East of England FRCPath Course Cytology Mock Exam

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Marking

Exam is marked out of 40

In reality the maximum achievable is 28

Pass mark is 20

Serious errors (1.0) are a problem

Maximising your marks

- Description = 1 mark so be BRIEF

- Diagnosis = 1.5 if fully correct

2.5 puts you on course for a baseline pass with no room for error

Other 1.0 marks for:

- Differential diagnosis (only if you need it) and immune table if relevant or other work up

- Comments

- Write 2 or 3 points demonstrating clinically relevant background knowledge

Tips

Low power scan,

- **Description** brief eg cellular sample with….
- **Diagnosis** give one! Eg atypical cells present.

Differential lies between….

- **Plan**

1. Make a cell block

2. Immunohistochemistry table
   - Know immunos for met adeno in pleural & ascitic fluid for males & females
   - Know meso versus adeno versus reactive mesos immuno panel

3. Clinical / radiological correlation and discuss at MDT with details!!

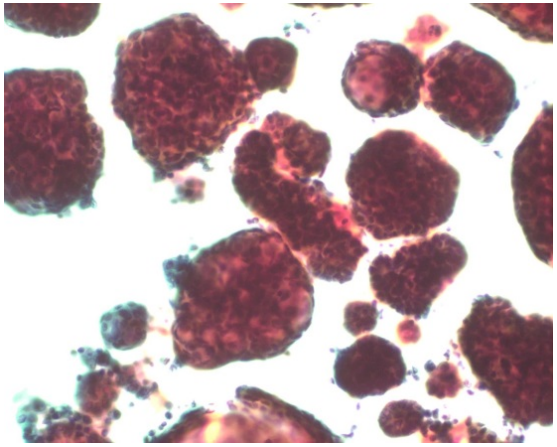
- **Comment**

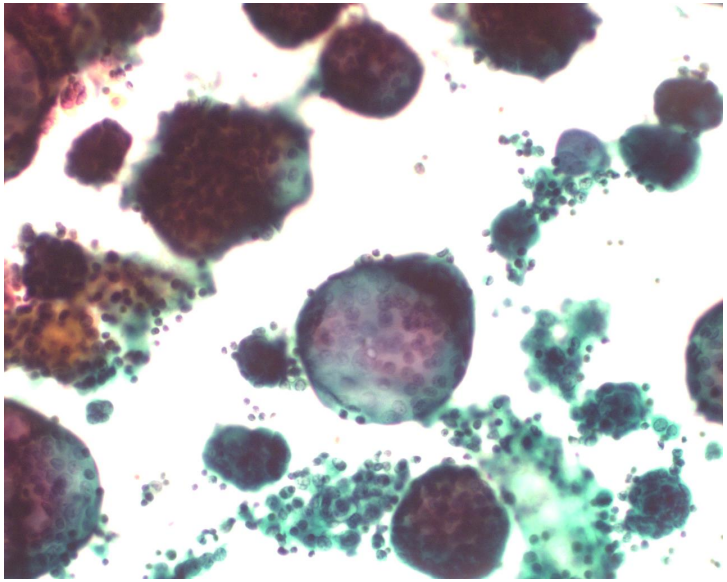
Aetiological factors, genetic associations, other things to consider….

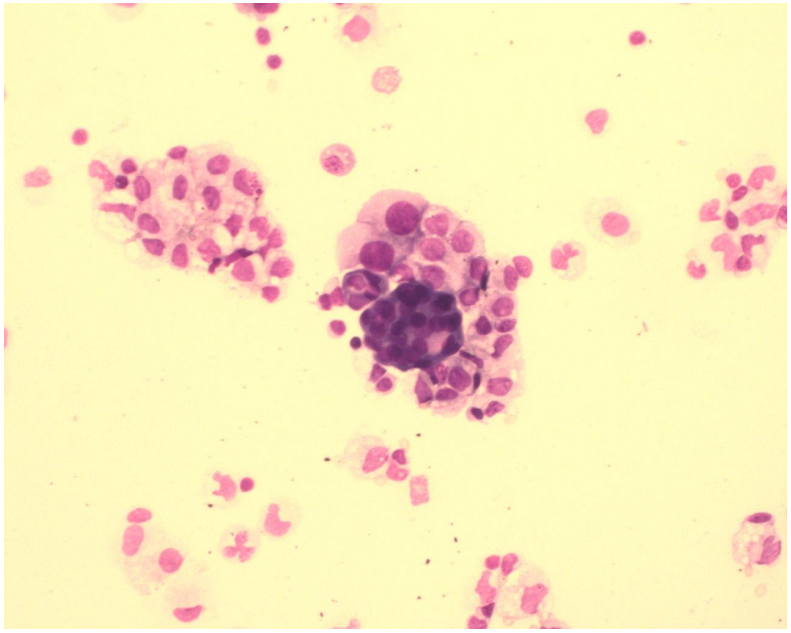
Case A1 (P89)

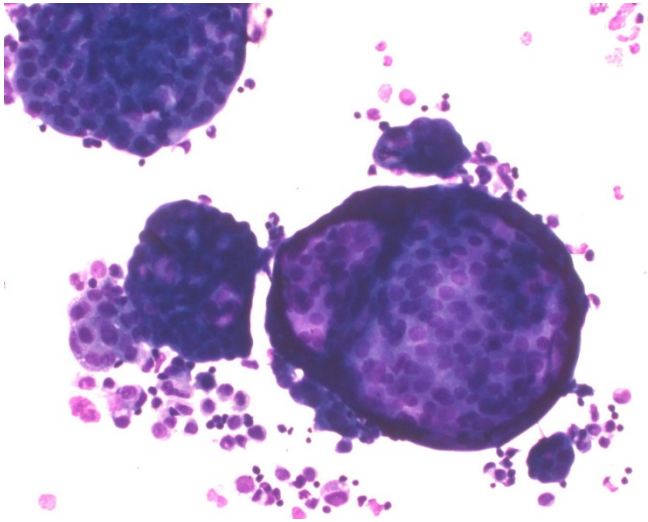
- 77 year old male, Pleural effusion
- Pleural fluid

