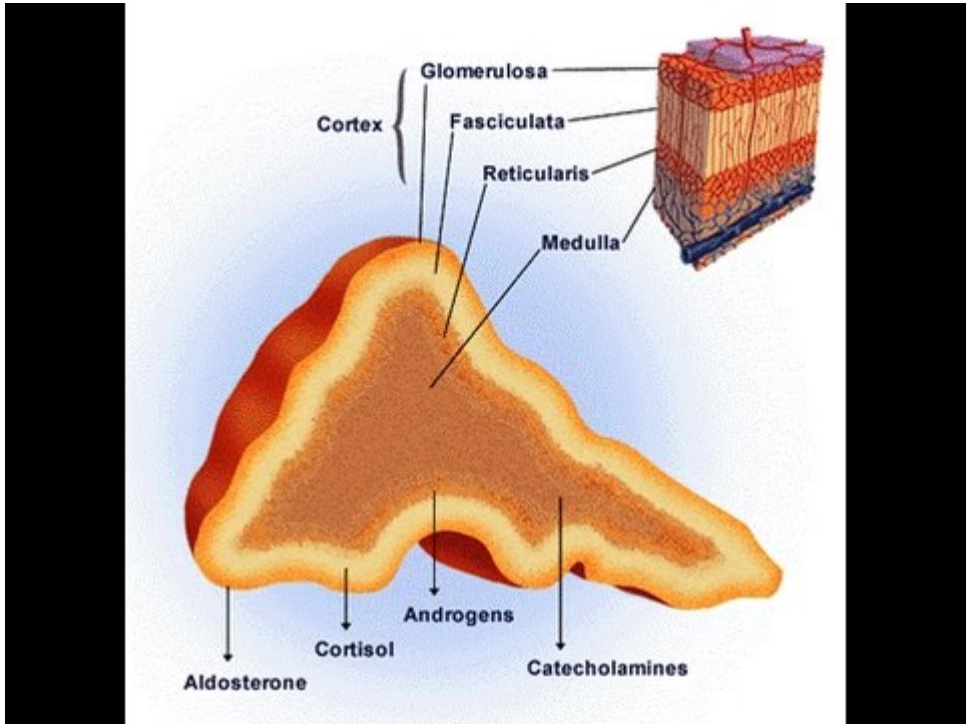
14/3/2016

Adrenal Gland Pathology

Master class

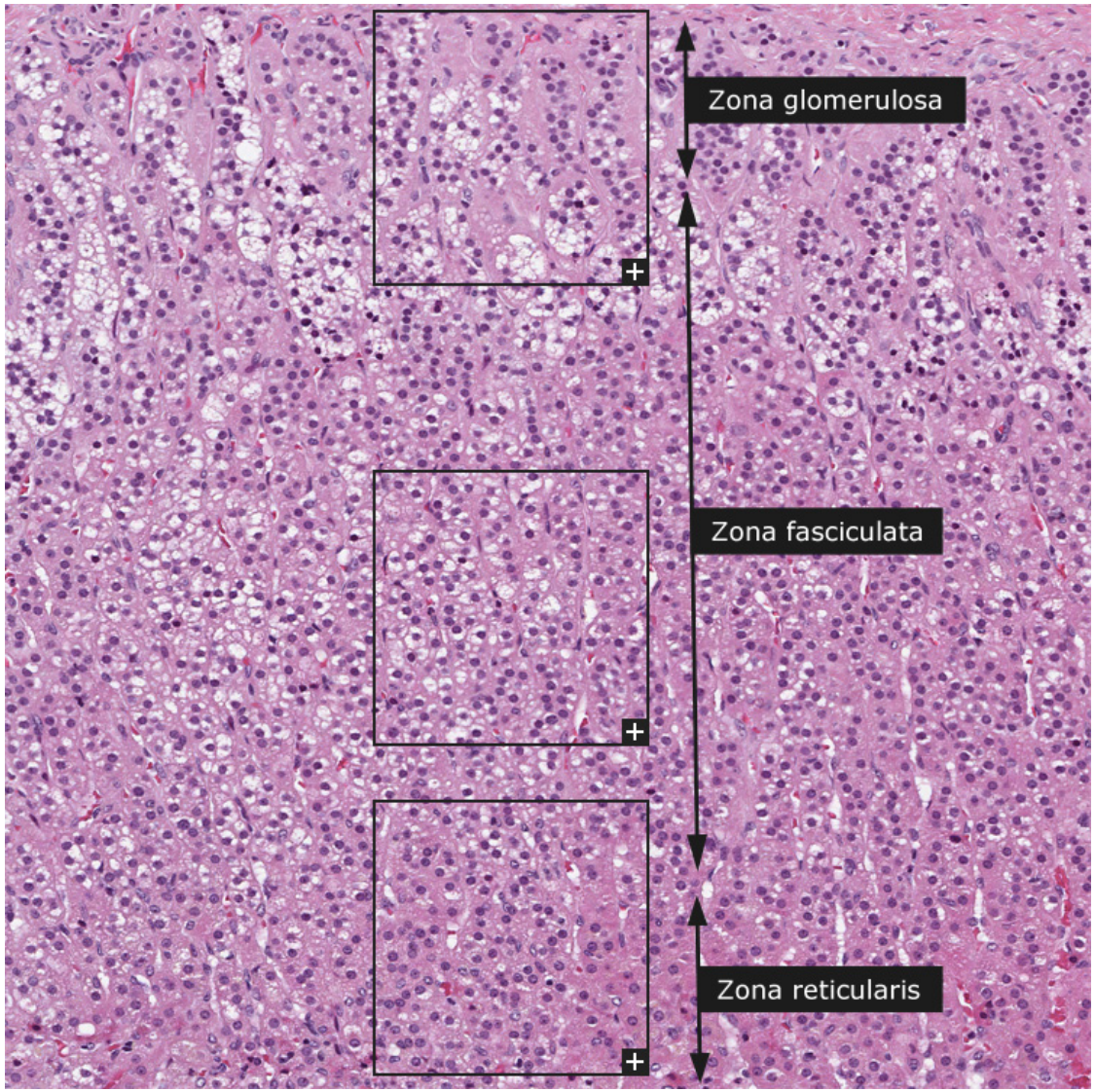
Dr Martine Poll Patey (CHU Reims)

Adrenal Gland



https://www.google.be/search?

