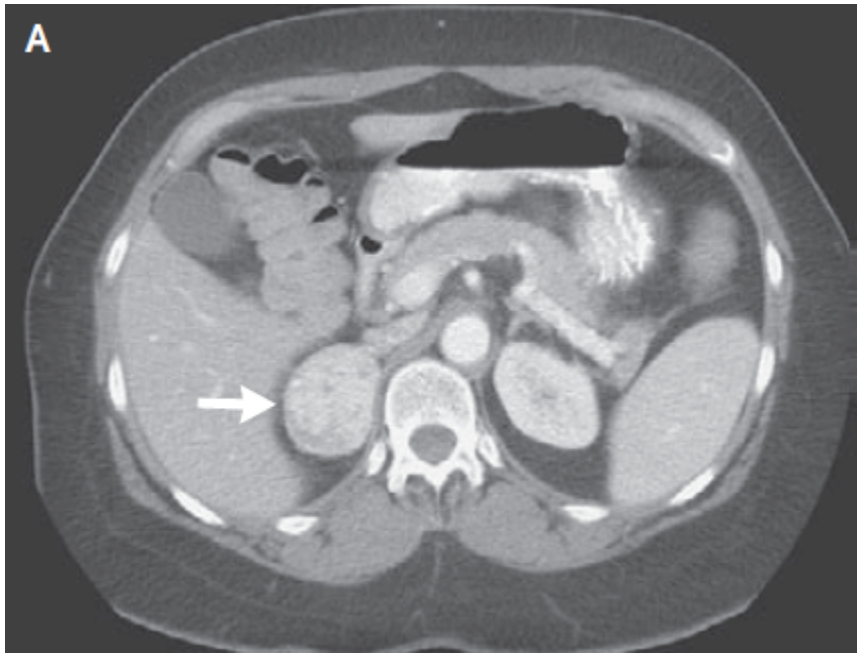
Management of Incidental Adrenal Lesions



Tommy Johnston

PCH Urology Audit Meeting

16/2/15

Adrenal Incidentaloma's (AI's)

Definition

Adrenal mass > 1cm in diameter discovered incidentally when investigating for something else

Widespread use of USS, CT and MRI has resulted in a dilemma for clinicians

Prevelance

- Autopsy studies (87,000) reported frequency of 6% (range 1-32%)
- Abdominal CT's series overall prevalence of 4%
- Risk increases with age
    - 20 -29 years = 0.2%
    - 70+ years = 7%
- CT series in pt's with extra-adrenal malignancy 6-20%

Adrenal Incidentaloma's

Majority are non-hypersecreting, benign adenomas (85%)

Adrenal hypersecreting or hormonally active (15%)

- Phaechromocytoma (5-8%)
- Cushing syndrome (5%)
- Conn's syndrome (1%)
- Androgen secreting tumours (<1%)

What are the chances of it being malignant?

- < 5% chance of it being a primary adrenal tumour
- < 1% of it being a metastasis if no prior Hx of primary cancer

Consensus view that all AI's should include thorough clinical, biochemical and radiological assessment

Clinical Assessment

Disorder	Symptoms	Signs
Cushing's syndrome	Patient may be asymptomatic if disease is subclinical; symptoms may include weight gain with central obesity, facial rounding and plethora, supraclavicular and dorsocervical fat pads, easy bruising, thin skin, poor wound healing, purple striae, proximal muscle weakness, emotional and cognitive changes (e.g., irritability, spontaneous tearfulness, depression, and restlessness), opportunistic and fungal infections, altered reproductive function, acne, and hirsutism	Hypertension, osteopenia, osteoporosis, fasting hyperglycemia, diabetes mellitus, hypokalemia, hyperlipidemia, and leukocytosis with relative lymphopenia
Pheochromocytoma	Patient may be asymptomatic; episodic symptoms may occur in spells (paroxysms) that can be extremely variable in presentation but typically include forceful heartbeat, pallor, tremor, headache, and diaphoresis; spells may be either spontaneous or precipitated by postural change, anxiety, medications (e.g., metoclopramide, anesthetic agents), and maneuvers that increase intraabdominal pressure (e.g., change in position, lifting, defecation, exercise, colonoscopy, pregnancy, and trauma)	Hypertension (paroxysmal or sustained), orthostatic hypotension, pallor, retinopathy grades 1 to 4, tremor, and fever
Primary aldosteronism	If hypokalemia is present, nocturia, polyuria, muscle cramps, and palpitations may be present	Hypertension, mild or severe; possibly hypokalemia and mild hypernatremia
Adrenocortical carcinoma	Symptoms may include mass effect (e.g., abdominal pain) and symptoms related to adrenal hypersecretion of cortisol (Cushing's syndrome), androgens (hirsutism, acne, amenorrhea or oligomenorrhea, oily skin, and increased libido), estrogens (gynecomastia), or aldosterone (hypokalemia-related symptoms)	Hypertension, osteopenia, osteoporosis, fasting hyperglycemia, diabetes mellitus, hypokalemia, hyperlipidemia, and leukocytosis with relative lymphopenia
Metastatic cancer	History of an extraadrenal cancer	Cancer-specific signs