Case A1

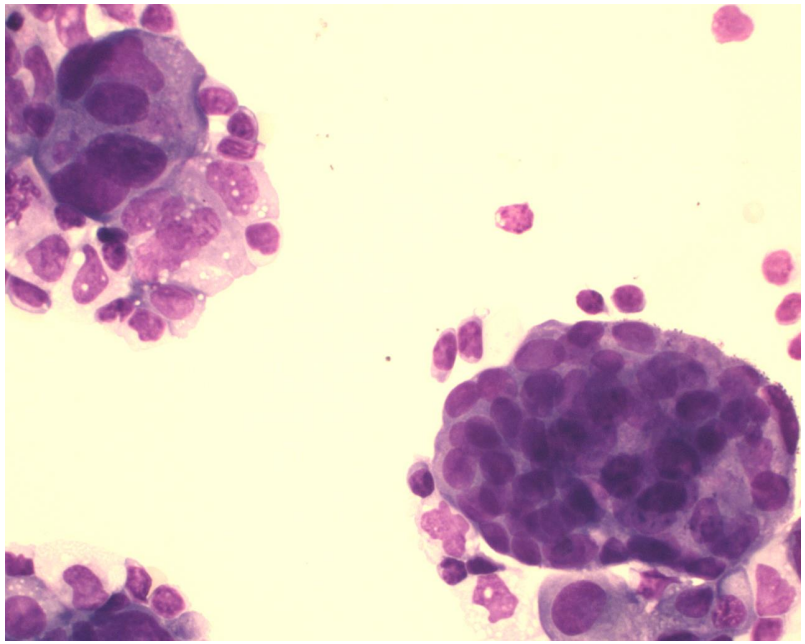


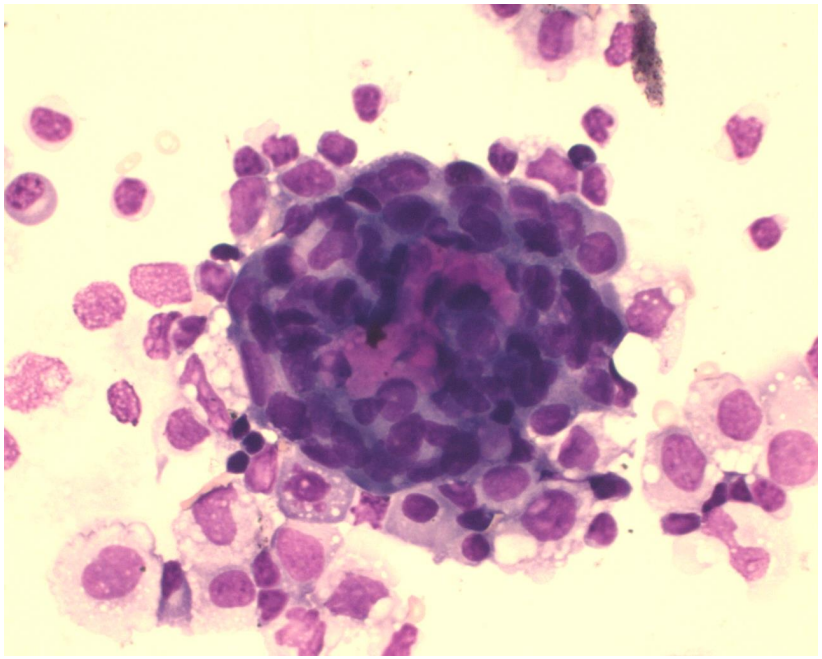




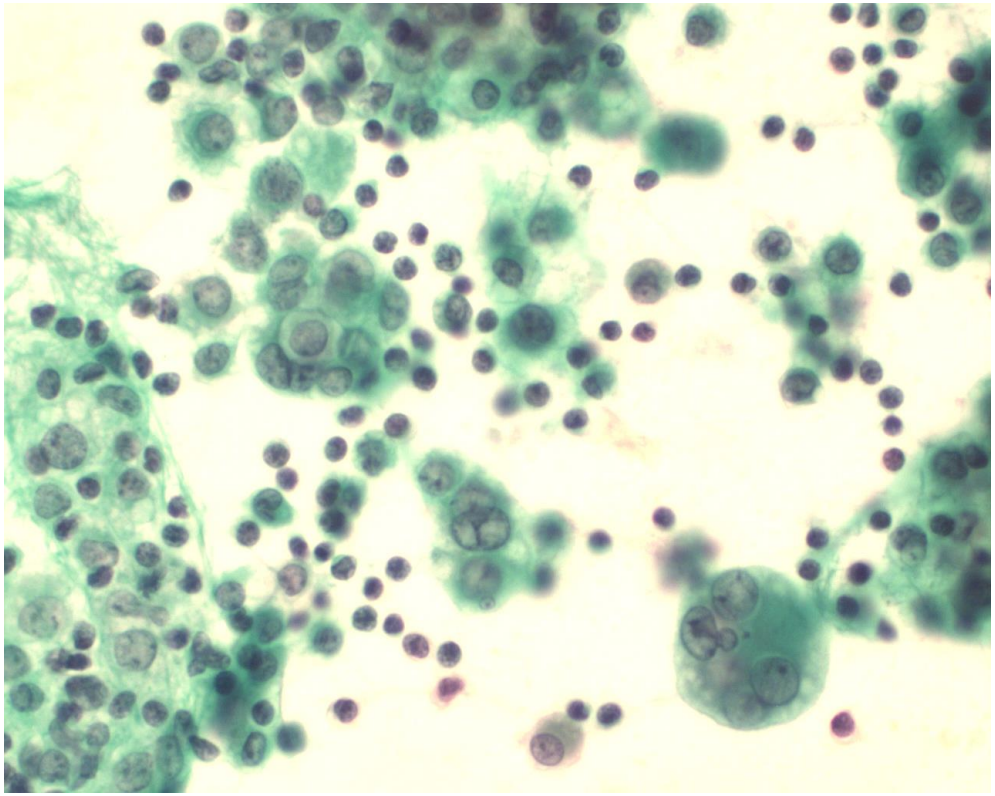


Case A1

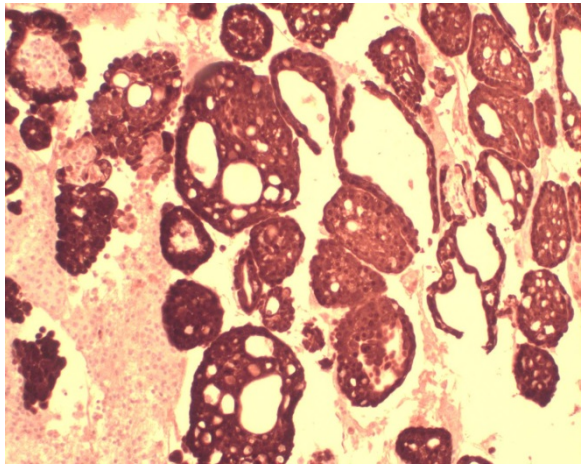




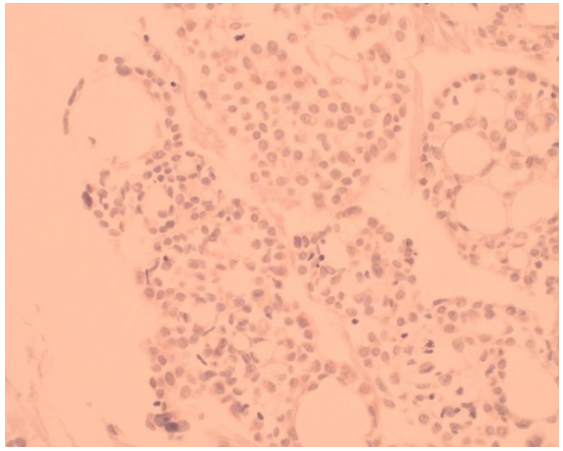
Case A1



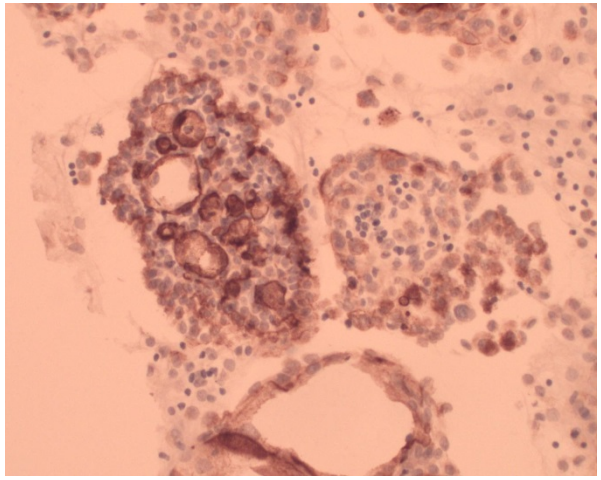
Case A1



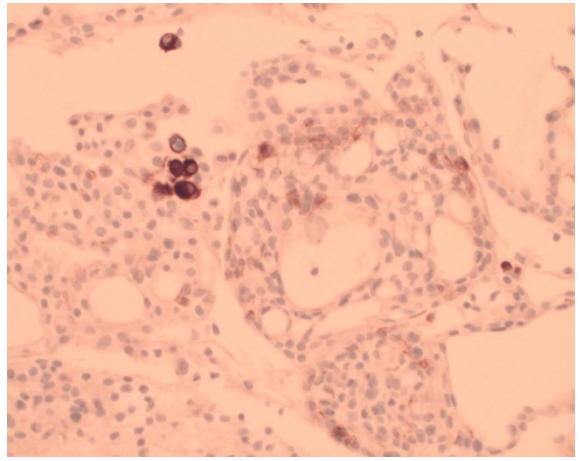
Calretinin



BER EP4



EMA



Desmin

Case A1

Description A

The specimen is cellular with many three dimensional groups of atypical epithelioid cells. These have dense cytoplasm, show some nuclear pleomorphism and membrane irregularities. Occasional cells have irregular macronucleoli.

Diagnosis

Atypical mesothelial proliferation, which would be supportive of a malignant mesothelioma in the correct clinical context.

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Case A1

Plan

1. Make a cell block
2. Perform immunohistochemistry

	Ber EP 4	MO C31	CK5/6	calretinin	D2-40	EMA	BAP-1	Desmin
Mesothelioma	-	-	+	+	+	Strong memb & cytopla	-	-
Reactive mesothelial cells			+	+	+	Weak cytoplas	+	+
Met ca	+	+	-	-	-	+	+	-

3. Clinico-radiological correlation - is there pleural thickening?

Case A1

Comments

A panel of antibodies is helpful as not 100% sensitive and specific

Definitive diagnosis on biopsy is advisable.

MDT discussion re surgery, chemotherapy, radiotherapy, palliation, clinical trail entry

Mesothelioma is associated with asbestos exposure.

Males>females 4:1 (occupation / paraoccupation exposure / Iatrogenic eg radiotherapy to chest wall)

Patients entitled to compensation.

Published models vary, but mesothelioma deaths may have peaked between 2011-2015.

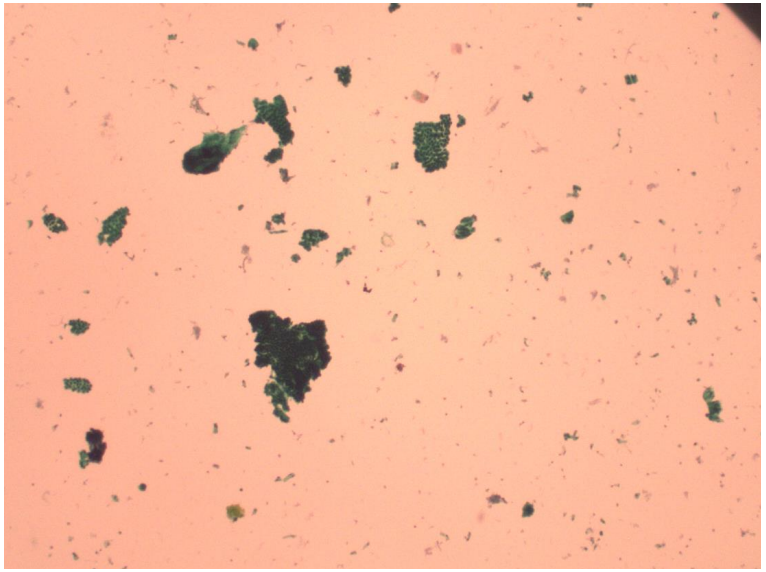
	1	1.5	2	2.5	3	Diagnosis
A1	benign	atypia	suspicious	malignant	Favour mesothelioma	Atypical mesothelial proliferation, supportive of mesothelioma in the correct clinical context.

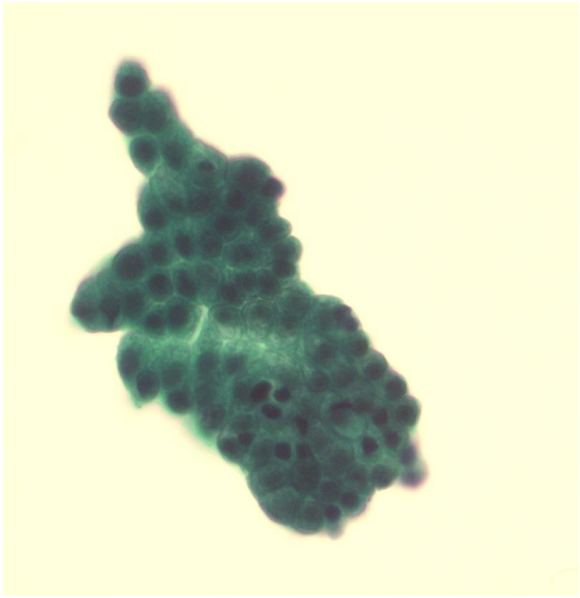
Case A2

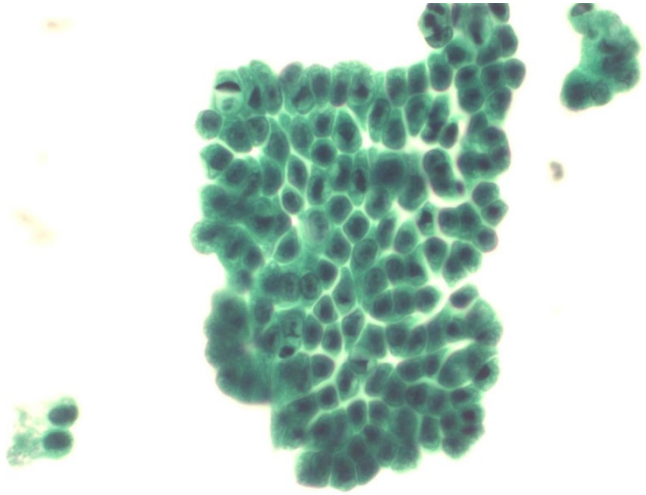
A. Bile duct brush

- 45 year old male, primary sclerosing cholangitis. Bile duct stricture ?malignancy