Histology of Cortex



Mineralocorticoids

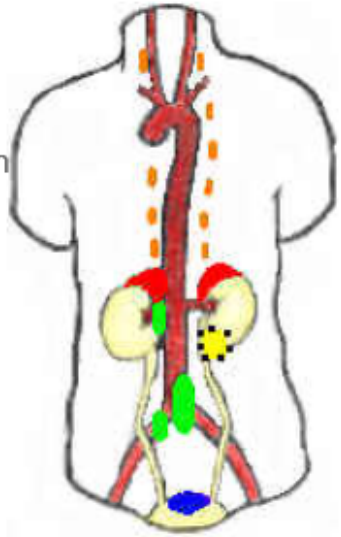
Glucocorticoids

Sexs Steroids

Abnormal localisation of adrenal tissue

Here's a look at the extra-adrenal sites of pheochromocytomas:

- Within the sympathetic nerve chain along the spinal cord (**orange spots**)
- Overlying the distal aorta (the main artery from the heart) (**green spots**)
- Within the ureter (collecting system from the kidney **(yellow spot)**
- Within the urinary bladder **(blue spot)**
- Remember, 90% are in the adrenal glands **(red spots on the kidneys)**



http://www.endocrineweb.com/conditions/pheochromocytoma/pheochromocytoma-ten-percent-tumor

Adrenal lesions in adults

- Cortical lesions:

Adrenal Cortical Hyperplasia/ Hypoplasia

ACA: Adrenal Cortical Adenoma

ACA: Adrenal Cortical Carcinoma

- Medullary lesions

Hyperplasia

Pheochromocytoma

Myelolipoma

Vascular Lesions

- Infections (TB) , Metastasis, …

Adrenal Cortical Hyperplasia

- Increased number of cells in the cortex
- Sybtypes:

