions were nearly 20 mm bigger than benign ones. Radiological 40.67% (24 out 59 patients) of AMs are smaller than 40 mm and 71.18% (42 out 59 patients) smaller than 60 mm. We performed 25 (42.37%) open and 34 (57.67%) laparoscopic ADX (Table 1).

Preoperatively, 19 (32.27%) patients out of 59 diagnosed were non-functional AMs, and others were 9 Cushing' syndromes, 4 Conn syndromes, 6 pheochromocytomas, 3 myelolipomas, 8 ACCs, 6 metastases from lung, 2 from renal cancer, one from colon and one metastasis from breast cancer. According to clinical evaluations, preoperatively we diagnosed 42 benign and 17 malign lesions, but histopthalogic analysis revealed only 44 benign and 15 malign lesions. We found 37 out of 45 benign lesions were women but 11 of 15 malign lesions were men. Histopathologic analysis revealed 28 (47.45%) of all 59 patients were adrenocortical adenomas, 5 pheochromocytomas, myelolipomas and one pseudocyst, endothelial cyst, ganlioneuroma, and adrenal medullar hemorrhage. Three out of 12 patients diagnosed as benign lesions before operation revealed malign, and 4 out of 8 malign suspected lesions revealed benign lesions after histopthalogic analysis (Table 2). Malign ones were 5 ACCs, 5 metastases from non-squamos lung cancer, 2 renal cell carcinoma, one colon metastases, one dendritic cell sarcoma, and one lymphoma (Table 2 and Table 3). In addition, three out of five our ACCs were hormone active.

Although age of ACC patients are nearly 15 years younger than lung cancer metastases (46.6 to 60.2 years) but much more larger in size (98.8 to 57.6 mm). Renal cell and colon cancer metastases were larger than both ACC and lung cancer metastases but lymphoma (180 mm) and dendritic cell sarcoma (190 mm) are much large than all of them. We interestingly found that although three lung cancer metastases were adenocancer metastases, the other two were very rarely seen lung cancers; one was metastasis of poorly differentiated lung carcinoma showing enteric differentiation and other one was pleomorphic lung carcinoma. In addition, one renal cell carcinoma was metastases to contralateral adrenal site. Both lymphoma and very rarely seen dendritic cell carcinoma of adrenal tumors were adjudged to operation with miss diagnosis of AAC (Table 3).

Management of the adrenal masses

We performed laparoscopic operation in 20 out of 24 lesions smaller than 40 mm and 33 out of 42 patients with tumors less than 60 mm, but we performed laparoscopic operation on 14 lesions bigger than 40 mm and only one patient whose lesion was bigger than 60 mm (Table 4).

Discussion

Prevalence of AMs tends to increase with age and up to

Table 2: Comparisons of the clinical and histopathologic diagnoses of patients operated due to adrenal masses.

	Clinical Diagnosis	Histopthalogic Diagnosis Adrenocortical Adenoma
Non-Functional Adenoma	19	28
Cushing's Syndrome	9	
Conn Syndrome	4	
Pheochromacytoma	6	5
Myelolipoma	3	7
Ganglioneuroma	0	1
Pseudocyst	0	1
Endotheliaal Cyst	0	1
Adrenal Medullary Hemorrhage	0	1
Adenocortical Carcinoma	8	5
Metastases From Lung Cancer	6	5
Metastases From Renal Cell Carcinoma	2	2
Metastasis From Breast Cancer	1	0
Metastasis From Colon Cancer	1	1
Dendtritic Cell Sarcoma	0	1
Lymphoma	0	1
Total Patients	59	59

Table 3: Remarkable properties of histopathologically malign lesions.