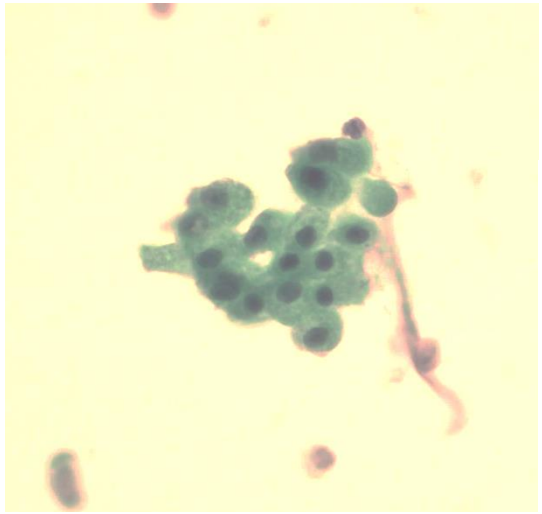
Case A2

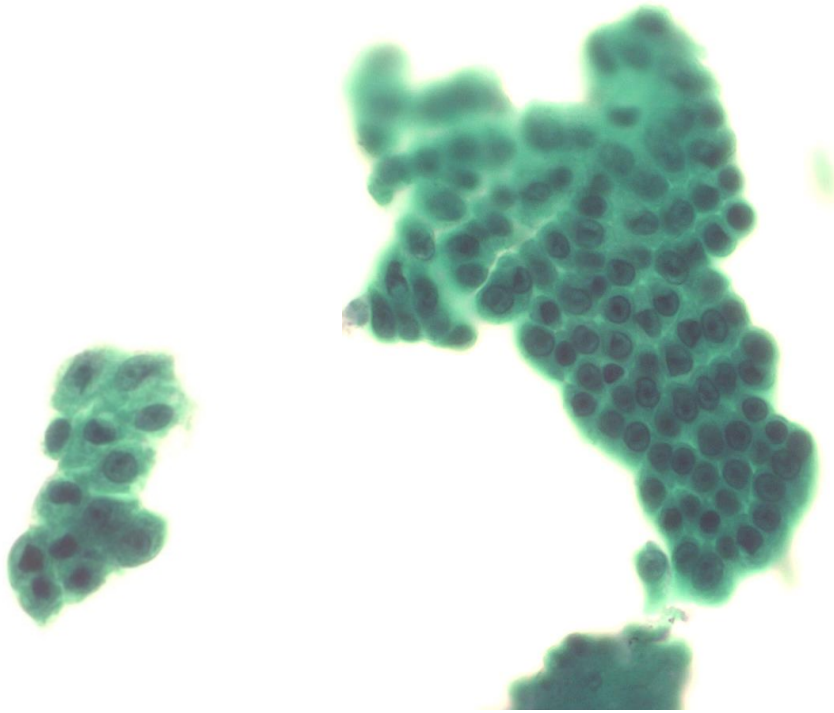




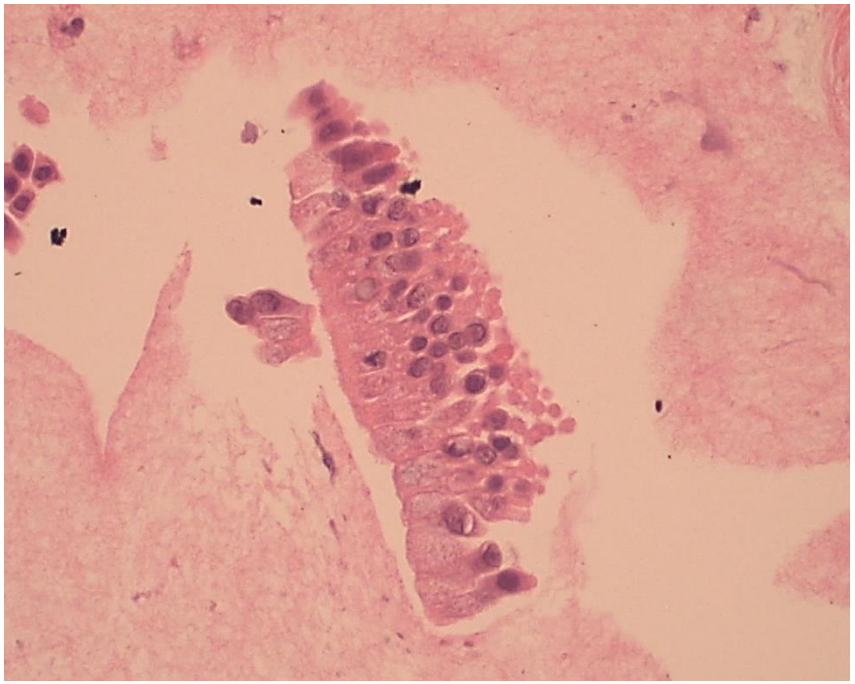


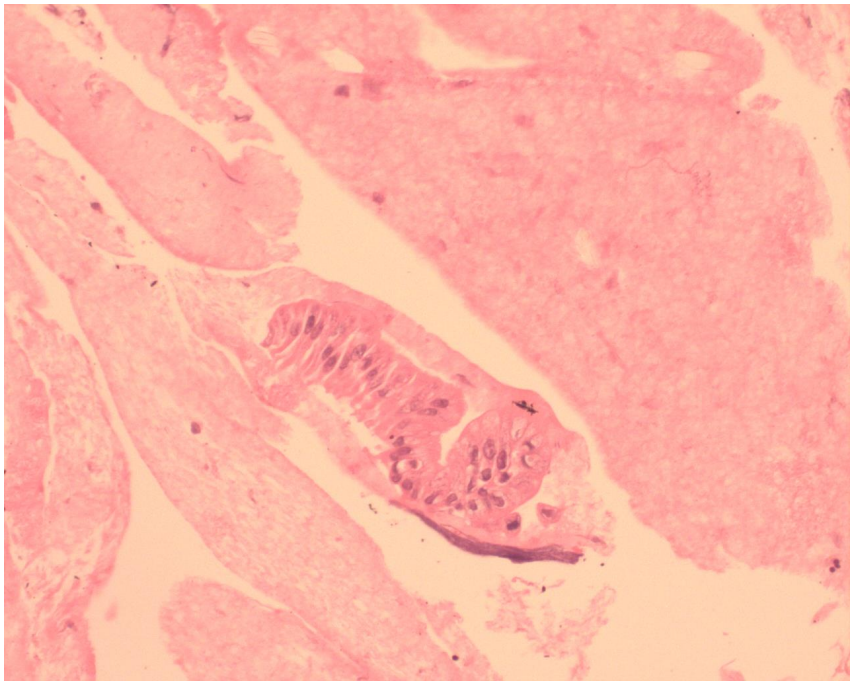
Case A2





A2





Case A2

(b8) 45M Primary sclerosing cholangitis. Bile duct stricture

Description

This is a highly cellular sample containing biliary type epithelium in flat sheets present, together with an occasional papillary group. There is some acute inflammation. The epithelium shows reactive changes. No high grade malignant cells are seen

Diagnosis

Benign biliary epithelium; no high grade malignant cells seen

Comments

Clinical / ERCP / imaging correlation is recommended. Consider EUSFNA of any mass lesions

Causes of benign bile duct strictures include gallstones, trauma (esp surgery) pancreatitis, primary sclerosing cholangitis

Diagnosis is multidisciplinary and the management will depend on careful correlation with ERCP findings, imaging and clinical history.

If there is ongoing clinical concern or non-correlation repeat cytology / biopsies should be considered.

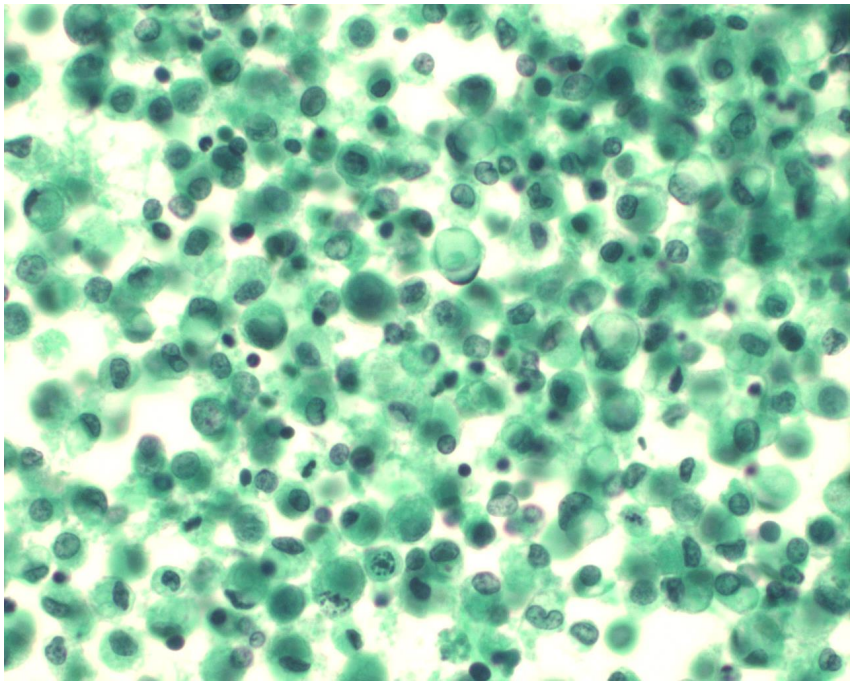
	1	1.5	2	2.5	3	Diagnosis
A2	malignant	suspicious	atypia	benign		Benign biliary brushing