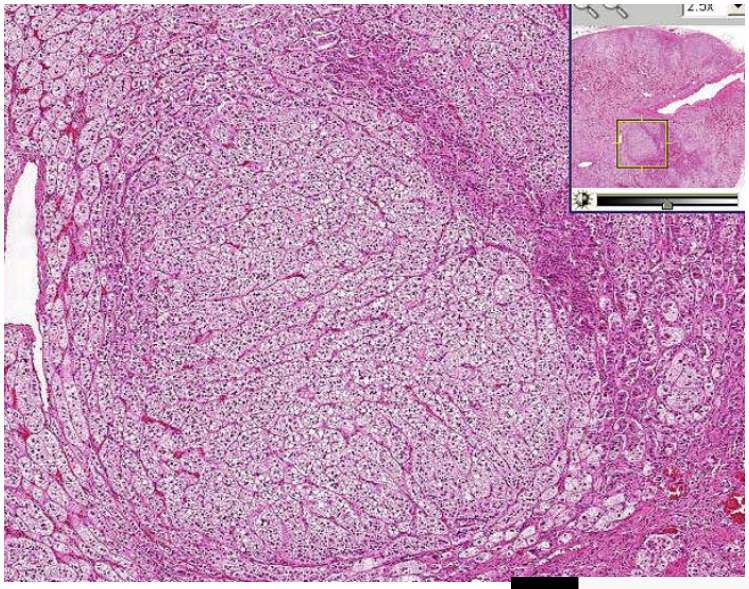
Diffuse with occasional small nodules

Micronodular: less than 0,5 cm and not more than 1 cm

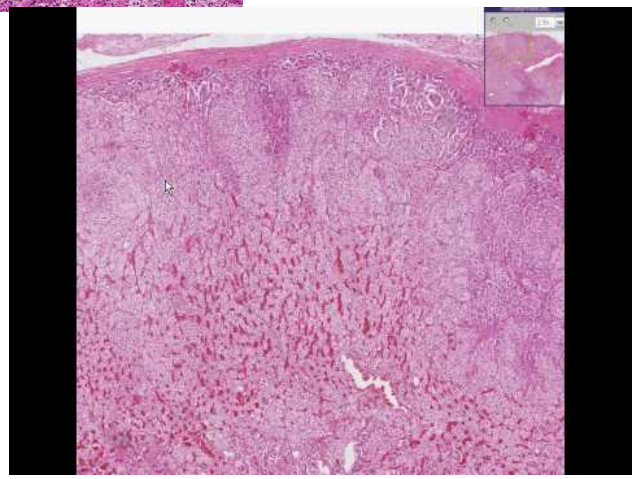
Macronodular: less than 1 cm

Mixed patterns

- Rarely unilateral process
- Some cases with pigmented cells

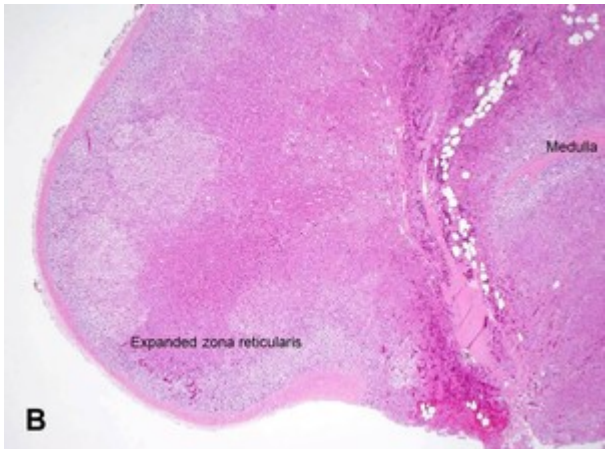


Micro Nodular Hyperplasia



Macro Nodular Hyperplasia

Diffuse Hyperplasia



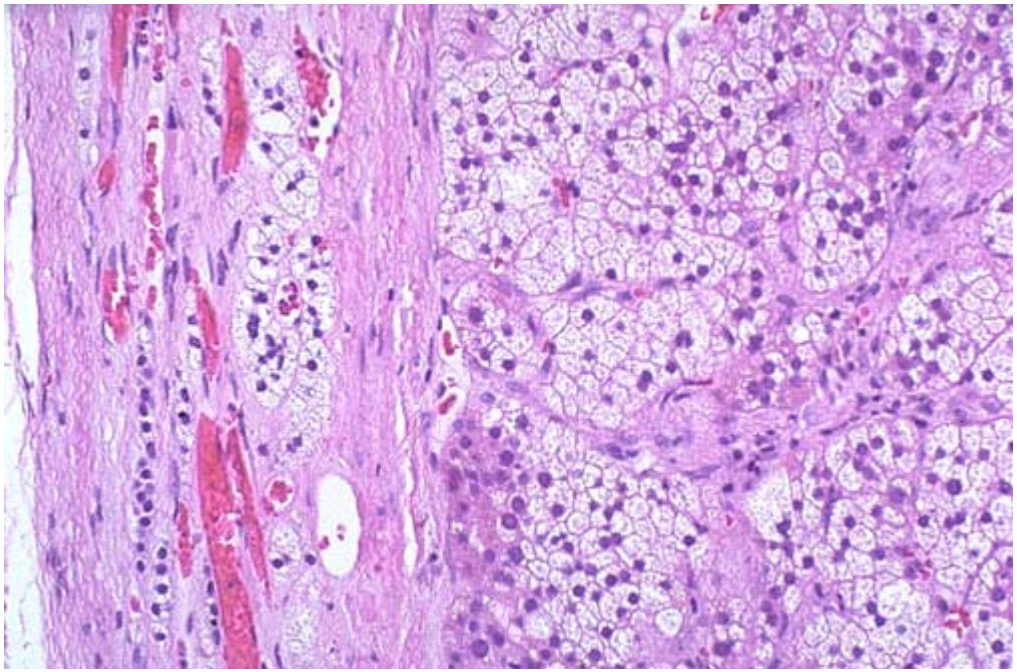
Endocrine Syndromes in AC Hyperplasia

- Zona glomerulosa: Hyperaldosteronism
- Zona fasciculata: Cushing, …
- Zona reticularis: Virilization

ACA

- More common in women.
- Same incidence right and left side
- Functional or not Functional (Incidentaloma)
- Sometimes difficult differential with Adrenal Macronodular Hyperplasia: Solitary lesion in a non hyperplastic background is adenoma.
- May have degeneration: cystic and/ or hemoraghe and fibrosis

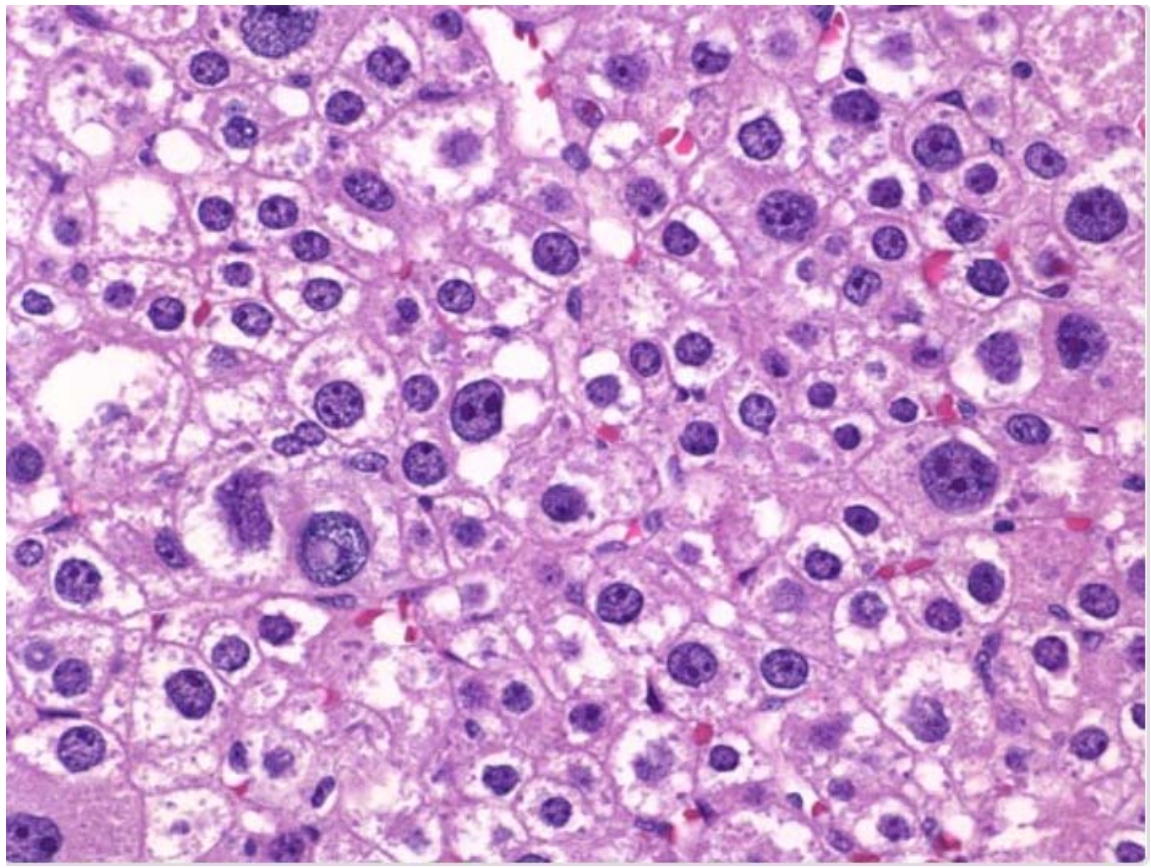
ACA



Microscopically, the adrenal cortical adenoma at the right resembles normal adrenal fasciculata. The capsule of this benign neoplasm is at the left. There may be minimal cellular pleomorphism within adenomas.

