

Adrenal cystic lesions: Report of 12 surgically treated cases and review of the literature

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ABSTRACT. Adrenal cysts are rare (0,064%-0,18% in autopsy series) and less than 500 cases have been reported in the western literature. Incidental diagnosis of adrenal cysts, however, is reported with increasing rates. We observed 12 patients with adrenal cyst. Each of them had a careful laboratory and instrumental evaluation; all the patients were operated. In our series about 67% of the patients were symptomatic (6 patients with abdominal pain, 1 with palpable mass, 1 with hemorrhagic shock). No biochemical alteration was observed. Conversely we observed an unusual subclinically hyperfunctioning cystic adenoma, potentially progressive to a clinically recognizable endocrine syndrome. US, CT and MRI had a sensitivity of 66,7%, 80% and 100% respectively. Adrenalectomy was performed in all patients. The pathological findings

were: 1 epithelial cyst (cystic adenoma), 2 endothelial cysts (vascular cystic ectasia with adenomatous adrenocortical hyperplasia and 1 vascular cyst) and 9 pseudocysts. On the basis of these results, we conclude that a careful hormonal, morpho-functional and instrumental evaluation is indicated in all adrenal cysts, even if the available diagnostic procedures, even when combined, cannot always define their nature. Surgical excision, when possible by laparoscopic approach, is indicated in presence of symptoms, endocrine abnormalities (even when subclinic), complications, suspicion of malignancy and/or large size (>5 cm). Adrenal gland must be excised *en bloc*, also because of the possible presence of other adrenal lesions.

(J. Endocrinol. Invest. 21: 109-114, 1998)

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INTRODUCTION

Adrenal cystic lesions are rare: since the first autopsy report of Greiselius (1) in 1670, less than 500 cases have been described in the world literature, including autopsy and clinical series (2, 3).

In the past the real incidence in the general population was supposed to be higher than usually believed, because of the difficult diagnosis of clinically silent lesions (4-6). Recently, the common use of ultrasonography (US), computerized tomography (CT) and magnetic resonance imaging (MRI) has resulted in increased diagnosis of serendipitous adrenal masses and, among these, of cystic lesions (2, 3, 7, 8).

Adrenal cysts are a heterogeneous group of lesions with different etiology and pathogenesis, as demonstrated by several attempts of classification (1, 9-11): careful diagnostic evaluation is mandatory to select the appropriate management, which is still controversial (10, 12, 13).

The authors report their clinical experience with 12 cases and a review of the literature.

MATERIALS AND METHODS

From April 1978 to January 1997, 146 patients with adrenal lesions were observed at the Department of Surgery of the Catholic University School of Medicine in Rome; 12 of them (8,2%) had adrenal cysts. There were 6 women and 6 men, with average age of 40 years (range 15-62 yr). None of them had clinical signs of adrenal disease at the time of diagnosis. Symptoms retrospectively related to adrenal neoplasm (e.g. vague abdominal and lumbar pain, dyspepsia) were reported in 6 patients. One patient presented, with acute abdominal and lumbar pain, acute anemia and hemorrhagic shock. An abdominal palpable mass was found in 2 patients, one of them complained of lumbar pain.

Key-words: Adrenal cyst, adrenal incidentaloma, adrenal surgery, adrenal pseudocyst, adrenal neoplasm, adrenal tumour, pre-Cushing syndrome, cystic adenoma.

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Accepted: November 24, 1997

Three patients were hypertensive, with non-stable arterial pressure values.

In 10 patients a careful hormonal evaluation was obtained, including 24-hr urinary cortisol, aldosterone, 17-hydroxycorticosteroids, 17-ketosteroids, vanilmandelic acid (VMA), metanephrine, catecholamine, homovanillic acid; basal plasma cortisol and its diurnal variation; determination of plasma aldosterone and renin activity both after overnight recumbency and after 4 hr upright posture; plasma dehydroepiandrosterone-sulphate (DHEAS). In 2 cases a single-dose overnight dexamethasone suppression test was carried out.

US was performed on all patients, CT on 10 and MRI on 2; angiography was carried out in 2 cases, an iv pyelography in 2.

In 3 patients ⁷⁵Se-selenomethyl-cholesterol adrenal scintigraphy (in 1 case after oral administration of dexamethasone) and in 2 ¹³¹I-MIBG scanning were performed. A CT-guided biopsy of the mass was obtained in 1 case.

All the patients have been operated: we adopted an anterior transperitoneal subcostal approach in 9 patients, a lombotomic extraperitoneal approach in 2 cases; a laparoscopic adrenalectomy was performed in the last patient.