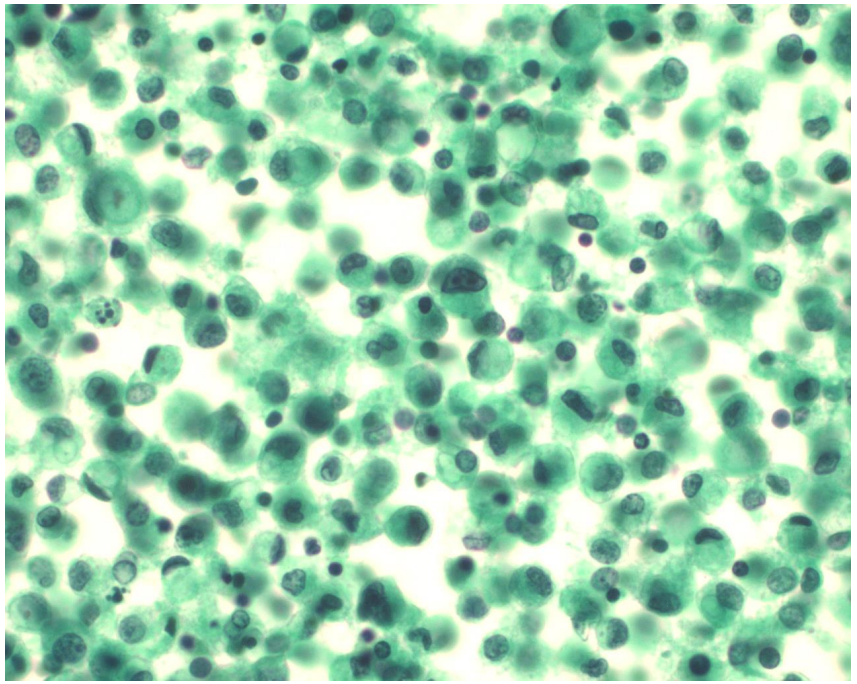
Case A3

Case A3 Ascitic fluid

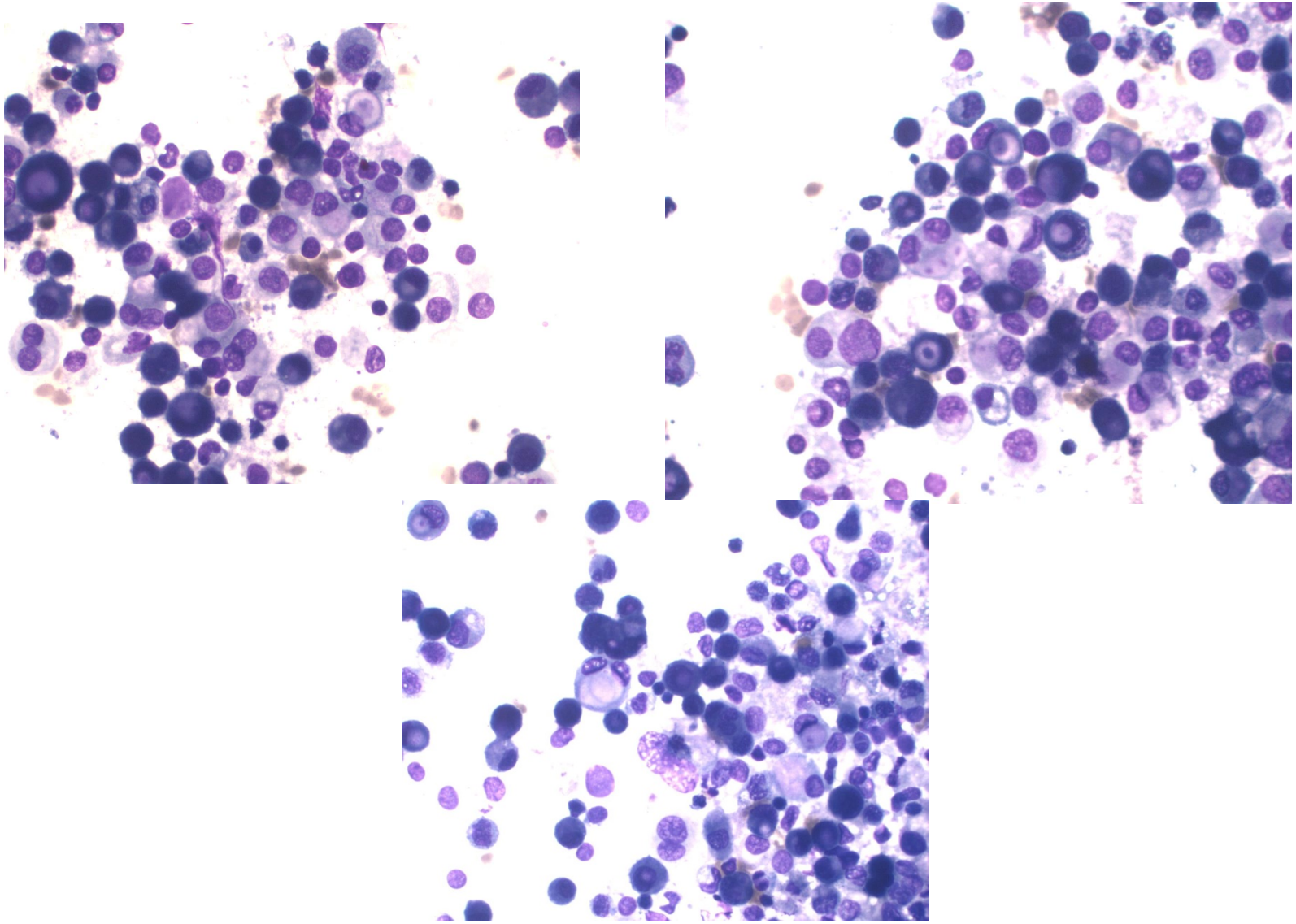
- 71 yr female
- Ascites

Case A3



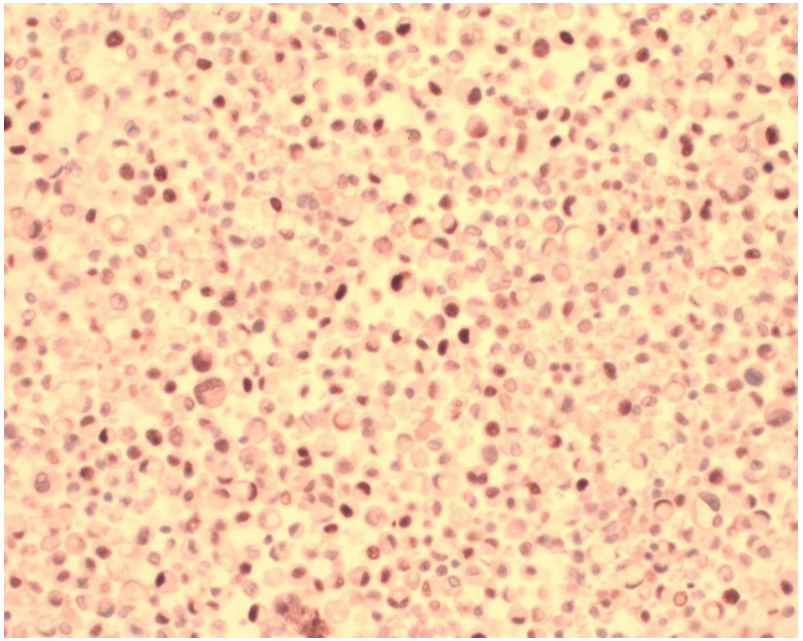


A3

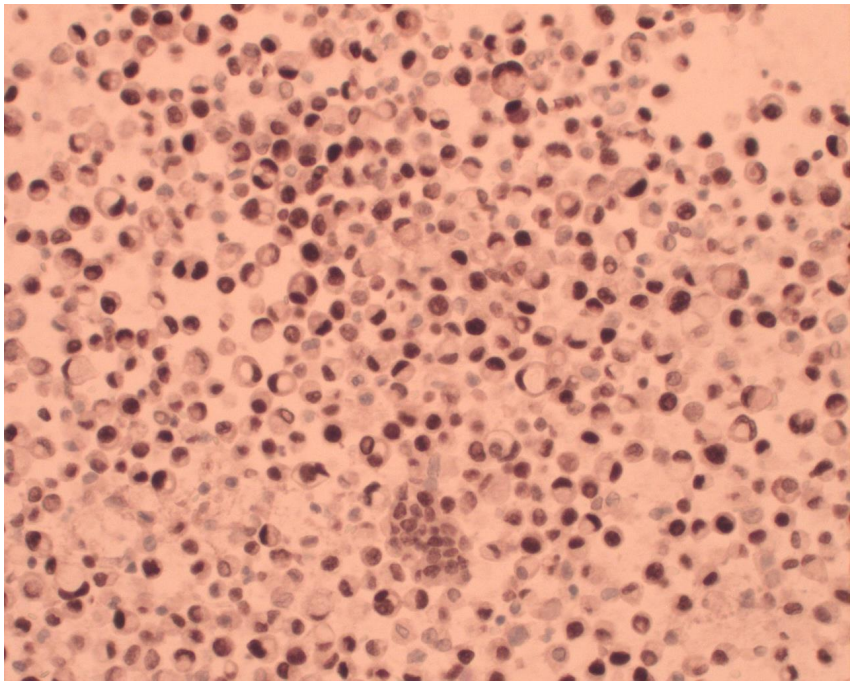


A3

Oestrogen receptor



Gata 3



Case A3 (F97)

Description

The specimen contains single atypical cells with mild nuclear pleomorphism, eccentric nucleoli, some membrane irregularities, intracytoplasmic lumina and occasional signet ring cells. Scant cells show targetoid mucin patterns. Mesothelial cells and inflammatory cells are also present

Diagnosis

Ascitic fluid: Metastatic adenocarcinoma

Plan

1. Correlation with imaging studies and clinical history is essential to determine primary site
2. Make a cell block
3. Perform immunohistochemistry to determine / support a primary site

Given the morphological appearances, a lobular breast carcinoma or upper GI primary should be considered in first instance in this case

Case A3 (F97)

Immuno panel (female with malignant ascites)

	CK7	CK20	CDX2	ER	WT1	PAX8	CA19.9	CEA	TTF1
lung	+	-	-	-	-	-	+/-	-	+
Gynae	+	-	-	+	+ (serous)	+	+/-	-	-
UGI	+	+/-	-/+	-	-	-	+	+	-
LGI	-	+	+	-	-	-	+/-	+	-
Breast	+	-	-	+/-	-	-	-	-	-

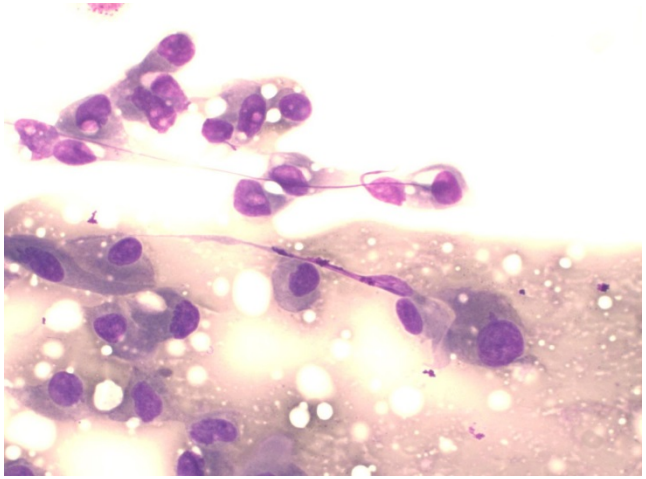
Gata3 for breast

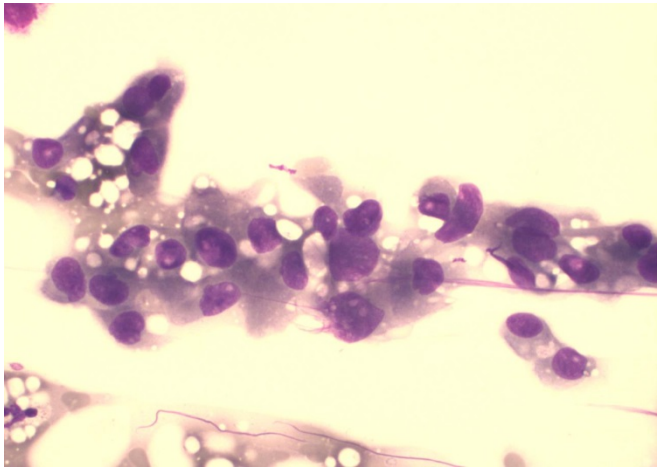
	1	1.5	2	2.5	3	Diagnosis
A3	benign	atypia	suspicious	malignant	Metastatic adenocarcinoma –good case to get 3.5, with comments	Metastatic adenocarcinoma