Pathology Outlines.com

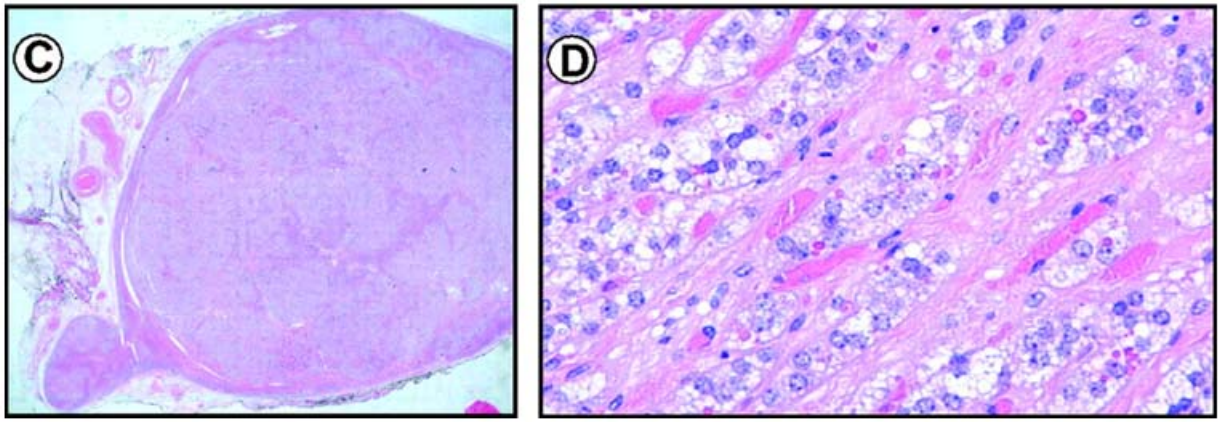
ACA



After a careful search, no evidence of necrosis or increased mitotic activity was found. The tumor cells, however, did exhibit focal cytologic atypia.

Pathology outlines.com

Clear cells of Adrenal Cortical Adenoma
See: pathology outlines com



Aderville Cabassi et al. Hypertension. 2012;59:e18-e19

(see white arrow; 10 days after delivery). **C**, Low– and (**D**) high–power magnification of clear cells of the adrenal cortical adenoma (hematoxylin/eosin; original magnification: ×10; ×400).

Published online before print
December 5, 2011, **doi:**
10.1161/HYPERTENSIONAHA.111.187237

Hypertension
February 2012vol. 59no. 2 e18–e19

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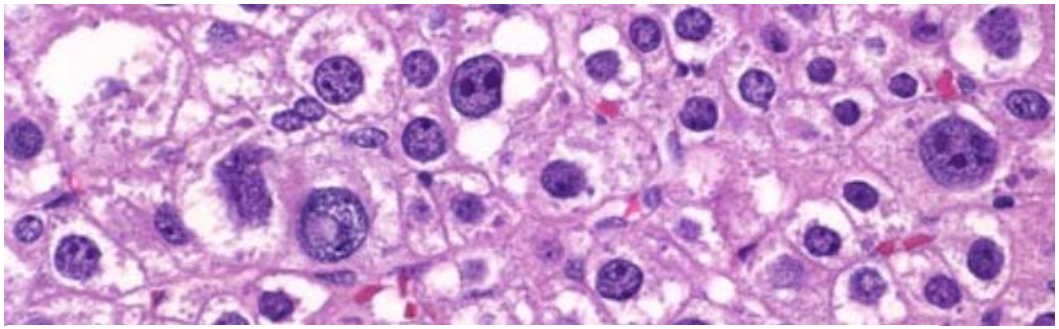
Adrenal gland and paraganglia
Adrenocortical adenoma
General

Prognostic Factors

- Distinguishing ACA from adrenocortical carcinoma (ACC) is difficult particularly in children, and several systems have been proposed
- In general, most reliable factors include size, necrosis, mitotic activity, atypical mitoses (Mod Pathol 2011;24:S58)
- **Weiss System** (Am J Surg Pathol 1984;8:163): most widely used criteria
  - Criteria (≥3 criteria indicates malignancy): high mitotic rate, atypical mitoses, high nuclear grade, low percentage of clear cells, necrosis, diffuse tumor architecture, capsular invasion, sinusoidal invasion, venous invasion
- Modified Weiss System (Am J Surg Pathol 2002;26:1612): >5 mitoses per 50 high powered fields, <25% clear cells, atypical mitotic figures, necrosis, and capsular invasion
  - Calculation:
    - 1 point each for the presence of atypical mitotic figures, necrosis, and capsular invasion
    - 2 points each for the presence of >5 mitoses per 50 high powered fields and <25% clear cells
    - Total score ranges from 0 to 7, and score of >3 highly correlates with subsequent malignant behavior



Comments:
There were occasional enlarged hyperchromatic nuclei with one or more prominent nucleoli.

Comments:
This adrenal adenoma presented as a 6.0 cm solid homogenous vascular mass in an 18 year old boy. After a careful search, no evidence of necrosis or increased mitotic activity was found. The tumor cells, however, did exhibit focal cytologic atypia.

