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Adenomatoid tumour of the adrenal gland: a case report and literature review

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Adenomatoid tumour (AT) is a rare, benign neoplasm of mesothelial origin, which usually occurs in the genital tract of both sexes. Occasionally these tumours are found in extra genital locations such as heart, pancreas, skin, pleura, omentum, lymph nodes, retroperitoneum, intestinal mesentery and adrenal gland. Histologically ATs show a mixture of solid and cystic patterns usually with focal presence of signet-ring like cells and scattered lymphoid infiltration. The most important thing about these tumours is not to misdiagnose them as primary malignant or metastatic neoplasms. We present a case of an adrenal AT in a 29-year-old asymptomatic male. The tumour was an incidental finding during abdominal CT-scan for an unrelated condition.
We also present a review of the literature concerning adrenal gland AT and give possible differential diagnosis.

Key words: adenomatoid tumour, adrenal gland, immunophenotype.

Introduction

Adenomatoid tumour (AT) is a benign neoplasm of mesothelial origin [1-3]. The usual place of its appearance is the male and female genital tract, most often epididymis in men and fallopian tube in women [4, 5]. Extragenital ATs have occasionally been described in heart [6], pancreas [7], skin [8], pleura [9], omentum [10], lymph nodes [11], retroperitoneum [12], intestinal mesentery [13], periadrenal soft tissue [14] and adrenal gland [15-31].

We report the clinicopathological and immunohistochemical findings of an incidentally discovered AT of the right adrenal gland in a 29-year-old man.

Material and methods

The resected adrenal gland with tumour was fixed in a 10% buffered formaldehyde solution. Representative sections of the tumour were embedded in paraffin. Tissue samples were cut into approximately 4 µm thick sections by microtome, placed on glass slides and stained with haematoxylin end eosin for histopathological examination. Additional sections were made for immunohistochemical analysis (for details see Table I).

Proliferative activity of the tumour was determined using immunohistochemical staining for nuclear protein MIB-1 (Ki-67). The proliferative activity rate (MIB-index) was calculated as a percentage of nuclei positive for MIB-1 in five areas of 100 cells each.

Clinical data were obtained from the patient's files in the Endocrinology and Surgery Departments.

Results

Clinical and macroscopic findings

A 29-year-old male was admitted to the hospital with the diagnosis of inguinal hernia. The pre-operative imaging procedures revealed a well circumscribed, mostly solid, 4 µm tumour of the right adrenal gland. The right adrenal gland with the tumour was removed.

The material sent for the histological examination weighted 34 g and consisted of fatty tissue and

Table I. Primary antibodies used for immunohistochemical staining

Antibody	Pretreatment	Dilution/ Incubation time	Detection method	Manufacturer
AE1/AE3	citrate buffer	1/50 (30')	LAB VISION	Dako
CK5/6	EDTA	1/50 (30')	EN VISION	Dako
CK7	citrate buffer	1/50 (30')	EN VISION	Dako
CK20	citrate buffer	1/50 (30')	EN VISION	Dako
calretinin	citrate buffer	1/100 (60')	EN VISION	Novocastra
D2-40	citrate buffer	ready to use (30')	EN VISION	Polgen
CD31	EDTA	1/20 (60')	EN VISION	Dako
CD34	citrate buffer	1/50 (30')	LAB VISION	Dako
factor VIII	citrate buffer	1/50 (60')	EN VISION	Dako
Ki-67	citrate buffer	1/50 (night)	LAB VISION	Dako

enlarged adrenal gland. On cross-sections a mass 4 cm in the biggest dimension arising from not-widened 3.5 cm long adrenal gland was seen (Fig. 1). The tumour was solid and well circumscribed. Its cut surface was smooth, greyish-white and partly yellow without haemorrhage or necrosis.