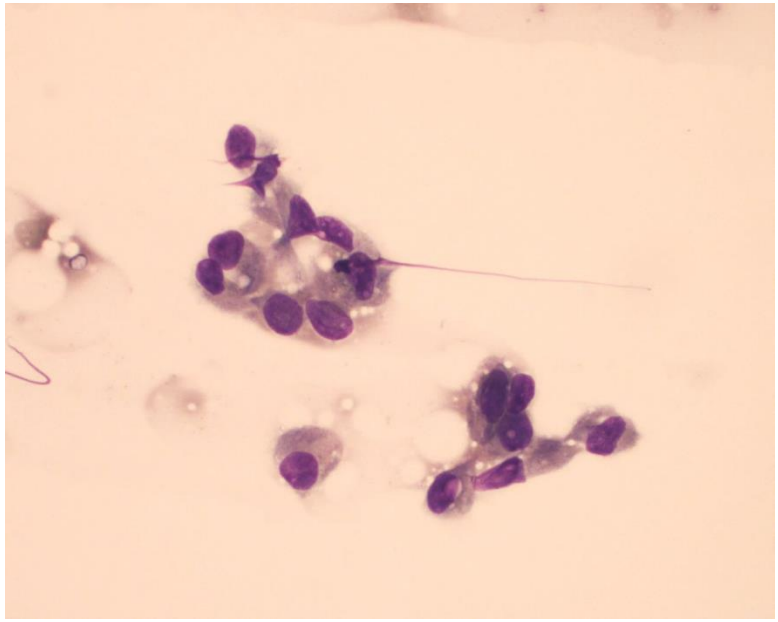
Case A4

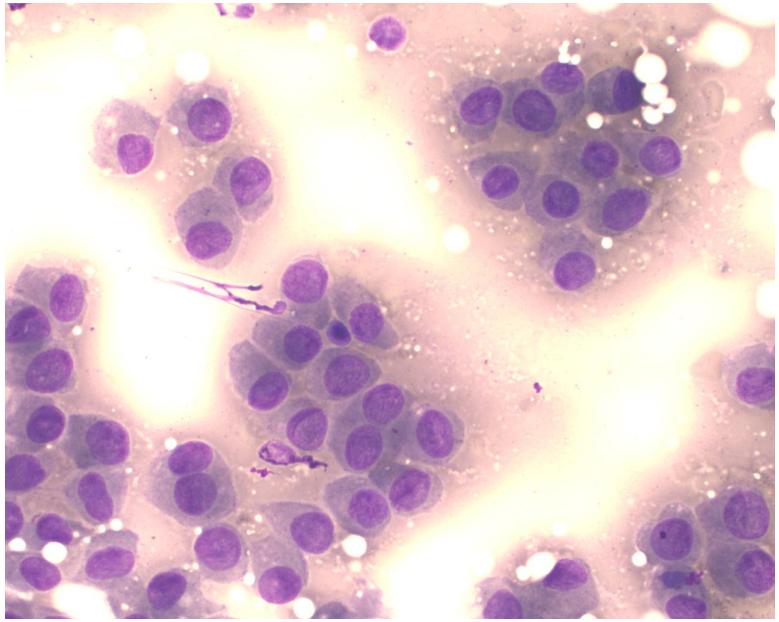
- Thyroid FNA
- Solitary thyroid nodule

Case A4

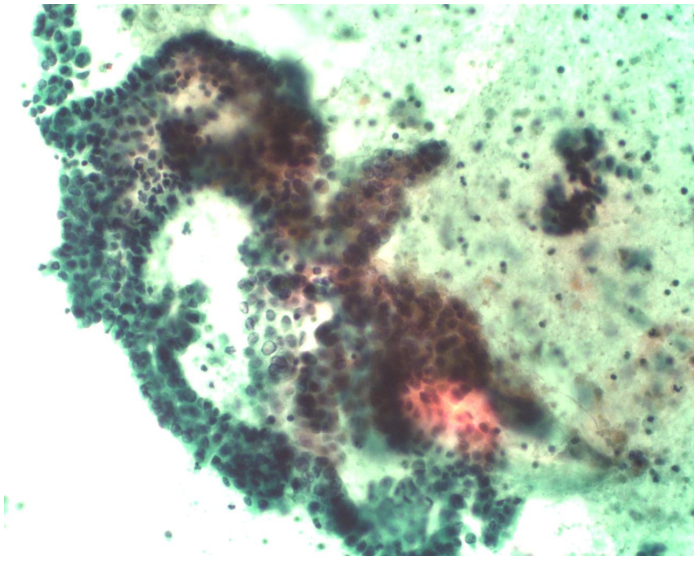


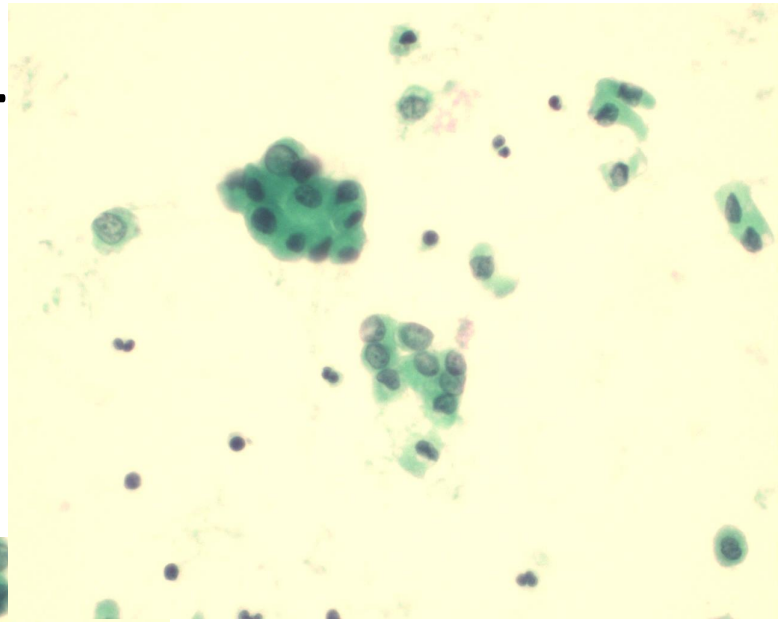


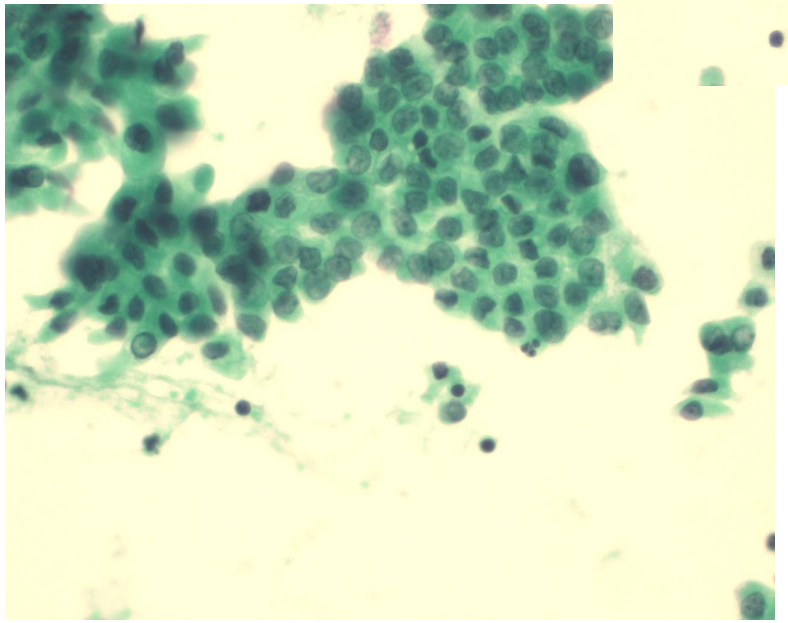




A4







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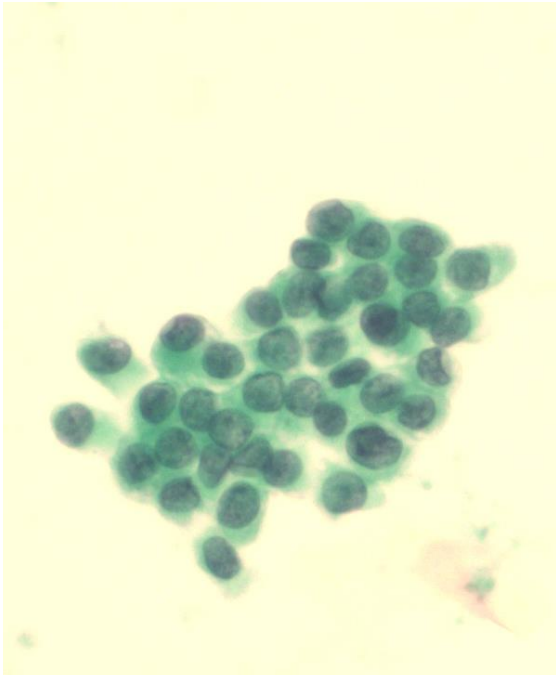
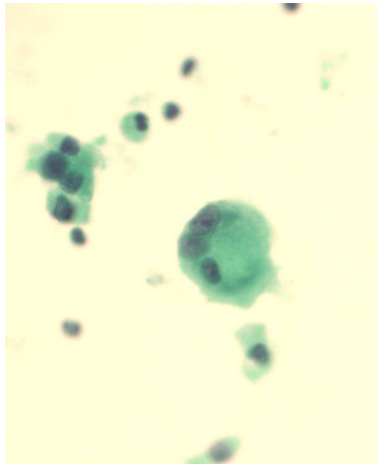




Case A4

Description

The aspirate includes abundant clusters of epithelial cells with deeply staining cytoplasm, in sheets and forming papillary structures, associated with thick colloid. Very occasional nuclear grooves and pseudoinclusions are seen.

Diagnosis

Papillary thyroid carcinoma (THY 5)

Comments

MDT discussion – management will depend on radiological tumour size and assessment of stage.

Total thyroidectomy is recommended if >4 cm in diameter, or multifocal disease, bilateral disease, extra-thyroidal spread, familial disease, clinically or radiologically involved nodes and / or distant metastases (BTA guidelines 2014)

PTC is the commonest well differentiated thyroid malignancy (75-85% cases)

Often in young females

Prognosis very good in young patients

Multifocality common

Lymphatic spread more common than haematogenous spread

It is associated with radiation exposure

20% chromosomal translocations involving RET proto-oncogene (encoding thyrosine kinase receptor) activating MAPK/ERK pathway - esp seen in children & post radiation exposure

30-50% point mutation in BRAF oncogene activating MAPK/ERK pathway

	1	1.5	2	2.5	3	Diagnosis
A4	benign	atypia	suspicious	Papillary thyroid carcinoma		Papillary thyroid carcinoma

Case A5

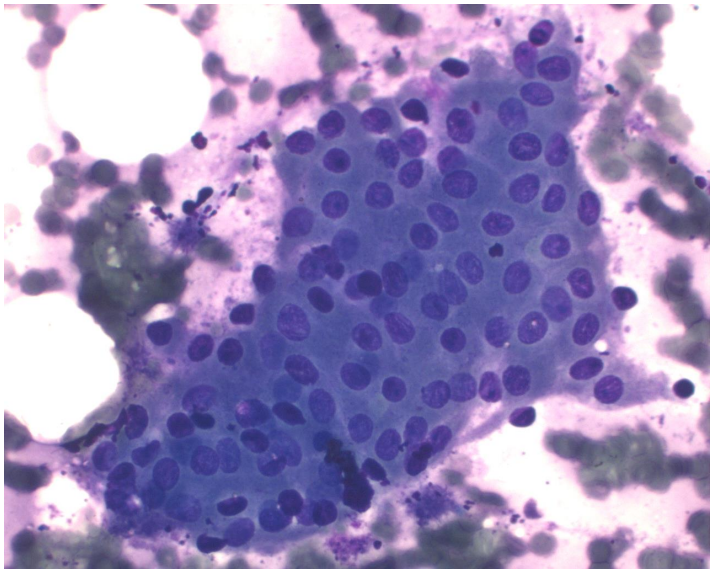
FNA Parotid

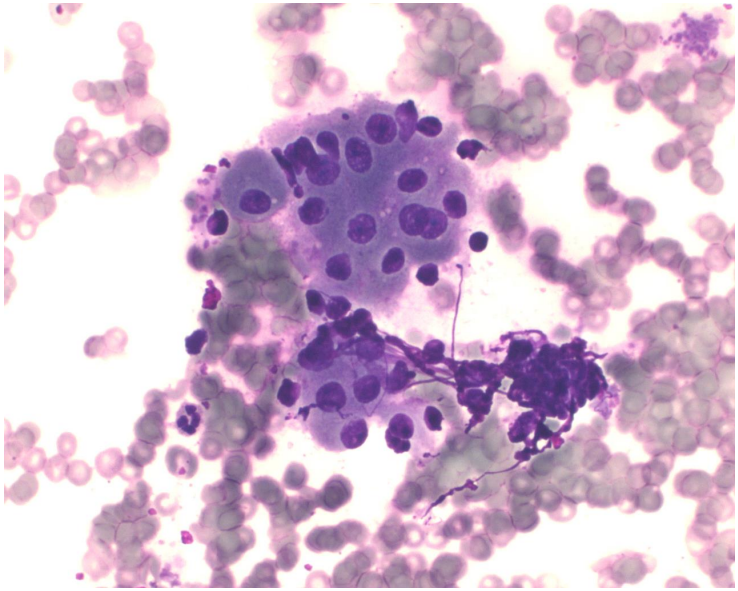
Case A

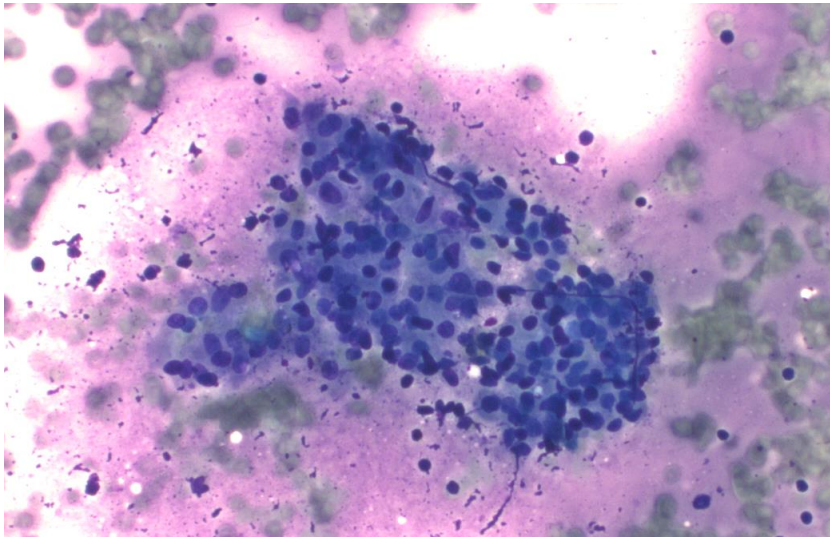
70 year old male parotid nodule – increased uptake on PET screening (for a lung lesion)