Biochemical assessment

1. **24 hour catecholamines/metanephrines** (Phaeochromocytomas)

- Sensitivity 95% and specificity of 95%
- Fractionated metanephrines 98% sensitive (only used to confirm Dx)

2. **Overnight 1mg Dexamethasone suppression test**

- Sensitivity 70-100% and specificity of 90%
- Test of choice to rule out Cushing's or Sub-clinical Cushing's syndrome
- > 138nmol/l = Cushing's if clinical features or Sub-clinical if no symptoms
- **Note** subset of Cushing's syndrome pt's may have normal results

3. **Aldosterone – renin ratio**

- Sensitivity 90% and specificity of 90%
- Best test for Conn's syndrome (ARR high or high normal)
- Must stop B-blockers (false positives) and aldosterone antagonists (false negatives)

Confirmatory hormonal testing is recommended in all +ve screening tests to limit false positive results and unnecessary surgery

Radiological Assessment

Computer tomography

- Risk of adrenal cancer related to size: **<2cm = 2%; 4-6cm = 6%; 6cm+ = 25%**
- Calcifications, haemorrhage and necrosis rarely seen in benign adenoma's
- Characteristic malignant/phaechromocytomas features:
  - Size > 3cm
  - Heterogeneous texture
  - Increased vascularity
  - Attenuation of > 10 HU on unenhanced CT
  - Decreased contrast washout at 10 – 15mins (< 50%)
  - Overlap between benign and malignant in 10 – 30% (indeterminate)

- Benign adenoma's:
  - < 10HU (98% specific for benign) as usually greater proportion of fat
  - > 50% washout10mins of contrast medium has sensitivity and specificity of 95-98% for benign

Note: No role for MRI if use contract washout protocol on CT

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The Incidentally Discovered Adrenal Mass

William F. Young, Jr., M.D.

Table 3. Characteristics of Adrenal Incidentalomas on Imaging (Imaging Phenotype).*

Variable	Adrenocortical Adenoma	Adrenocortical Carcinoma	Pheochromocytoma	Metastasis
Size	Small, usually ≤3 cm in diameter	Large, usually >4 cm in diameter	Large, usually >3 cm in diameter	Variable, frequently <3 cm
Shape	Round or oval, with smooth margins	Irregular, with unclear margins	Round or oval, with clear margins	Oval or irregular, with unclear margins
Texture	Homogeneous	Heterogeneous, with mixed densities	Heterogeneous, with cystic areas	Heterogeneous, with mixed densities
Laterality	Usually solitary, unilateral	Usually solitary, unilateral	Usually solitary, unilateral	Often bilateral
Attenuation (density) on unenhanced CT	≤10 Hounsfield units	>10 Hounsfield units (usually >25)	>10 Hounsfield units (usually >25)	>10 Hounsfield units (usually >25)
Vascularity on contrast-enhanced CT	Not highly vascular	Usually vascular	Usually vascular	Usually vascular
Rapidity of washout of contrast medium	≥50% at 10 minutes	<50% at 10 minutes	<50% at 10 minutes	<50% at 10 minutes
Appearance on MRI†	Isointense in relation to liver on T_2-weighted image	Hyperintense in relation to liver on T_2-weighted image	Markedly hyperintense in relation to liver on T_2-weighted image	Hyperintense in relation to liver on T_2-weighted image
Necrosis, hemorrhage, or calcifications	Rare	Common	Hemorrhage and cystic areas common	Occasional hemorrhage and cystic areas
Growth rate	Usually stable over time or very slow (<1 cm per year)	Usually rapid (>2 cm per year)	Usually slow (0.5 cm to 1.0 cm per year)	Variable, slow to rapid