Pheochromocytoma

- “Paraganglioma” derived from chromaffin cells of adrenal medulla
- More right side, M=W, Any age (most 40 year)
- Clinical aspect: Hypertension, Tachycardia,..
- Urine: Elevated catecholamine levels

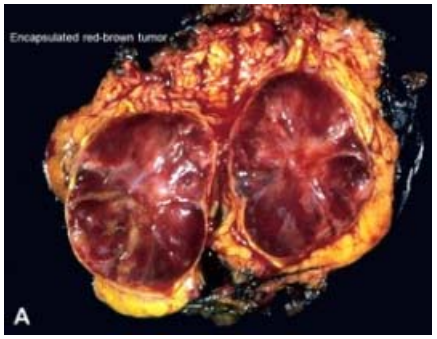
- Can be sporadic or MEN 2a, 2b, Carney triad,…

Pheochromocytoma is the 10% tumor

10 percent of all Pheochromocytomas are:
Malignant (90% are benign)
Bilateral (found in both adrenal glands: 90% are arise in just one of the two adrenal glands)
Extra-Adrenal (found within nervous tissue outside of the adrenal glands ... see below)
In Children (90% are in adults)
HERIDITARY: 30-40%
Recur (10% or slightly less, will come back 5 to 10 years later)
Associated with MEN syndromes (patients with rare syndromes of endocrine tumors.)
Present with a stroke (10% of these tumors are found after the patient has a stroke)

http://www.endocrineweb.com/conditions/pheochromocytoma/pheochromocytoma-ten-percent-tumor

- Gross: encapsulated yellow-white to red-brown, soft, fleshy tumor (image A).



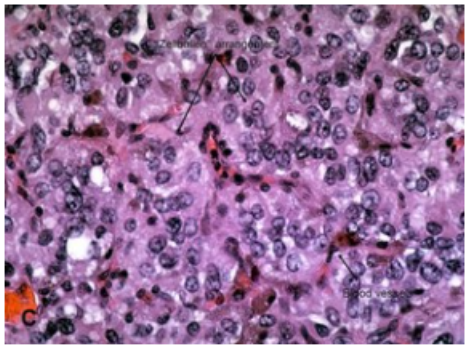


Image C
(click on the image above)

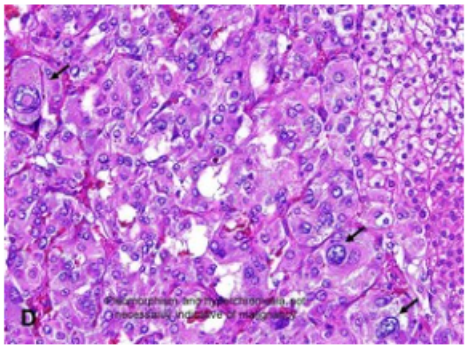


Image D
(click on the image above)

- Histology:
  - Well-defined nests (zellballen) of polygonal cells surrounded by a delicate fibrovascular stroma
    (image B) & (image C).
  - Cells have considerable variation in size and shape, and often demonstrate faintly basophilic (blue) finely granular cytoplasm.
  - Pleomorphism, hyperchromasia, and mitotic figures may be present and do not necessarily indicate malignancy (image D).
  - Eosinophilic globules (PAS positive) can be seen.
  - The only definitive evidence of malignancy is metastatic disease.
- Immunohistochemistry: synaptophysin+, chromogranin+ and S100+ (+ only in sustentacular cells intermingled with malignant chromaffin cells).

https://www.auanet.org/education/modules/pathology/adrenal-gland/pheochromocytoma.cfm

Am J Surg Pathol. 2002 May;26(5):551-66.

Pheochromocytoma of the Adrenal gland Scaled Score (PASS) to separate benign from malignant neoplasms: a clinicopathologic and immunophenotypic study of 100 cases.

Thompson LD[1].

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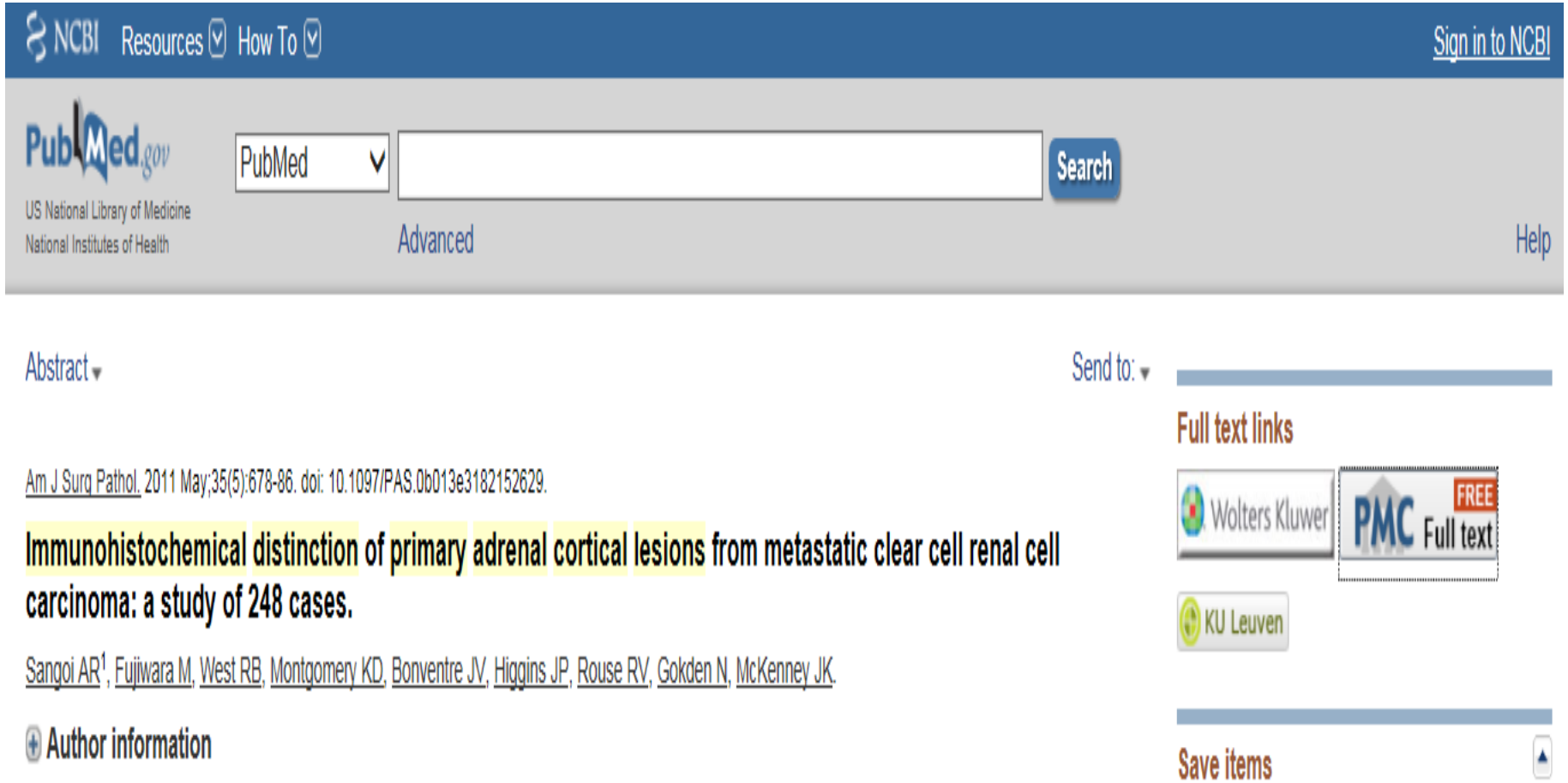
Abstract