Histological findings

The histological examination revealed an unencapsulated tumour consisting of a mixture of different patterns: gland-like spaces of various size, irregular outline and focal cystic dilation and solid nests of cells set in a fibrous stroma (Fig. 2). The tumour structures were seen between nests of residual adrenocortical cells (Fig. 3). A discontinuous rim of compressed adrenal cortex was focally present around the tumour. Cells lining these irregular channels and tubular structures were mostly flattened resembling endothelial cells (Fig. 2). Some of them were plump with epithelioid features and abundant cytoplasm. Small groups of cells with the appearance of so-called signet-ring cells with round, intracytoplasmic vacuoles were also seen (Fig. 3). Nuclei were vesicular, occasionally with small nucleolus. None of the cells exhibited atypia or pleomorphism. Mitotic figures and necrosis were absent. Small lymphoid aggregates and foci of lipomatous metaplasia were focally present within the tumour (Fig. 4). The adrenal medulla had typical histological structure without evidence of the tumour cells. Mucicarmin stain did not reveal any presence of mucin within signet-ring like cells or in tumour channels. An immunohistochemical examination showed that the tumour cells exhibited strong expression of cytokeratin

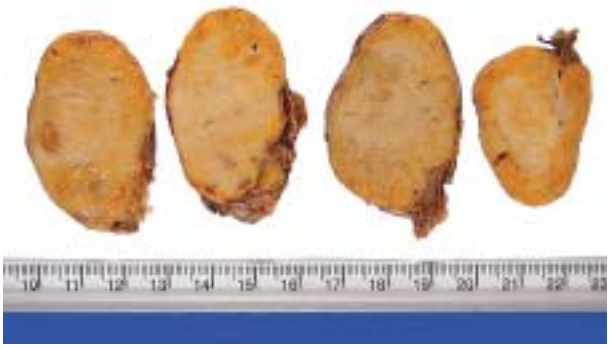

Fig. 1. Cut surface of the adrenal gland showing a solid, well circumscribed tumour with smooth, greyish-white surface

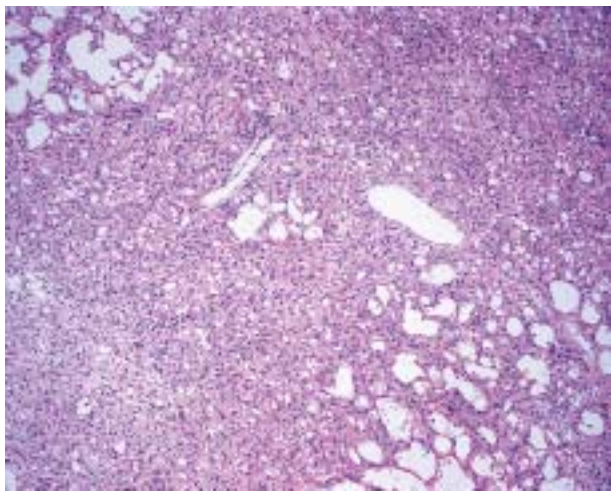

Fig. 2. Adrenal AT composed of mixture of patterns: fenestrated channels of varied size and irregular outlines, and solid nests of cells (HE, 10×)

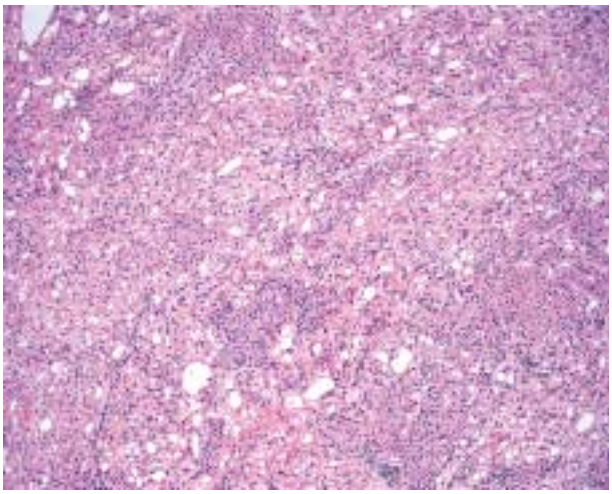

Fig. 3. Tumour structures intermingled with residual adrenal cortical tissue (HE, 10×)