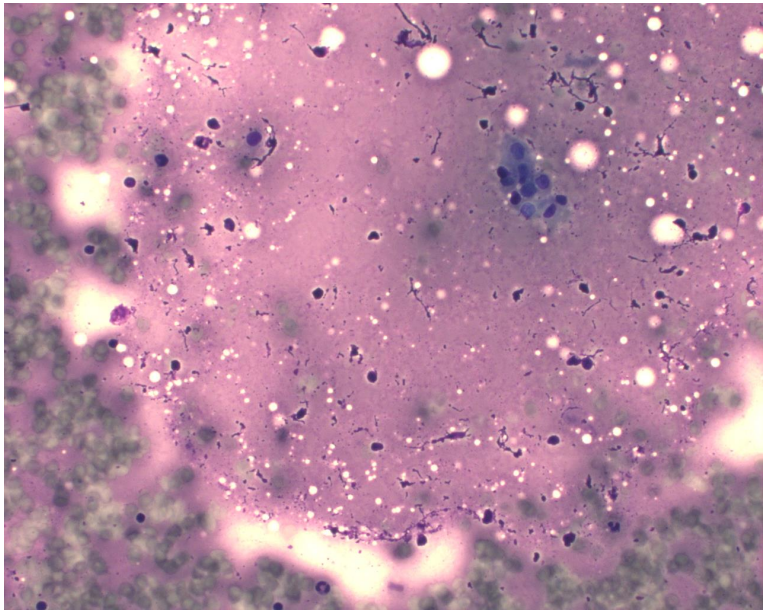
- FNA Parotid

Case A5

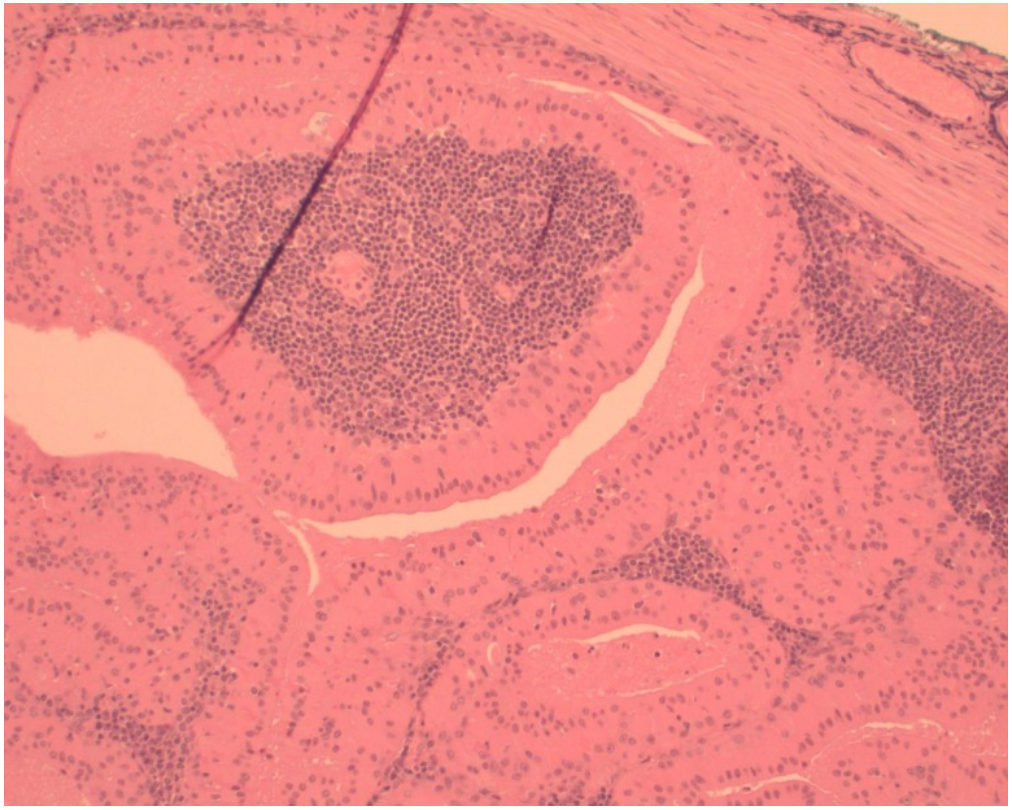








Case A5 - Resection



Case A5 (H30

Description

The aspirate contains sheets of oncocytic epithelial cells in a background containing lymphocytes.

Diagnosis

Warthin's tumour

Comments

Warthin's tumour has a preponderance for older male smokers (60-70yrs).

Usually in tail of parotid

2nd most common benign parotid tumour (after PSA)

It can be multifocal (10-20%) and occasionally bilateral (5-15%).

Presentation usually painless and slow growing, but minority may be painful and rapidly enlarging esp if infarcted.

In the presence of a clear FNA diagnosis and radiological correlation, clinical follow up rather than surgery may be discussed with the patient.

Can occasionally see squamous metaplasia with atypia – recognised diagnostic pitfall as can be confused with a cystic metastatic squamous cell carcinoma.

	1	1.5	2	2.5	3	Diagnosis
A5	malignant	suspicious	atypia	Benign with Warthin's in DD	Confident Warthin's tumour	Warthins