No comprehensive series has evaluated the histologic features of pheochromocytoma to separate benign from malignant pheochromocytoma by histomorphologic parameters only. Fifty histologically malignant and 50 histologically benign pheochromocytomas of the adrenal gland were retrieved from the files of the Armed Forces Institute of Pathology. The patients included 43 females and 57 males, with an age range of 3-81 years (mean 46.7 years). Patients usually experienced hypertension (n = 79 patients). The mean tumor size was 7.2 cm (weight was 222 g). Histologically, the cases of malignant pheochromocytomas of the adrenal gland more frequently demonstrated invasion (vascular [score = 1], capsular [score = 1], periadrenal adipose tissue [score = 2]), large nests or diffuse growth (score = 2), focal or confluent necrosis (score = 2), high cellularity (score = 2), tumor cell spindling (score = 2), cellular monotony (score = 2), increased mitotic figures (>3/10 high power fields; score = 2), atypical mitotic figures (score = 2), profound nuclear pleomorphism (score = 1), and hyperchromasia (score = 1) than the benign tumors. A Pheochromocytoma of the Adrenal gland Scaled Score (PASS) weighted for these specific histologic features can be used to separate tumors with a potential for a biologically aggressive behavior (PASS > or =4) from tumors that behave in a benign fashion (PASS <4). The pathologic features that are incorporated into the PASS correctly identified tumors with a more aggressive biologic behavior. Application of these criteria to a large cohort of cases will help to elucidate the accuracy of this grading system in clinical practice

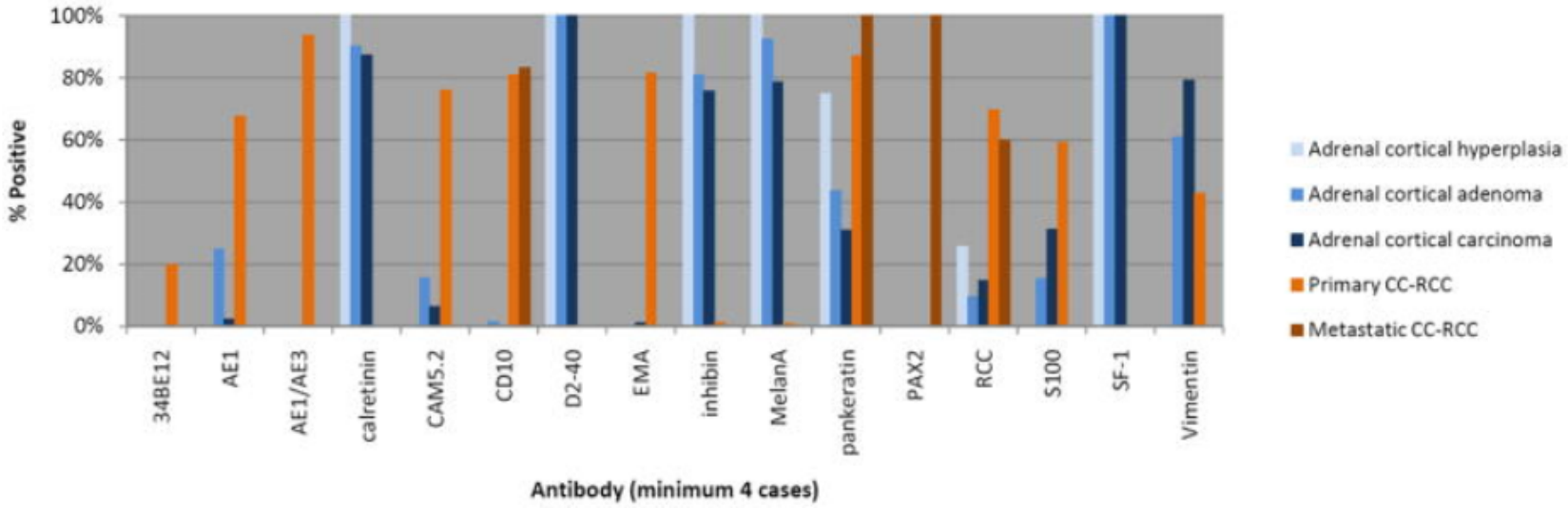
Free in Pub Med



Am J Surg Pathol. 2011 May; 35(5): 678–686.