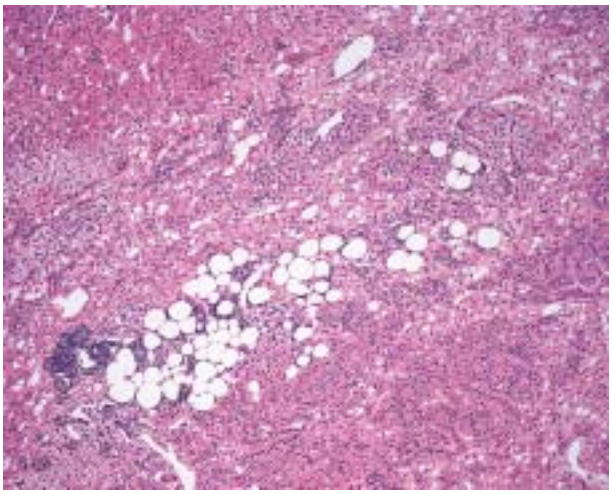

Fig. 4. Focal lymphoid aggregates and foci of lipomatous metaplasia within AT (HE, 10×)

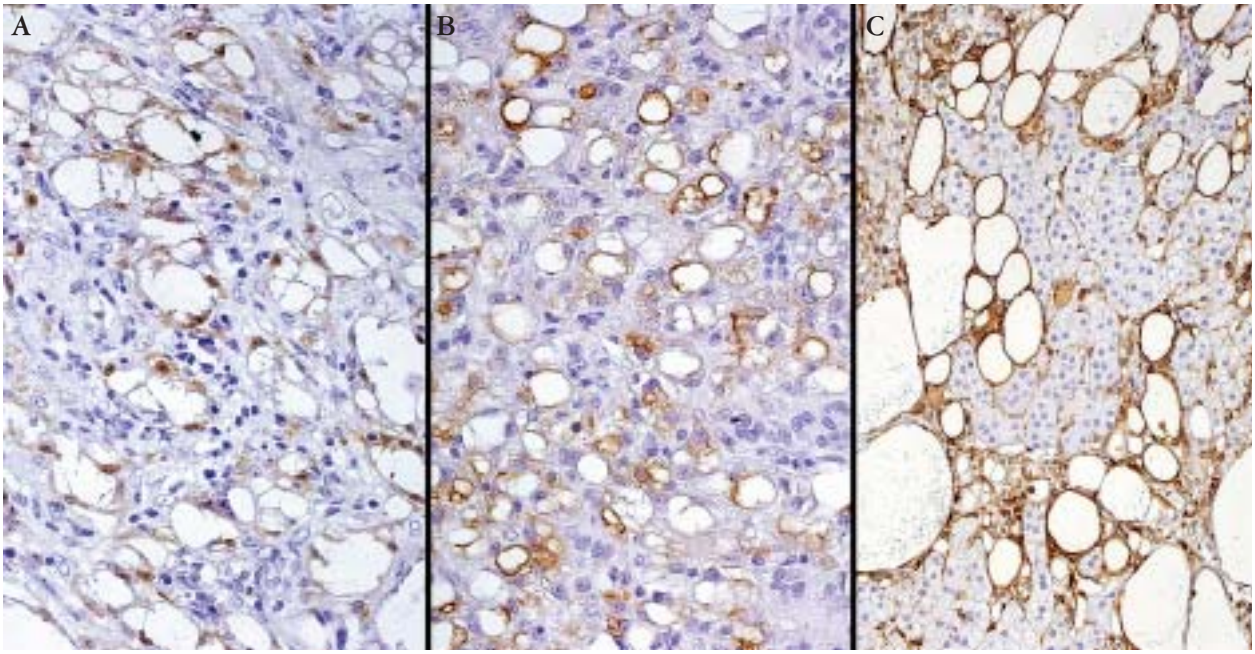

Fig. 5. Adrenal AT immunohistochemistry: A) calretinin, B) D2-40, C) Vimentin

AE1/AE3, CK7, calretinin (Fig. 5), D2-40 (Fig. 5) and vimentin (Fig. 5). Focal expression of cytokeratin CK5/CK6 was observed. Tumour cells did not express any vascular markers like: CD31, CD34 and Factor VIII or epithelial marker CK20. Proliferating activity measured by expression of proliferative marker Ki-67 (MIB-index) did not exceed 1% of cells.

Discussion

AT is a rare finding usually present in the genital tract. Adrenal gland AT is extremely rare: we could only find 27 cases reported previously in the literature [15-31]. Only four authors reported more than one case of AT [16-18, 28] with the biggest series consisting of 5 cases [18]. Characteristics of the 28 adenomatoid tumours reported previously together with our case are summarized in Table II.

ATs occurred in young adults mostly in the 3rd-4th decades of life. The average age of patients in all reported cases was 40, ranging from 24 to 64 years. Only 6 patients were older than 50.

Most of the patients with the adrenal gland AT were men. Only one tumour was reported in a woman [16]. A possible explanation for this disproportion can be connected with the differences in embryological development of the gonads in both

Table II. Clinicopathological features of adenomatoid tumours of the adrenal gland

PATIENT NO.	AGE	SEX	LATERALITY	DIAMETER	CLINICAL FINDINGS AND SYMPTOMS	CITATION
1.	26	M	R	15	IRF (suspicion of a giant echinococcus cyst of the liver)	[15]
2.	49	M	R	1.3	IFA	[16]
3.	57	M	L	3.8	IFA	[16]
4.	50	F	R	0.5	IFA	[16]
5.	40	M	L	6.0	IRF (found on CT scan during sarcoma staging)	[16]
6.	46	M	R	1.2	CT (symptoms: central and right flank abdominal pain)	[17]