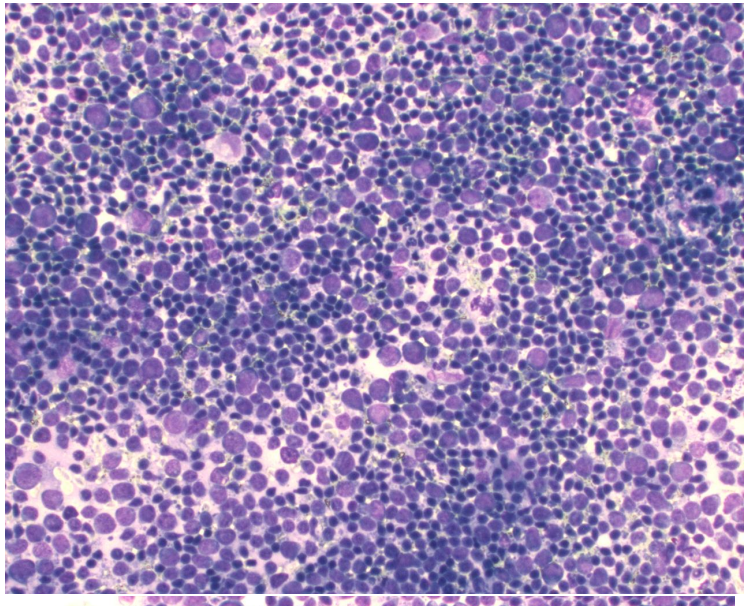
Case A6

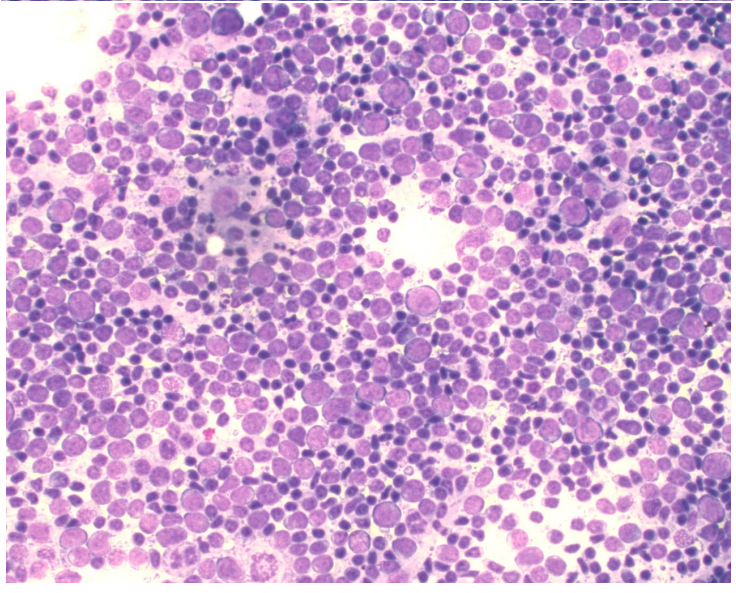
FNA Lymph node

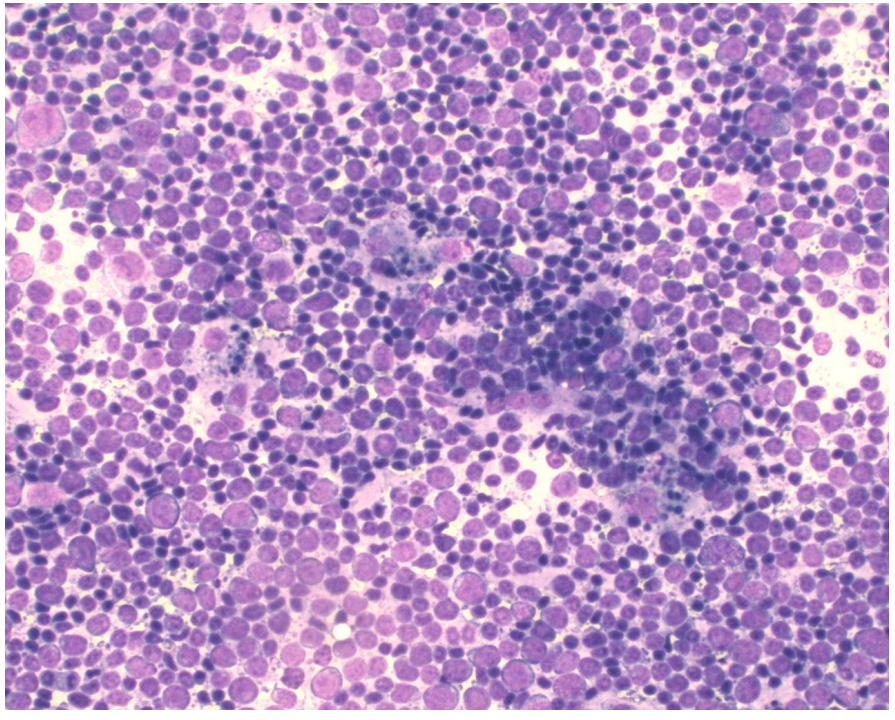
Case A6

- 50 year old female, enlarged lymph node left neck.
- FNA lymph node

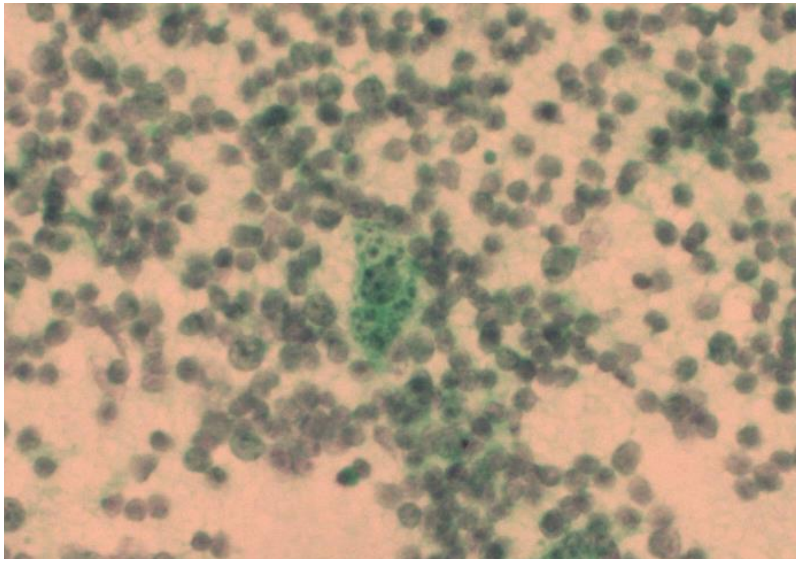
Case A6

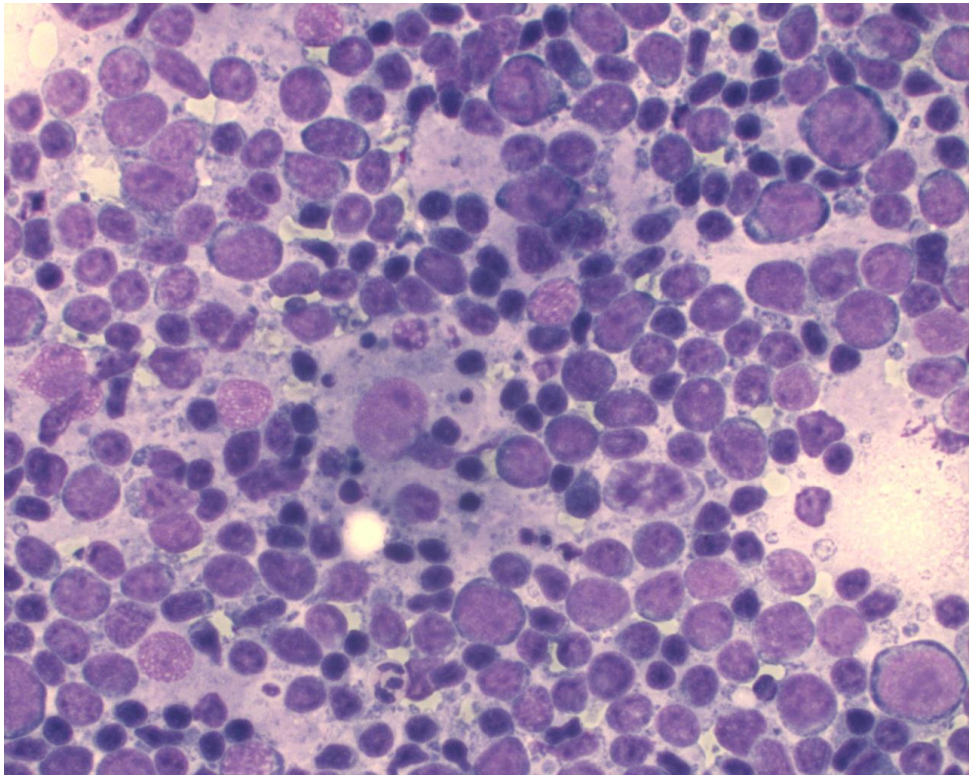


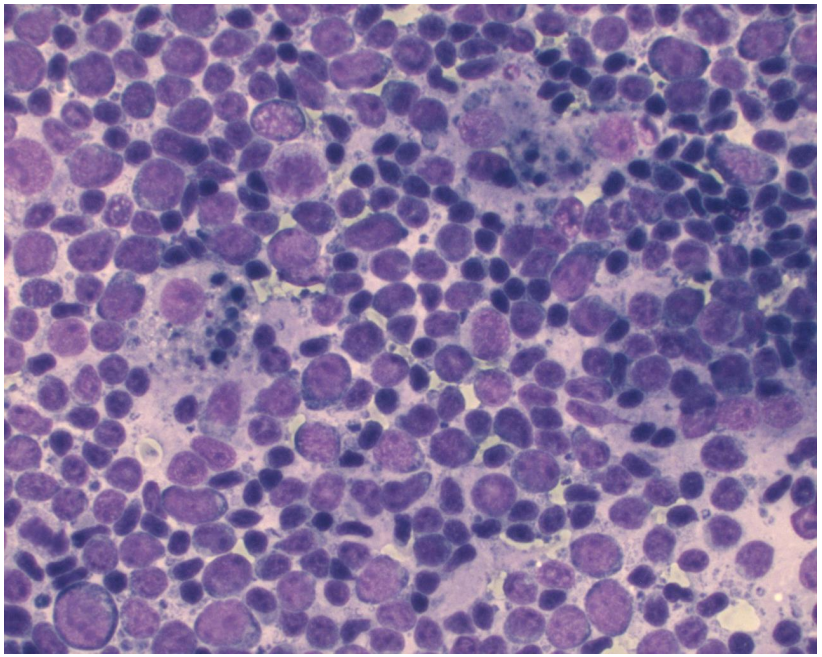




Case A6







Case A6

Description

The aspirate comprises a mixed population of small, intermediate and large lymphoid cells together with scattered tingible body macrophages. There is no metastatic malignancy and there are no granulomata.

Diagnosis

Reactive lymph node

Comments

Clinical / radiological correlation is recommended. Consider repeat aspiration for flow cytometry if the adenopathy / biopsy if the adenopathy persists after an appropriate of observation.

	1	1.5	2	2.5	3	Diagnosis
A6	malignant	Suspicious	atypia	Benign		Reactive lymph node

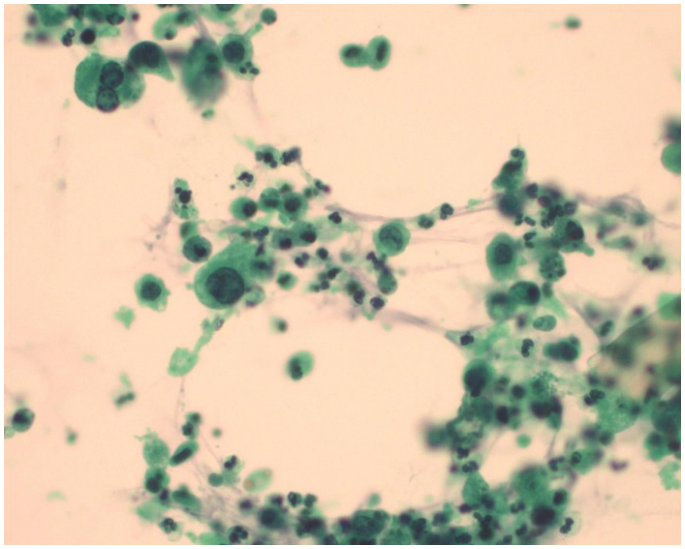
Case A7

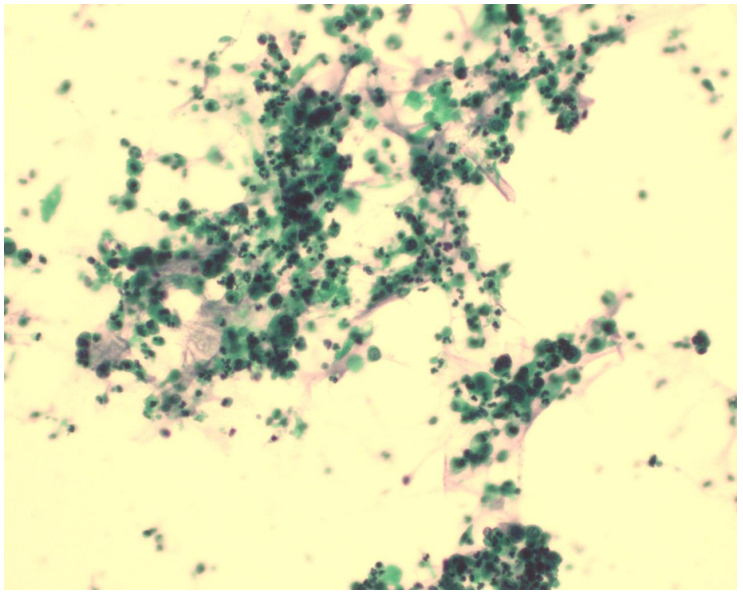
- Urine

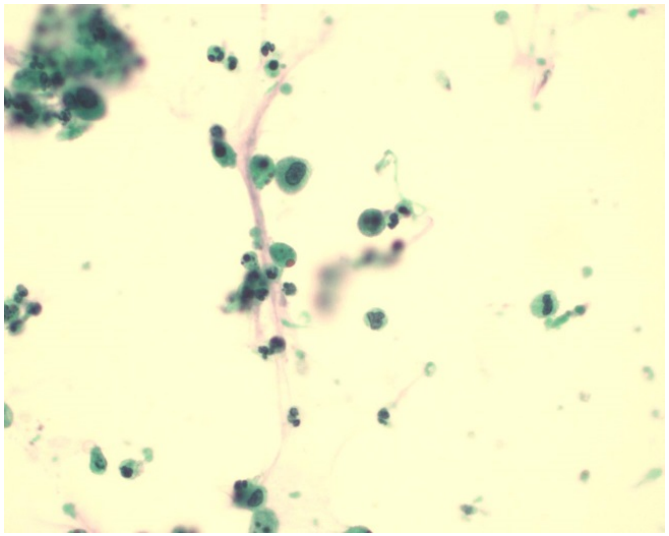
Case A7

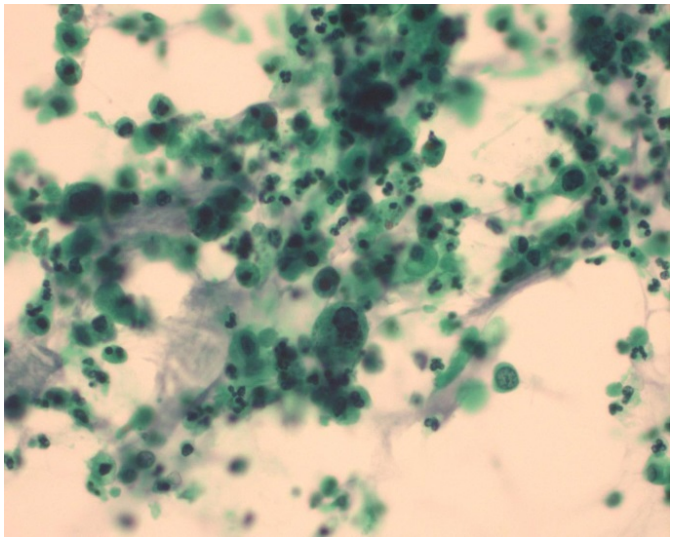
- 60 year male. Previous cystectomy. Ileal conduit. Haematuria.
- Cystoscopy NAD.