RESULTS

All the cysts were unilateral: 7 of them were on the right and 5 on the left. The mean diameter was 9,1 cm (range 3 to 30 cm).

Table 1 - Adrenal cysts: clinical presentation, diagnostic investigation and pathology in our experience.

Pat	Sex	Age	Clinical presentation	US	CT	MR	Angiography	IVU	Se-cholesterol scintigraphy	MIBG scintigraphy	Size (cm)	Pathology
1	F	42	Palpable mass	N ^a	N ^a	-	-	N ^a	-	-	15	Organizing hematoma
2	F	27	Abdominal pain	P	P	P	-	-	IP	-	7	Sclero-calcific wall cyst
3	F	34	Abdominal pain	P	P	-	-	P	-	-	8	Adrenocortical adenomatous hyperplasia + cystic vascular ectasia
4	M	51	Abdominal pain	P	-	-	P	-	-	-	10	Hemorrhagic cyst
5	M	62	Abdominal pain	N ^{a*}	N ^{a*}	-	N ^a	-	-	-	6,5	Organizing haematoma
6	M	39	Incidental finding	P	P	-	-	-	DP	N	5	Multilocular cyst
7	M	37	Incidental finding	P	P	P	-	-	-	-	6	Sclero-atrophic wall cyst
8	M	51	Incidental finding	P	P	-	-	-	-	-	8	Cystic involution in adrenal adenoma
9	M	51	Incidental finding	P	P	-	-	-	CP	-	3	Cystic adenoma
10	F	15	Acute, severe anemia, acute abdominal pain	N ^{c°}	-	-	-	-	-	-	30	Hemorrhagic cyst
11	F	32	Abdominal pain	N ^a	P	-	-	-	-	-	5	Vascular cyst
12	F	37	Abdominal pain	P	P	-	-	-	-	-	6	Fibro-calcific wall cyst

P= Positive (Adrenal Cyst); N= Negative; CP= Concordant Pattern; DP= Discordant Pattern; IP= Indifferent Pattern; ^a Hepatic Hydatid Cyst; ^b Adrenal Carcinoma; * FNAB: suspected malignancy; ^c sub-hepatic neoformation, with fluid corpuscular content, like a hemorrhagic collection of uncertain origin; [°] Chest x-ray: swelling diaphragmatic shape on the right side.

Laboratory findings

One patient complaining of abdominal pain, similar to a renal colic, had an acute, severe anemia due to intracystic bleeding (Hb 4.9 g/dl; RBC 1.710.000/mmc; Hct 14.9%). Plasma renin activity diminished without any change after 4-hr upright posture in a stable hypertensive patient. Moderate hypokaliemia was observed in a patient with a cystic adenoma which appeared tracer uptaking at ⁷⁵Se-selenomethyl-cholesterol scanning, performed after dexamethasone administration. No other significant biochemical alterations were observed.

Imaging studies

US showed a cystic adrenal lesion in 8 out of 12 cases (sensitivity 66.7 %), CT in 8 out of 10 (sensitivity 80%), and MRI in both the patients on whom it was performed.

False negative diagnosis was given by non-invasive imaging in three patients.

⁷⁵Se-selenomethyl-cholesterol scintigraphy, performed after oral administration of dexamethasone, showed uptake of radiotracer at the side of the mass (concordant imaging pattern) in a patient with a cystic right adrenal adenoma. A "cold" area between the right adrenal gland and the homolateral kidney was observed in the second case (discordant imaging pattern); in the third patient a bilateral symmetric uptake pattern was found. ¹³¹I-MIBG was negative in all cases.

The results of the performed diagnostic investigations are illustrated in Table 1.

Surgery and post-operative period

All the cysts were excised *en bloc* with the adrenal gland. Four patients needed transfusions during surgery. No other intraoperative complication was reported.

In the postoperative period one patient presented an acute cholecystitis, treated conservatively; no other surgical complications were observed.

The mean postoperative hospitalization was 9 days. Acute or late postoperative adrenal failure have not been observed.

Pathology

The observed histotypes were:

*1 epithelial cyst: 1 cystic adenoma, 3 cm in diameter;

*2 endothelial cysts: 1 vascular cystic ectasia associated with adenomatous adrenocortical hyperplasia (8 cm) and 1 vascular cyst (5 cm);

*9 pseudocysts: 1 adenoma with cystic involution (8 cm); 1 multilocular cyst (5 cm), 1 sclero-atrophic

wall cyst (6 cm); 1 sclero-calcific wall cyst (7 cm), 1 fibro-calcific wall cyst (6 cm), 2 hemorrhagic cysts (10 and 30 cm in diameter, respectively), and 2 organizing hematoma (6,5 and 15 cm, respectively).