Previously reported Findings

Figure 1



Review of previously reported immunohistochemical findings in adrenal cortical lesions and clear cell renal cell carcinoma. [2-6, 9-12, 16, 25, 27, 33, 34, 36, 41, 42, 44, 45, 50, 53, 54]

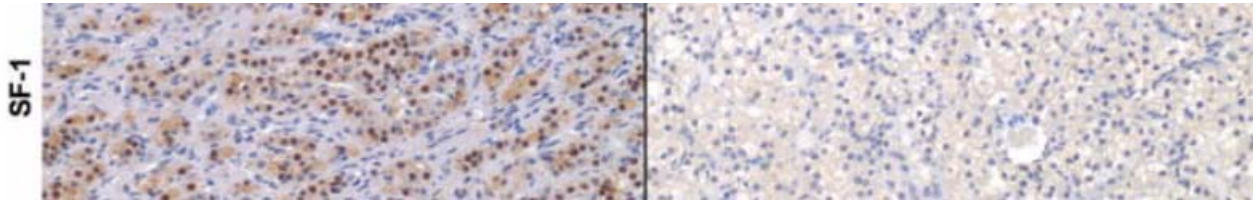
Table 2

Immunohistochemical Staining Results* for Metastatic Clear Cell Renal Cell Carcinoma versus Adrenal Cortical Lesion with Adrenocortical Markers

	Calretinin (C, N)	Inhibin (C)	MelanA (C)	SF-1 (N)	Synaptophysin (C)
CC-RCC (overall)	18/184 (10%)	17/184 (9%)	18/184 (10%)	0/184 (0%)	3/184 (2%)
CC-RCC (WD)	13/133 (10%)	11/133 (8%)	11/133 (8%)	0/133 (0%)	2/133 (2%)
CC-RCC (PD)	5/51 (10%)	6/51 (12%)	7/51 (14%)	0/51 (0%)	1/51 (2%)
ACL	56/63 (89%)	54/63 (86%)	54/63 (86%)	54/63 (86%)	37/63 (59%)

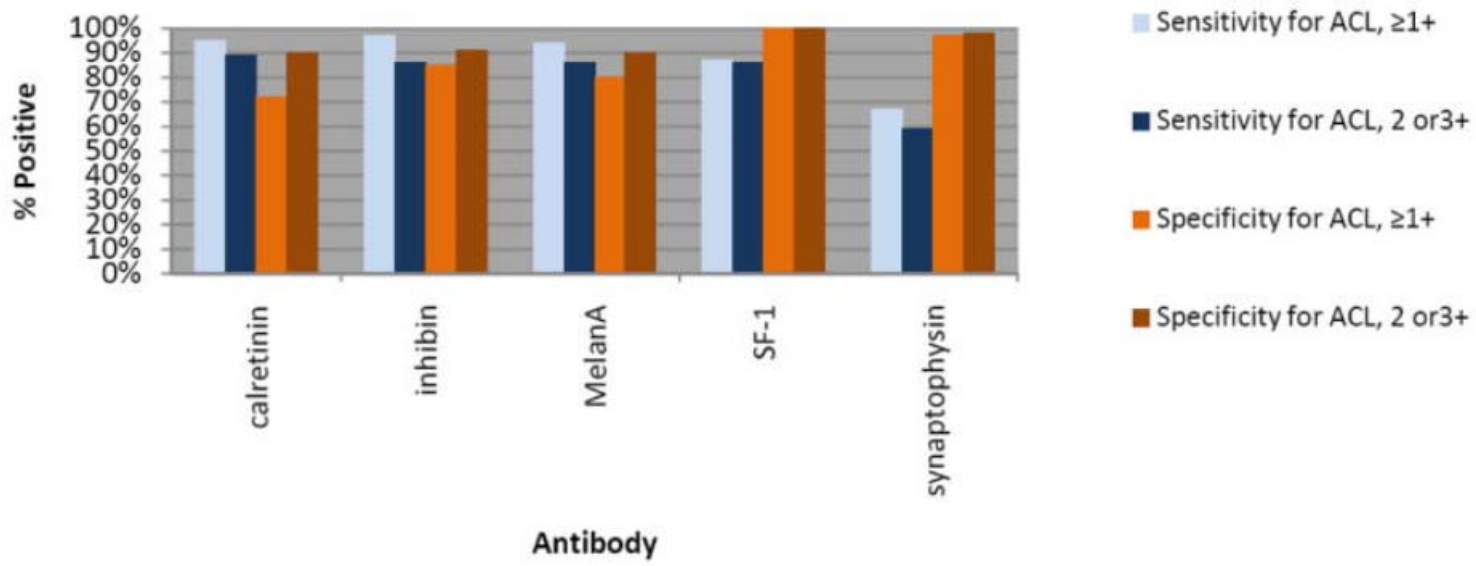
* ≥2+ staining intensity considered positive

CC-RCC = metastatic clear cell renal cell carcinoma, WD = well-differentiated, PD = poorly-differentiated, ACL = adrenal cortical lesion, C = cytoplasmic, N = nuclear



Am J Surg Pathol. 2011 May; 35(5): 678–686.

FIGURE 4



Sensitivity and specificity for adrenal cortical lesions versus metastatic CC-RCC by staining intensity threshold.

Table 3

Immunohistochemical Staining Results* for Metastatic Clear Cell Renal Cell Carcinoma versus Adrenal Cortical Lesions with Renal Epithelial Markers

	AE1/AE3 (M/C)	CAM5.2/AE1 (M/C)	CD10 (M/C)	EMA (M/C)	RCC (M/C)	CAIX (M/C)	hKIM-1 (M/C)	HNF-1b (N)	PAX-2 (N)	PAX-8 (N)	TIM-1 (M/C)
CC-RCC (overall)	101/184 (55%)	110/184 (60%)	142/185 (77%)	144/185 (78%)	33/185 (18%)	160/184 (87%)	153/185 (83%)	139/184 (76%)	91/185 (49%)	152/184 (83%)	68/184 (37%)
CC-RCC (WD)	64/133 (48%)	72/133 (54%)	103/133 (77%)	108/133 (81%)	28/133 (21%)	119/133 (89%)	110/133 (83%)	98/133 (74%)	70/133 (53%)	108/133 (81%)	50/131 (38%)
CC-RCC (PD)	37/51 (73%)	38/51 (75%)	39/52 (75%)	36/52 (69%)	5/52 (10%)	41/51 (80%)	43/52 (83%)	41/51 (80%)	21/52 (40%)	44/51 (86%)	18/53 (34%)
ACL	6/63 (10%)	5/63 (8%)	6/63 (10%)	0/63 (0%)	0/63 (0%)	2/63 (3%)	0/63 (0%)	0/63 (0%)	0/63 (0%)	0/63 (0%)	0/63 (0%)