Case A7

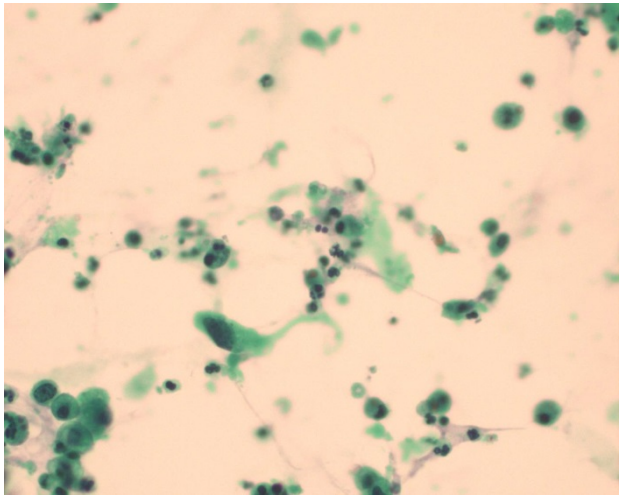


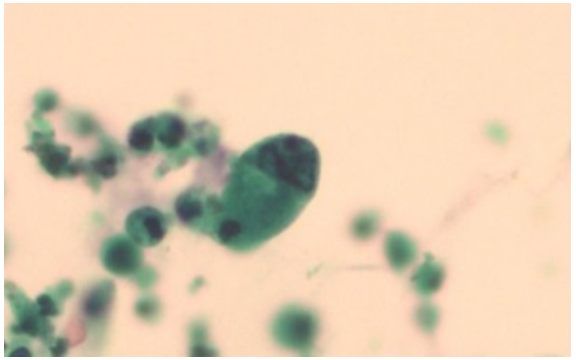


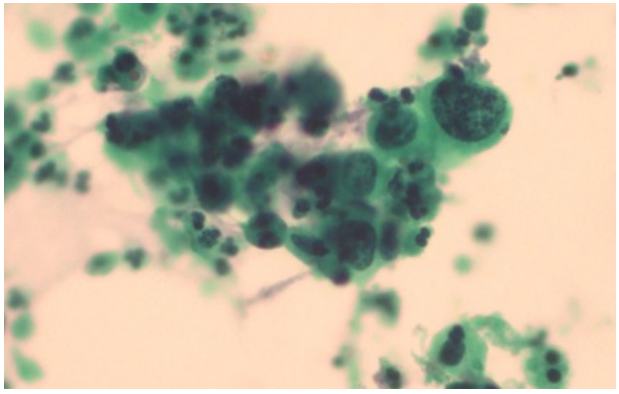


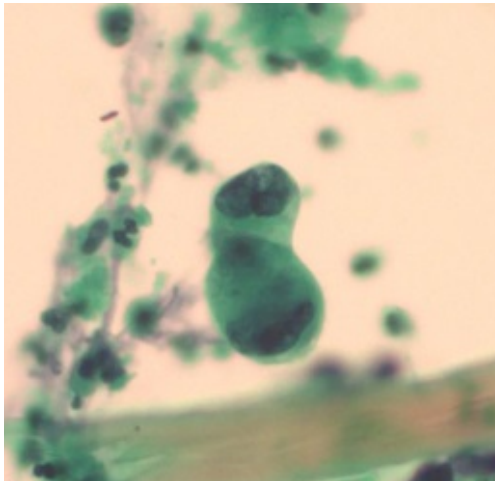


Case A7









Case A7

Description

This is a cellular sample comprising abundant degenerate cellular debris, together with extracellular mucin and neutrophils, in keeping with an ileal conduit sample. In addition there are scattered single atypical cells and occasional small groups showing increased nuclear : cytoplasmic ratios, coarse chromatin and irregular membranes. Some of these also show degenerate features. The appearances are in keeping with a recurrent high grade urothelial carcinoma.

Diagnosis

Ileal conduit urine: High grade urothelial carcinoma

Comments

The negative cystoscopy is noted. Further evaluation, including upper tract investigation is recommended.

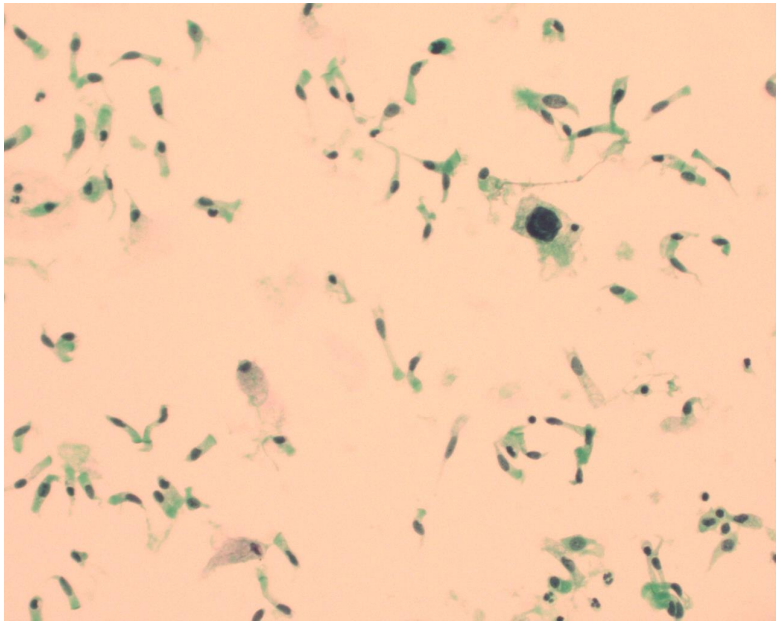
	1	1.5	2	2.5	3	Diagnosis
A7	benign	atypia	suspicious	malignant		Ileal conduit -High grade Urothelial carcinoma

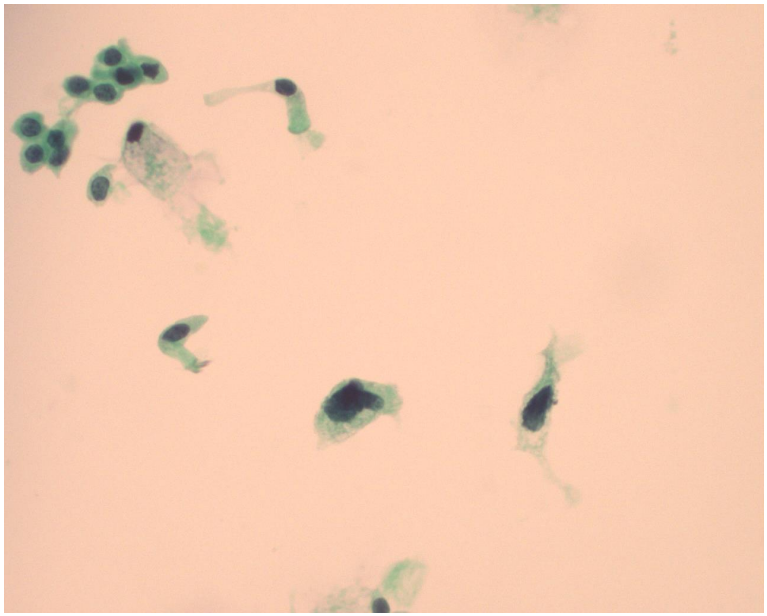
Case A8

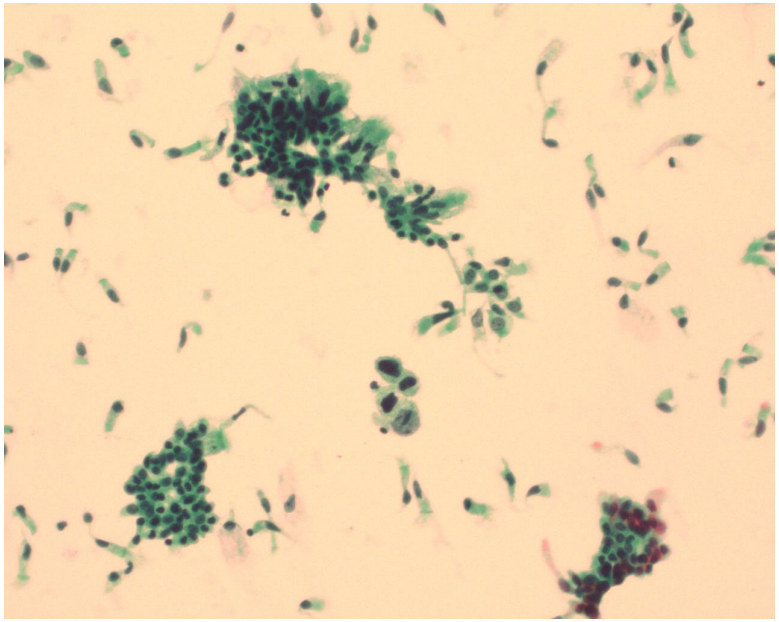
Case 8A

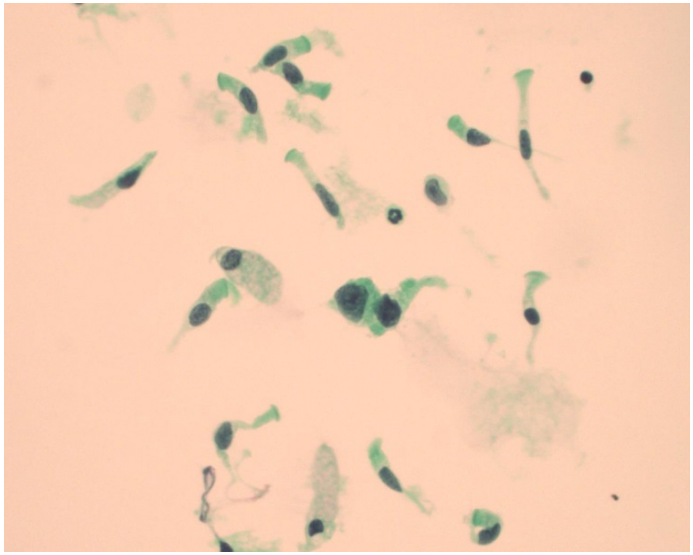
- 60 year old male, SOB
- Bronchial brush

A8









Case A8

Description

This is a cellular sample comprising many groups and single benign endobronchial cells, together with scant single atypical cells with increased nuclear: cytoplasmic ratios, hyperchromasia and irregular membranes.

Diagnosis

Non small cell carcinoma (adenocarcinoma)

Comments

Clinical / radiological correlation is recommended

Consider Alk ROS1 EGFR, PD-L1

EGFR (Next generation sequencing)

Frequent alterations occur in genes belonging to the receptor thyrosine kinase pathway involved in cell proliferation and survival , eg EGFR mutation leading to overexpression

Thyrosine kinase inhibitors eg Gefitinib are used as a first line therapeutic agent

ALK, ROS 1 (FISH)

Membrane associated tyrosine kinase receptors - recurrently involved in fusions or rearrangements

ALK mutations seen in 7% (EML4-ALK translocation of mutations in ROS 1 gene) – treat with ALK inhibitors eg Ceritinib

PD-L1 overexpression (IHC) (positivity based on percentage of positive cells)

Pembrolizumab is a therapeutic antibody that binds to and blocks PD-1 receptor located on lymphocytes. PD-L1 receptor prevents the immune system from attacking the body's own tissues (immuno checkpoint). Many cancers make proteins that bind to PD-1, thus shutting down the ability of the body to kill the cancer on its own. Inhibiting PD-1 on the lymphocytes prevents this, allowing the immune system to target and destroy cancer cells

Pembrolizumab is a first-line treatment if the cancer overexpresses PD-1, and the cancer has no mutations in EGFR or in ALK

	1	1.5	2	2.5	3	Diagnosis
A8	benign	atypia	suspicious	Malignant		BAL -Non small cell carcinoma (adenocarcinoma)

Cytology exam advice

- Look at lots (and lots) of cytology cases
- Look at lots of examples of each entity, cytology can be highly variable
- When doing histology pay attention to the cytomorphology.
- Beware of the range of reactive changes seen at each site eg, fluids, urine, resp, biliary tract
- Could the changes be reactive to therapy rather than malignant?
- Is there an infection? esp in immunosuppressed patients
- Beware clinical history can be helpful or even misleading!

Eg Fluid from a patient with a history of malignancy elsewhere. Don't be afraid to call it benign.

General advice

- Do not guess – in the patient's interest and your own, if you genuinely can't decide, consider calling it atypical explain the issue and how you would achieve a diagnosis

- Mentally prepare yourself - how you will avoid mid-exam panic and meltdown. Visualise this.

- Use your time wisely – write short descriptions

- Present your scripts as **clearly and neatly** as possible.

- Consider using a highlighter pen

Good luck!