DISCUSSION

Adrenal cysts are rare: their incidence ranges between 0.064% (5) and 0.18% (6). They represent about 4-22% of all the incidentalomas in different series (14). These lesions have been observed at all ages, with a peak incidence between the third and sixth decade, also in our experience (1, 3, 8-10, 15, 16). They seem to affect women 2 or 3 times more often than men (1, 9, 10, 17), but some authors reported different ratios (8). The cysts are usually unilateral (bilateral in about 8-15 % of all cases) without a side prevalence (1, 15, 18) and their size may range from the microscopic ones to those huge containing several litres of fluid.

The first remarkable pathogenetic classification of adrenal cysts was proposed by Terrier and Lecene in 1906 and simplified by Abeshouse: the division, repropoed by Foster (1), into 4 categories (Table 2) is now widely accepted, although the identification of these histologic types and their pathogenesis is still debated, particularly in presence of epithelial cysts and pseudocysts (10, 11, 19-22).

Recently, immunohistochemical findings suggested that some (and perhaps most of) adrenal pseudocysts originate as endothelial-lined vascular lesions and their origin from a degenerated adrenal neoplasm is unlikely (11). Conversely, in our experience, at least in one case the adrenal cyst originated from a degenerated adrenal adenoma.

Table 2 - Classification of the adrenal cysts.

Histologic type	Frequency in the world literature	Frequency in our experience
Parasitic cysts (Hidatid cysts)	7%	-
Epithelial cysts	9%	
Embryonal cysts		
Cystic adenomas		8,3%
True glandular cysts (Mesothelial cysts)		
Endothelial cysts	45%	16,7%
Lymphangiomatous cysts	42%	-
Angiomatous cysts	3%	
Pseudocysts	39%	75%

Most of the adrenal cysts are asymptomatic and incidentally diagnosed; symptoms and signs, when present, are usually related to the compression or displacement of abdominal organs (e.g. dull upper abdominal or lumbar pain, gastrointestinal and urinary symptoms, palpable mass, etc.) and they are more frequent when cysts are large (1, 10, 16). In our series symptoms and signs (abdominal pain, palpable mass) were present in 8 patients out of 12 (66.6%).

More rarely, symptoms are related to an endocrine dysfunction (Cushing syndrome, virilizing syndrome, pheochromocytoma syndrome, adrenal failure) (1, 8, 10, 12, 23).

Arterial hypertension, cured or dramatically improved after surgical removal of an adrenal cyst, has been sometimes described, even in absence of any endocrine activity (1, 4, 24); several pathogenetic mechanisms have been proposed (angulation or compression of the renal vessels, vasoactive or neuroendocrine stimulation) (4, 10, 24), but none of them is completely exhaustive. Three of our patients (25%) were hypertensive, but none showed post-operative resolution or improvement of arterial hypertension.

Adrenal cysts may be diagnosed when complicated. Massive retroperitoneal hemorrhage due to a ruptured adrenal cyst (eventually associated with compression of the liver and the infra-hepatic vena cava), and intracystic hemorrhage, sometimes associated with acute anemia and shock, have been reported (1, 17, 25-27). We observed a case of intracystic bleeding with acute anemia and haemorrhagic shock requiring an emergency laparotomy. Adrenal pseudocysts complicated by infection, occasionally associated with sepsis, have also been described (20, 28).

Laboratory findings are usually aspecific and not very useful for diagnosis (3, 8). However, an accurate hormonal evaluation is advisable in all patients with adrenal cysts because of the possible origin from benign or malignant adrenal neoplasms (8, 10).

The common imaging methods (chest x-ray, abdominal plain x-ray, IVU, aortography) may show only indirect signs of an adrenal lesion (altered diaphragmatic outline; calcifications - about 15% of the cases; displacement of the kidney, neovascularization or stretching of adrenal vessels): due to these technical limitations, a preoperative diagnosis of adrenal cysts was possible in the past only in a small number of cases (3, 2-7, 2%), even when symptomatic (1, 7, 8, 10, 15, 18). The introduction and the wide use in the clinical practice and the technical improvement of US, CT and MRI resulted

in increased frequency of diagnosis of adrenal masses, and among these of cystic neoformations, even if clinically mute (3, 7, 22). Features of adrenal cysts are similar to those of other organs (29, 30), however they present more complex aspects about their etiopathogenesis (29, 30). It is sometimes difficult to identify the origin of cystic neoformations, especially when large; in these cases it may be helpful to use multiplanar imaging methods, such as US and MRI, especially when they are integrated (29). Nevertheless, an exact preoperative diagnosis is not possible in all cases, as also results by our experience.