	Total Patients	Gender		Age Median year (min-max)	Size After Histopathologic Analysis mm (min-max)	Remarkable points
		Man	Woman			
ACC	5	4	1	46.6 (35-57)	98.8 (14-190)	• Three of them hormone active
Metastasis from Lung Cancer	5	5	0	60.2 (48-65)	57.6 (14-95)	• One Patient: Metastasis of non-small cell - enteric differentiation showing poorly differentiated lung cancer. • One Patient: Metastasis of pleomorphic carcinoma of lung.
Metastasis from Renal Cell Carcinoma	2	1	1	77 (72-82)	80 (40-120)	• One patient have metastasis to contralateral adrenal site
Metastasis From Colon Cancer	1	0	1	75	70	
Lymphoma	1	0	1	53	190	• Clinically misdiagnosed as an ACC
Dendritic Cell Sarcoma	1	0	1	58	170	• Clinically misdiagnosed as an ACC

Table 4: Comparisons of patients operated open or laparoscopic techniques for adrenal masses.

		Surgery Technique	
		Open	**Laparoscopic**
Total Patients		25	34
Site of the Mass	**Right**	10	17
	Left	15	17
Radiologic Size (mm)		72.9 (14-200)	36.6 (16-85)
40 mm	**<**	4	20
	≥	21	14
60 mm	**≤**	9	33
	>	16	1
Clinical Diagnosis	**Benign Suspected**	11	31
	Malign Suspected	14	3
Histopthalogic Diagnosis	**Benign Reported**	9	33
	Malign Reported	16	1
Size after Histopathologic Analysis (mm)		88.33 (14-190)	43.8 (10-90)

10% in the 8th decade [6,7]. In our research, median age is 52 and the youngest patient is at 17 and oldest one is 82-years-old. Although some researchers reported no differences between genders, others reported that women more often develop an AM, even three times more common in women than men patients [6]. Similarly, according to our data, AMs were two times more prevalent in women patients.

Most patients with AMs present hormone inactive, high lipid content and less than 4 cm in size. Most of AMs do not require surgical resection. On the other hand, nearly one fifth of AMs is hormone active and/or has malignancy risks. In previous analyses, the percentage of hormone inactive tumors was reported 70 to 94%, but we found 63.7% of AMs in our patients [6,8]. In addition, the clinically silent pheochromacytomas must be in mind in the surgical decision. The prevalence of pheochromocytoma in clinical and surgical studies reported 7 to 10% [5]. Although, subclinical Cushing' s syndrome and Conn syndrome are mostly reported hormonal conditions, we found Cushing' s syndrome and pheochromocytoma mostly in our patients [9].

The prognosis of ACC is generally poor, and the overall 5-year survival rate after diagnosis is 7% to 65% [10]. Given these facts, it is important to promptly determine whether or not a tumor discovered as an AM is an ACC. The incidence of ACCs in the general population is only 1- /1,000,000/year and ACCs constitutes 1.4% of the AMS [11]. In a cohort study,

ACC was diagnosed in 8.4% of subjects referred for ADX [12]. In some series, the mean malignancy rate was reported between 3.5% and 34% due to varying selection criteria but it was 8.4% of our patients [13].

Determination of the malignant potential of an AM is more difficult. The size criteria for malignancy are not definitive and are derived from some selected series. The actual size of an AM is important, but it can be underestimated at least one cm by modalities such as CT and MRI scans. We know that the risk of malignancy in an AM increases with the size [6]. National Institute for Health and American Association for Clinical Endocrinologists reported the risk of ACC at 25% for AMs with the diameter more than 6 cm, 5% for AMs for between 4-6 cm, and 2% for smaller than 4 cm in size [4]. On the other hand, some AMs are in high-density, hormone-inactive but smaller than 4 cm or in low-density, hormone-inactive and between 4 and 6 cm without radiological signs of malignancy. ADX was recommend in the case of AMs more than 3 cm in diameter in young patients, whereas more than 5 cm in older patients [14]. The rate of malignancy of the AMs with diameters of less than 4 cm, 4-6 cm, and more than 6 cm to be 0%, 2.9%, and 13.6% [15]. In our study, histopathologically benign lesions are much smaller than malign lesions, the average diameters of ACC were 98.8 mm. In our study one ACC and one lung metastasis lesions are both 14 mm in size that is very small AMs than expected to be malignant.