Other assessment tools

PET

- Useful in detecting metastasis in patients with previous oncological Hx
- Metabolically active lesions take up FDG versus benign lesions

Fine-needle aspiration cytology

- Not recommended for routine workup
- Most commonly used for AI's in pt's with Hx of extra-adrenal disease
- MUST exclude phao first as risk of hypertensive crisis or severe haemorrhage

Management

Adrenalectomy

- Functioning tumour
- Non-functioning tumour > 4cm
- Non-functioning tumour < 4 cm with calcification, haemorrhage or necrosis
- Non-functioning tumour with positive PET or FNAC if solitary
- Must take into account patient age, co-morbidities and clinical judgement

Follow-up for non-functioning with favourable CT features

- Use clinical judgement when assessing 4 – 6cm size
- Re-imaging at 3 – 6, 12 and 24 months
- Repeat hormones annually
- If no change after 24 months, discharge
- If increase > 1cm or becomes hormonally active, surgery

Note: 2 – 8% non- functional to functional in 2 years in AI's > 3cm
Growth rate > 1cm in 5 – 25% of AI's, of which 5% will malignant when excised

Guidelines for the management of the incidentally discovered adrenal mass

CUA GUIDELINE

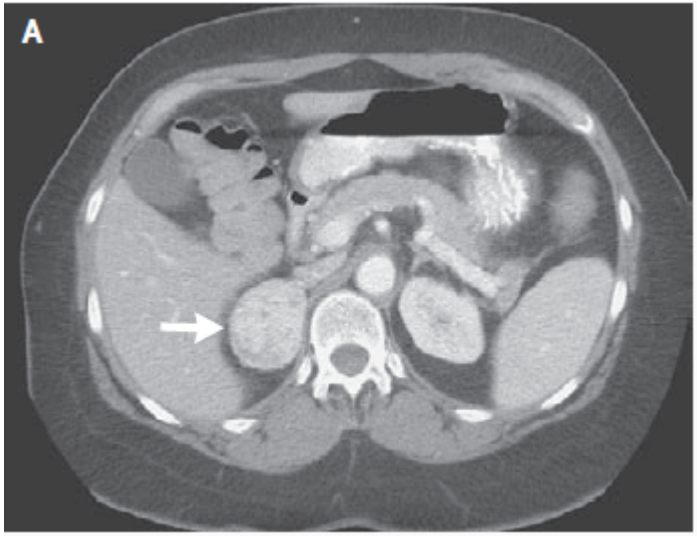
Anil Kapoor, MD, FRCSC; Topher Morris, BMSc;* Ryan Rebello, MD, FRCSC†*

*Division of Urology, Department of Surgery, McMaster University, Hamilton, ON; †Department of Radiology, McMaster University, Hamilton, ON

Table 1. Long-term follow-up of adrenal incidentalomas

Study	Average mass size (cm)	Follow-up (years [range])	Mass increase	Mass decrease	Malignancy	Hyperfunction	Overt disease
Giordano et al. 2010[46]	2.22	3 (1-10)	7/118	2/118	0/118	0/102	0/118
Comlekci et al. 2010[47]	2.5	2 (0.5-11)	30/162	8/162	0/162	6/162	0/162
Vassilatou et al. 2009[48]	2.5	5.2 (1-12.8)	20/77	6/77	0/77	NC	4/77
Fagour et al. 2009[16]	2.4	4.3 (2.7-5.9)	5/51	1/51	0/51	3/27a	3/51
Tsvetov et al. 2007[49]	2.6	2	11/88	0/88	1/88	0/88	0/88
Bulow et al. 2006[50]	2.5	2.1 (0.3-9)	17/229	12/229	0/229	4/229	3/229
Bernini et al. 2005[42]	2.5	4 (1-7)	32/115	24/115	0/115	NC	0/115
Emral. et al. 2003[21]	NG	2	0/60	0/60	0/60	0/60	0/60
Libe et al. 2002[43]	2.5	2.1 (1-10)	13/64	0/64	1/64b	0/64	0/64
Barzon et al. 2002[51]	3.6	4.6 (1-12)	19/130	2/130c	0/130	6/130	4/130
Grossrubatscher et al. 2001[52]	2.5	2.0 (0.5-6.5)	22/53	6/53	0/53	0/53	0/53
Favia et al. 2000[53]	4.4	2.8 (0.5-5)	NG	NG	0/90	0/90	0/90
Rossi et al. 2000[54]	3.26	2.8 (0.5-7.1)	5/32	0/32	0/32	1/32	0/32
Siren et al. 2000[55]	2.5	7.1 (2-16.3)	4/27	7/27	0/27	0/27	0/27
Mantero et al. 2000[29]	NG	>1	14/53	NG	0/53	1/53	1/53
Terzolo et al. 1998[56]	2.5	>1	0/53	0/53	0/53	0/53	0/53
Barry et al. 1998[57]	2	7.0 (0.1-11.7)	4/91	0/91	0/224	0/224	0/224
Terzolo et al. 1997[30]	NG	1	1/41	0/41	0/41	0/41	0/41
Bastounis et al. 1997[58]	3.2	3.6 (1-5.3)	2/60	0/60	0/60	0/60	0/60
Bencsik et al. 1995[59]	<3	1.5 (0.3-3.4)	1/27	0/27	0/27	0/27	0/27
Herrera et al. 1991[60]	NG	2.0 (0.1-5.6)	5/159	4/159	0/159	0/287	NG
Total			212/1690	72/1690	1/1913	21/1809	15/1754
			12.5%	4.3%	0.05%	1.2%	0.9%