7.	33	M	L	1.7	IRF (CT during workup for hypertension)	[17]
8.	33	M	R	4.2	IRF (CT)	[17]
9.	37	M	L	3.1	IFS	[18]
10.	31	M	R	3.2	IRF	[18]
11.	31	M	–	3.5	IRF (investigation in the course of hypertension)	[18]
12.	64	M	L	1.2	IFA	[18]
13.	44	M	L	3.2	IRF (investigation in the course of hypertension)	[18]
14.	24	M	L	1.1	IRF (during investigation for Cushing syndrome)	[19]
15.	30	M	L	3.0	IFA	[20]
16.	54	M	L	6.5	IRF (investigation in the course of pneumonia)	[21]
17.	31	M	R	4.0	IRF	[22]
18.	42	M	L	2.5	IRF	[23]
19.	54	M	R	3.6	IRF	[24]
20.	51	M	R	3.0	IRF (investigation in the course of hypertension)	[25]
21.	28	M	R	9.0	IRF (investigation in the course of acute cholecystitis)	[26]
22	42	M	L	14.5	IRF (during evaluation of renal colic)	[27]
23.	47	M	R	7.0	IRF (CT performed for diverticulitis)	[28]
24.	52	M	R	5.5	IRF (investigation in the course of hypertension)	[28]
25.	44	M	L	3.5	IRF (investigation in the course of hypertension)	[29]
26.	34	M	R	3.0	IFA	[30]
27.	33	M	L	1.7	IRF (investigation in the course of hypertension)	[31]
28.	29	M	R	4.0	IRF	our case

M – male, F – female, R – right adrenal gland, L – left adrenal gland, IRF – incidental radiographic finding
IFA – incidental finding during autopsy, IFS – incidental finding during surgery for unrelated reasons

sexes, especially different role of mesonephric ducts in males and females [20] together with the hypothesis that ATs arise from inclusions of pluripotential mesenchyme cells associated with the Mullerian tract [1, 17-19]. The mesonephric duct in men slowly transforms into a duct of epididymis and remains in that form. The mesonephric duct in women regresses early during the embryogenesis [20]. The possibility of penetration of pluripotential mesenchyme cells from the developing mesonephric duct to different locations (e.g. adrenal glands) in women is much less probable than in men.