One of the AMs was clinically misdiagnosed as an AAC before operation and reported a follicular dendritic cell sarcoma after histopathologic analysis. Follicular dendritic cell sarcoma is an uncommon tumor and was originally described as a non-lymphomatous primary lymph node malignancy in 1986 [16]. Usually arises in lymph nodes of the cervical, mediastinal, or axillary areas, but rarely in extranodal sites such as small intestine, mesocolon, pancreas, liver, mesentery and the abdominal wall [17]. Retroperitoneal ones have been only sporadically reported. On contrast enhanced CT scan, follicular dendritic cell sarcoma usually appears homogeneous masses but, like ACC, heterogeneity as a result of necrosis or hemorrhage can be seen [18]. Complete surgical resection is the treatment of choice but chemotherapy and radiation therapy modalities have been also used to treat follicular dendritic cell sarcoma.

Adrenal is the fourth frequent site of metastases from malignant cancers. Breast, lung, prostate, colon and renal cancer, and melanoma prefer to metastases to adrenal. In our study, 8 patients out of 13 malignant AMs were metastases. One cancer patient cohort study reported up to 50% to 75% of AI was metastases and postmortem series reporting the incidence up 38% [19,20]. The prevalence of metastatic lesions among AI reported up to 2.5% [4]. Metastases to adrenal glands are more in men and we also found that metastatic lesions dominated in men [21].

Non-squamaous lung carcinomas often metastases to adrenal and we operated 5 such adrenal metastases including two very rare pleomorphic and adenocarcinoma with enteric morphology. Pleomorphic carcinoma is a rare and aggressive pulmonary malignancy and metastases to the brain, liver, adrenal tissue, and bone have been reported. Other rarely seen lung adenocarcinoma with enteric morphology is a special type of primary adenocarcinoma which shares some identical components with colorectal carcinoma. Its metastases to adrenal also well expected. In addition, we have operated intraglandular metastases of two RCC and one colon cancer to adrenal and one of RCC was to contralateral site. While ipsilateral intra-glandular adrenal metastasis of renal cell carcinoma is well known due to its anatomical location, but isolated contralateral adrenal metastasis is extremely rare. In autopsy studies, only up to 2.5% found to have the contralateral adrenal gland as the sole site of metastasis [22].

Many research reported significant survival improvement and pain palliation with surgical interventions in some metastatic AMs [22]. Multidisciplinary oncologic evaluation and patient's functional status are important before deciding any surgical interventions. In our study, we performed ADX in five from lung, two intraglandular metastases from renal cell and one colon cancers for curative intention after multidisciplinary consultation.

Nowadays, laparoscopic ADX is the preferred surgical technique to resect any AMs. With the recent advances, a robotic approach is also an important option. With the advantages of less blood loss, quicker recovery and hospitalization, the laparoscopic approach has improved surgical results compared to the open ADX [23-25]. Even, laparoscopic ADX was recommended and shown it a feasible, safe and superior treatment option for pheochoromacytoma [26]. However, both laparoscopic and robotic ADX for adrenal malignancies remains uncertain on oncologic outcomes [27,28]. Open surgery is recommended when the tumor is large or suspected to be malignant [6]. On the other hands, data from some series have shown that minimal invasive ADX could be performed in some selected metastases [29,30]. We generally preferred laparoscopic operations to masses less than 60 mm and benign but the median size of our AMs resected with laparoscopic ADX was 43.8 mm (10-90 mm) and open was 88.33 mm (14-190 mm). In addition, we performed laparoscopic operation in three malignant suspected lesions but only one of them was reported histopathologically as a lung cancer metastasis.

In conclusion, adrenal is a site of many non-functional and also hormone active benign and malignant lesions and metastases. Adrenal masses should be resected if hormone active or malignancy present. Laparoscopic surgery is feasible in benign lesions and also in some of the malignant lesions. Rarely seen lung cancer metastases, contralateral site renal cell carcinoma metastasis and also some rare sarcoma can be encountered when evaluating an adrenal mass.

Conflict of Interest

We all authors declare that there is no conflict of interest.

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