Case studies

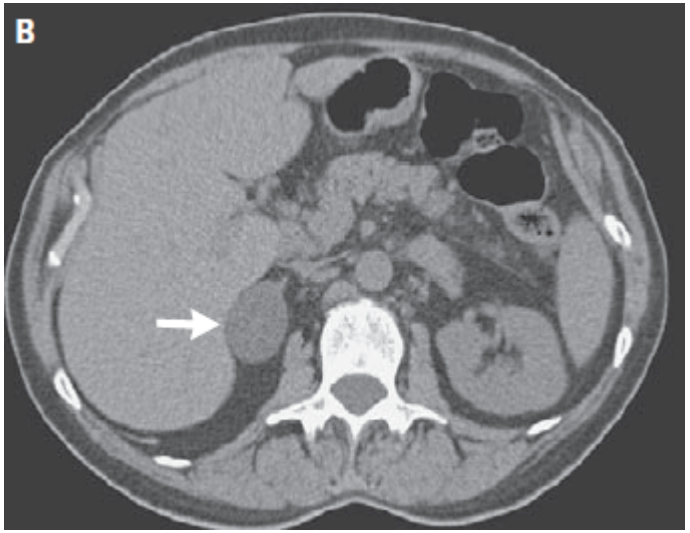


Patient 1 - 48F with ? appendicitis

CT - Right contrast-enhanced 4.5 cm in diameter
Heterogeneous (vascular)
Unenhanced CT attenuation was 40 HU
Contrast-medium washout < 50%/10 mins

No symptoms or signs of pheochromocytoma

Both urine/plasma elevated normetanephrine levels

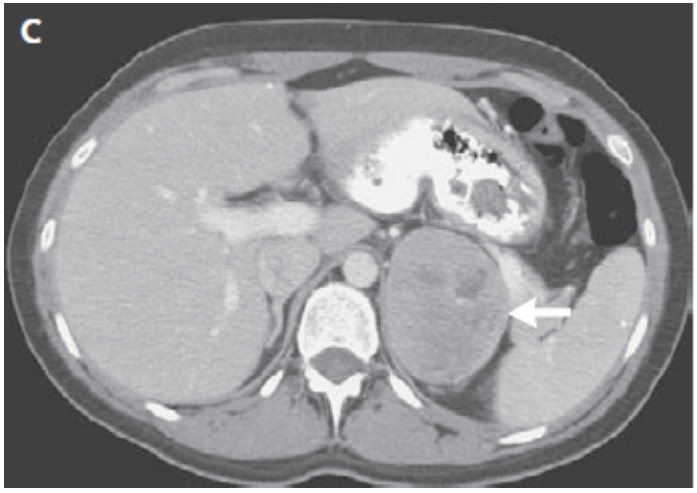


Patient 2 - 62F with abdominal pain

CT - Right adrenal 3.6cm x 2.5 cm mass
Unenhanced CT attenuation was < 10 HU
Contrast-medium washout > 50%/10 mins