* ≥2+ staining intensity considered positive

CC-RCC = metastatic clear cell renal cell carcinoma, WD = well-differentiated, PD = poorly-differentiated, ACL = adrenal cortical lesion, C = cytoplasmic, M = membranous, N = nuclear

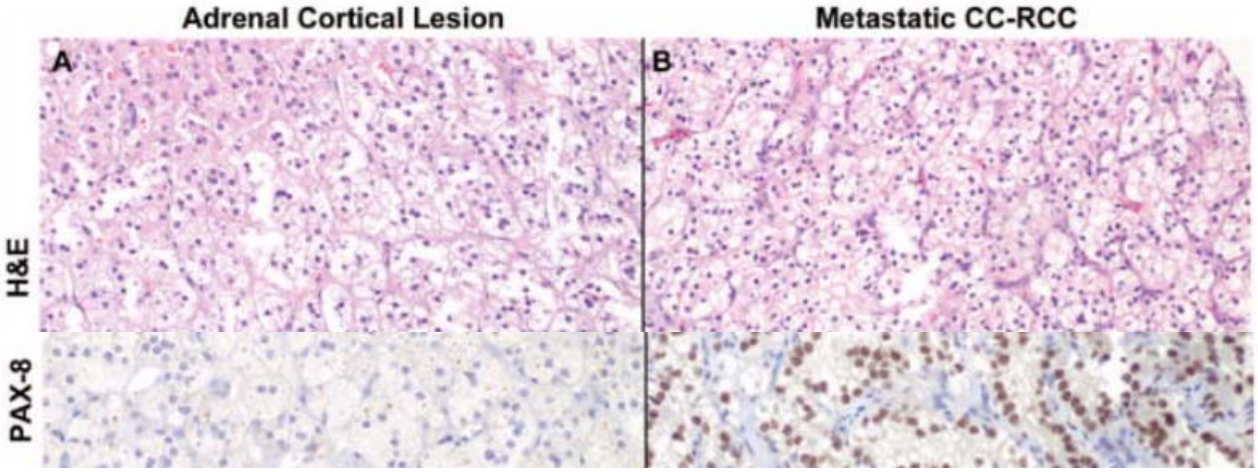
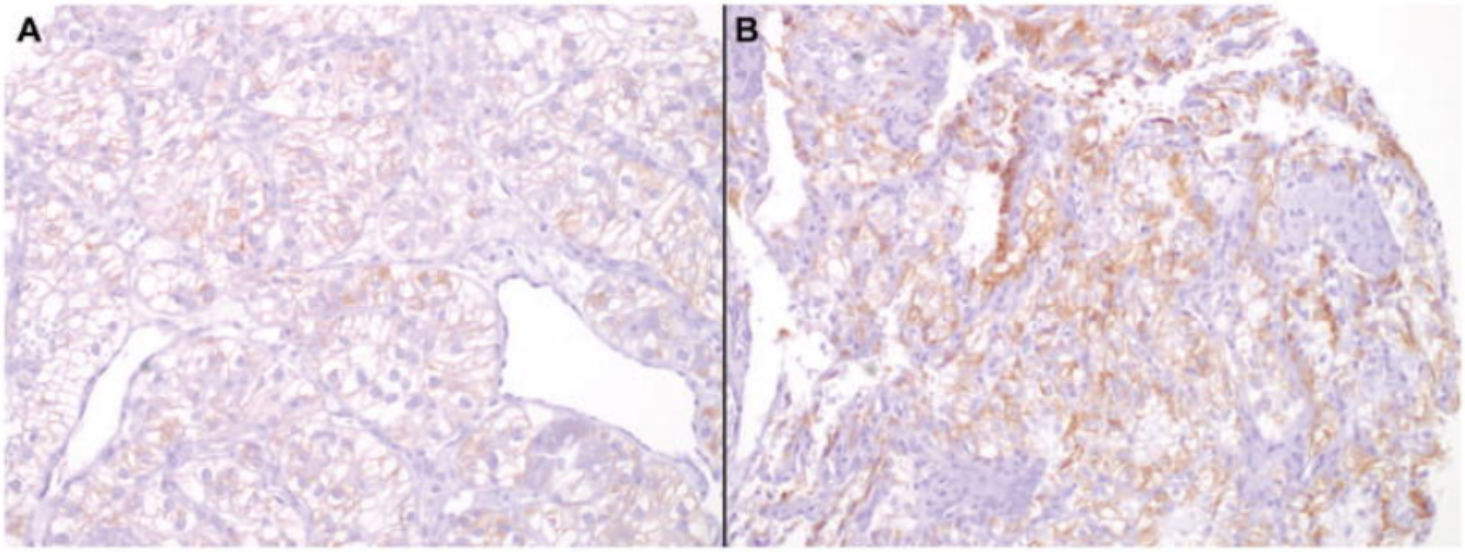


Figure 3



MelanA immunoreactivity in metastatic clear cell renal cell carcinoma (CC-RCC). Weak cytoplasmic staining (1+) in several cases of metastatic CC-RCC was seen with MelanA, calretinin, and (A) inhibin. This may cause significant interpretation problems in small biopsies if a ≥2+ staining threshold is not required. Given that occasional cases of metastatic CC-RCC may show stronger staining (2+) with these 3 markers (B, melanA in this case), the addition of the nuclear marker SF-1 helps improve diagnostic specificity for adrenal cortical lesions versus metastatic CC-RCC.