Adrenal ATs were almost equally distributed between the right and left adrenal glands (14 : 13), in one case, data were not available. Almost all cases were discovered incidentally during radiographic examination [15-19, 21-29, 31], surgery for an unrelated reason [18] or during autopsy [16, 18, 20, 30].

ATs demonstrated a great degree of size variation: the smallest described examples were about 1 cm in diameter [16-19], the biggest one had about 15 cm [15]. 21 reported ATs were smaller than 5 cm and all were asymptomatic [16-20, 22-25, 28-31] as well as two the biggest tumours [15, 27]. Only one patient had symptoms which could be connected to adrenal mass [17]. The patient with central and right flank abdominal pain had a coexisting big adrenal cyst (11 cm in diameter) with only small AT 1.2 cm in diameter in the cyst wall. The symptoms were more probably connected with the big cystic mass in the abdomen than with the small solid area of AT in the cyst wall [17].

ATs were round, usually well circumscribed, gray or greyish-white with light-yellow areas. In some of them irregular cystic spaces had been macroscopically visible [16, 21, 23, 27].

The immunohistochemical profile was consistent with the one described in ATs in usual locations (genital tract) and was typical for the tumuor of mesothelial origin: calretinin +, CK5/6+, CK7+, vimentin+, D2-40+, CD31–, CD34–.

Diagnosing difficulties of AT may arise when this tumour occurs in sites different from its usual location which is the urogenital tract. The adrenal AT tumour can mimic all other entities occurring in this place like: adenomas, carcinomas, pheochromocytomas, myelolipomas, benign cystic lesions and metastases from distant locations. It may also be easily misdiagnosed as vascular neoplasm: lymphangioma or angiosarcoma. Differential diagnosis includes all these entities.

Numerous irregular cystic spaces lined with flattened cells may suggest a vascular neoplasm, especially lymphangioma. However, the cells are positive for CK and they lack reactivity for the usual vascular markers (CD31, CD34, factor VIII), which excludes vascular tumours. It is important that ATs may show reactivity for D2-40, a marker which is known to be positive in endothelia of lymphatic vessels. At least in two cases reported in the literature ATs were primarily diagnosed as lymphangiomas [18].

Histologically all ATs presented a local pseudoglandular pattern often with an infiltrative appearance at the periphery which could lead to it being confused with adenocarcinoma. In case number 1 described by Isotalo [18] AT was incorrectly diagnosed as adenocarcinoma (the diagnosis from a frozen section). The final diagnosis from permanent sections was correct. Adenocarcinomas of the adrenal gland show striking nuclear pleomorphism, the mitotic figures are easily found and the cells are cytokeratin positive but they do not show co-expression of cytokeratin and calretinin (nuclear staining). The MIB-index in any reported AT was not higher than 3% (the highest one reported by Isotalo [18]). MIB-index in malignant primary and metastatic adrenal tumours is usually much higher.

Mucin stain may be helpful in excluding the neoplastic nature of signet-like looking cells. Such cells in AT are mucin negative. Signet-ring cell carcinoma (usually metastatic from a stomach) shows nuclear pleomorphism and cells contain a lot of acid mucin: dark blue droplets in Alcian-PAS. Cystic adenomas which are considered in differential diagnosis do not express CK and D2-40. Excluding cases of ATs found incidentally during autopsy, the local resection of the tumour was curative for all patients. No local recurrences or metastatic spread of AT have ever been reported.

In summary, ATs in extra genital sites like adrenal gland are very uncommon. Nonetheless, such diagnostic possibility should always be considered in order to avoid misdiagnosing them as primary or metastatic malignant tumours.

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