Negative urine/plasma normetanephrine levels

Case studies



Patient 3 - 27F flushing and loose stools

CT - Left adrenal mass 7 x 5 x 6 cm

- Heterogenous and contrast enhancing
- Unenhanced CT attenuation was > 10 HU
- Contrast-medium washout < 50%/10 mins

Non-functioning on hormonal testing

Management Algorithm

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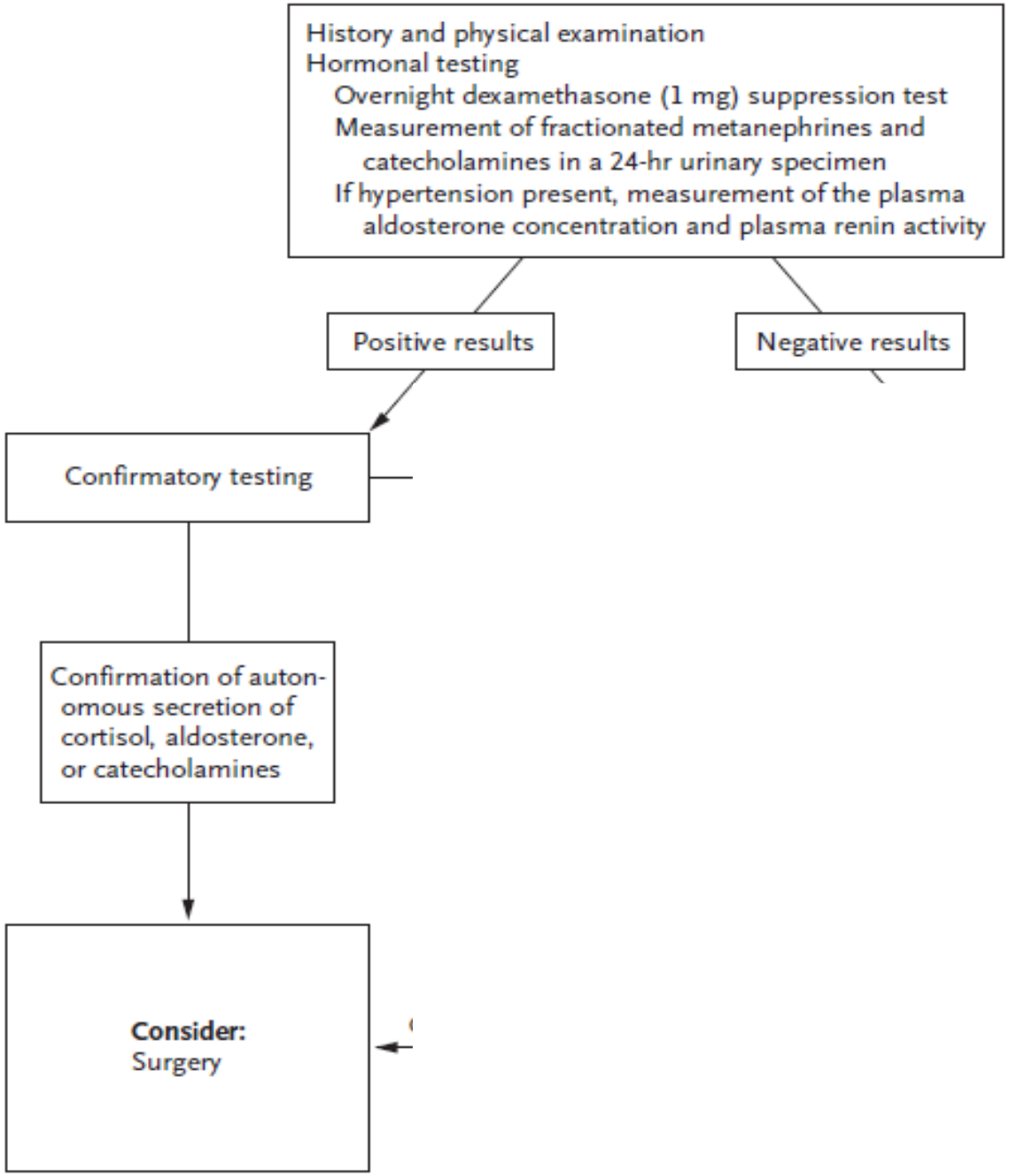

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AACE/AAES Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN ASSOCIATION OF ENDOCRINE SURGEONS MEDICAL GUIDELINES FOR THE MANAGEMENT OF ADRENAL INCIDENTALOMAS