Recently, NP-59 and Selenomethyl-cholesterol scintigraphy have been widely used to functionally evaluate non-hypersecreting adrenal masses (31-33). Gross et al. described three different scintigraphic patterns: an asymmetric, increased or lateralizing accumulation of the radiotracer to the side of the adrenal mass (concordant pattern) is characteristic of functioning, but nonhypersecretory benign adrenal lesions (i.e. adrenocortical adenomas); destructive or space-occupying lesions (i.e. malignant adrenocortical neoplasm, cyst, hemorrhage, adrenomedullary lesion) show decreased or absent radiotracer uptake (discordant pattern); a normal scintigraphic scan, without significant lateralization of tracer, is characteristic of small size or extraadrenal lesions (31).

However, in our experience, only 2 of 3 cysts resulted as no-tracer uptaking at selenomethyl-cholesterol scintigraphy. In the third case a selenomethyl-cholesterol scan, performed after oral administration of dexamethasone, showed surprisingly an exclusive tracer uptake within the lesion with suppression of the normal contralateral glandular parenchyma, in absence of any endocrine alteration. This unusual finding could be related to either histological type (cystic adenoma) or to the relative small size of the lesion. Such subclinical endocrine hyperfunction is very similar to that one described only in solid incidentalomas and defined as "Sub-Clinical Cushing Syndrome" or "Pre-Cushing Syndrome" (31, 34-37). We could hypothesize that this functioning, but not hypersecretory, cystic adenoma could eventually autonomize producing a clinically recognizable endocrine syndrome.

On the basis of this case, we emphasize that an accurate endocrinological evaluation is mandatory for patients with incidental diagnosed adrenal lesions and, in selected cases, a study of the pituitary-adrenal axis should be carried out through a dexamethasone suppression test, since a subclinical hyperfunction is possible. Moreover, in our opin-

ion, ^{131}I -MIBG scintigraphy may be helpful for cysts of suspicious pheochromocytomatous origin.

In clinical practice percutaneous adrenal cyst puncture, under either fluoroscopic or US or CT guidance (15, 29), has been sometimes used to evaluate (cystography, cytologic examination) or treat (aspiration of the cystic fluid, sclerotherapy) patients with cystic adrenal lesions prior to or instead of surgery (15, 29); however this is an invasive procedure and has a significant morbidity (29).

There is no general agreement about the management of adrenal cysts. Some authors propose surgery in all cases (10) due to the impossibility of an accurate diagnosis, others adopt a less aggressive and conservative approach (2, 3, 7, 8, 29).

Our opinion is influenced by several considerations. First of all, in the current clinical practice an exact diagnosis of nature of an adrenal lesion is not possible in all cases. Morpho-dimensional criteria, adopted for solid incidentalomas, are not helpful in cystic lesions: benign cysts of massive proportions have been described. A cystic degeneration of an adrenal neoplasm, benign or malignant, primitive or secondary, may occur, as demonstrated in our experience, contrary to what was recently supposed by other authors (11). Moreover, a neoplastic degeneration of epithelial cysts and, recently, an adenoma-carcinoma sequence for adrenocortical neoformations has been supposed (22, 38). Clinical evidence of endocrine dysfunction may occur (1); we, also observed an unusual subclinical hypersecreting cystic adenoma and adrenal cysts may coexist with an adrenocortical hyperplasia (as we observed) or with a functioning adenoma (39).

A correlation between adrenal cysts and hypertension is not uncommon, although still unclear. Finally, adrenal cysts may develop life threatening infective or hemorrhagic complications, requiring an emergency operation (17, 20), particularly when large.

Therefore, we conclude that surgical management, in absence of absolute contraindications, is advisable for all symptomatic cysts and when suspected malignancy, hormonal secretion or large dimension (>5 cm) are present. Asymptomatic, non-functioning small sized cysts (<5 cm) require a conservative management, and a periodic US or CT follow-up; analysis of intracystic fluid may be useful.

Conversely, we think that percutaneous aspiration of the symptomatic cysts of large dimension is unadvisable, because recurrences, even after sclerotherapy, have been frequently described and cytologic examination of the cyst fluid does not have high diagnostic accuracy (2, 29, 40).

Several surgical interventions have been proposed

(e.g. excision of the cyst alone or with a small part of glandular parenchyma; marsupialization of the cyst, etc.): we believe that adrenalectomy *en bloc*, preferably by a laparoscopic approach, is indicated in all cases, because of its low morbidity and the possible coexistence with other adrenal lesions (i.e. adenomatous hyperplasia, adenoma).

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