Higher Specialist Diploma

Cellular Pathology

Examination – September 2022

Short Answer Questions

60 minutes

Attempt all four questions

Instructions to candidates

1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

2. Record your candidate number, the question number and the page number in the spaces provided on the answer sheets

3. Begin each new answer on a new page

4. Each question is worth 25 marks

1.

a. Upon reviewing HER2 staining, the control slide shows an identical level of staining on the 2+ and 3+ sections. Speculate on how this might have occurred and indicate your plan to investigate and resolve this issue? (15 Marks)

b. Your NEQAS EQA results are returned to the lab, and for the Grocott stain, you have been given a score of 3. What will you do in this situation? (10 Marks)

2. A prostatectomy specimen is examined, and no sign of cancer is found – despite a malignant core biopsy. Explain how you would investigate this discrepancy, and what corrective measures you would put in place to prevent a recurrence.

3. You have been asked to validate and verify a new predictive antibody test within your department. Discuss and explain the steps you would need to go through to complete this requirement.

4. A sentinel lymph node specimen has been compromised following formalin fixed and paraffin embedding. The resulting sections cut from the blocks reveals holes and tearing of the tissue. Critically assess the investigations that you would conduct to try to identify the cause of the error(s).

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Essay Paper

120 minutes

Attempt 2 out of 5 questions

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1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

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3. Begin each new answer on a new page

4. Each question is worth 100 marks

1. Discuss the importance and value of the growing role of biomedical scientists in performing histological dissection.

2. ‘An image paints a thousand words!’ Critically discuss the impact and benefits of digital pathology within cellular pathology.

3. Discuss and evaluate the histological investigations of bone marrow trephine biopsies.

4. Discuss and critique the identification of infectious agents within cellular pathology.

5. Discuss the importance and implications of the 2 Week cancer pathway for patient management within cellular pathology.

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Case studies

120 minutes

Attempt all case studies

Instructions to candidates

1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

2. Record your candidate number and the page number in the spaces provided on the answer sheets

3. Begin each new case study on a new page

4. Each case study is worth 100 marks

5. For these case study questions you are strongly advised to answer the questions as they arise during the case study to avoid later information impacting adversely on your answers to the earlier questions by presuming an "outcome".

SEEN CASE STUDY

1.

An 83-year-old male patient presents with a distinctive multifocal pigmented lesions on his back (2-3mm in diameter). The lesions are closely cropped and appear to be clinically irregularly pigmented. A skin ellipse biopsy is performed in order to remove the multifocal lesions. A marker stitch is placed at one pole. The clinical diagnosis suggests metastatic deposits with unknown primary.

a. Describe the procedure for histological dissection of a skin ellipse with a marker stitch provided for orientation purposes (15 marks)

On review of the HE stained sections from the specimen the multifocal lesions present with similar microscopic findings. (See Figures One and Two)

FIGURE 1 Low Power HE Stained Section

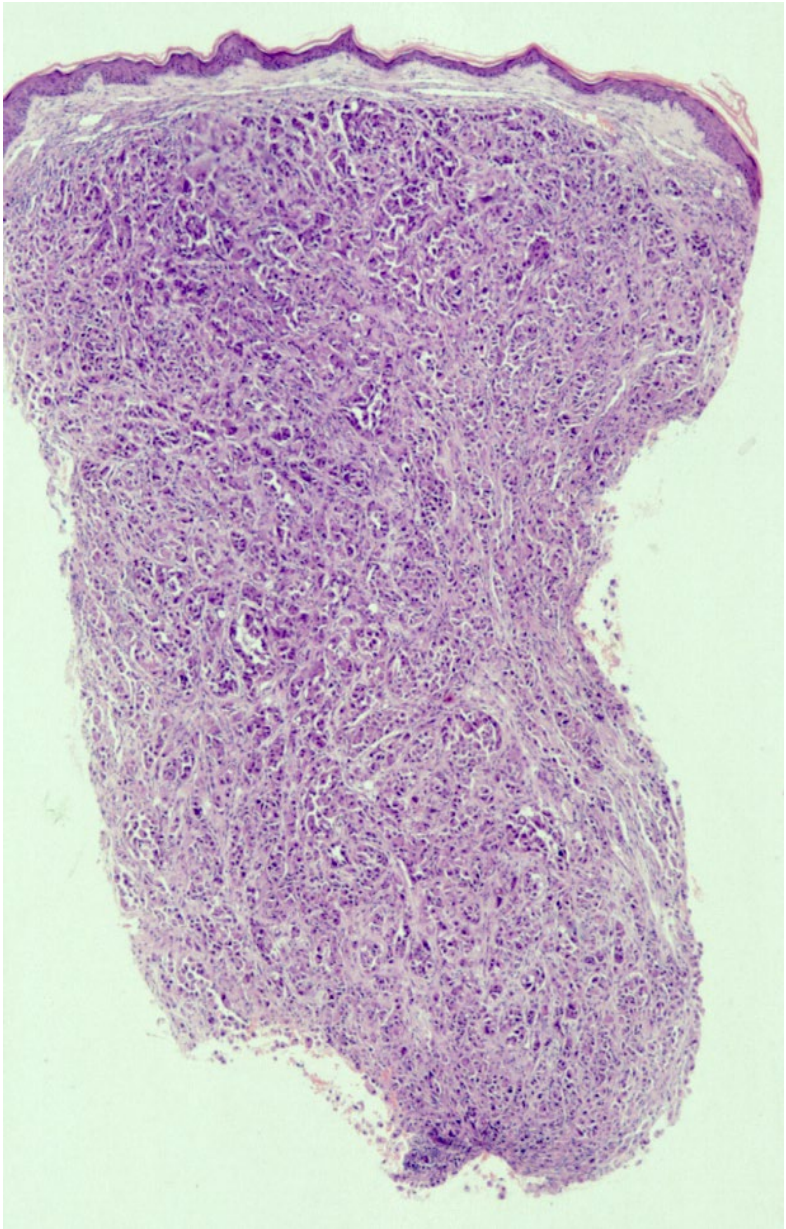
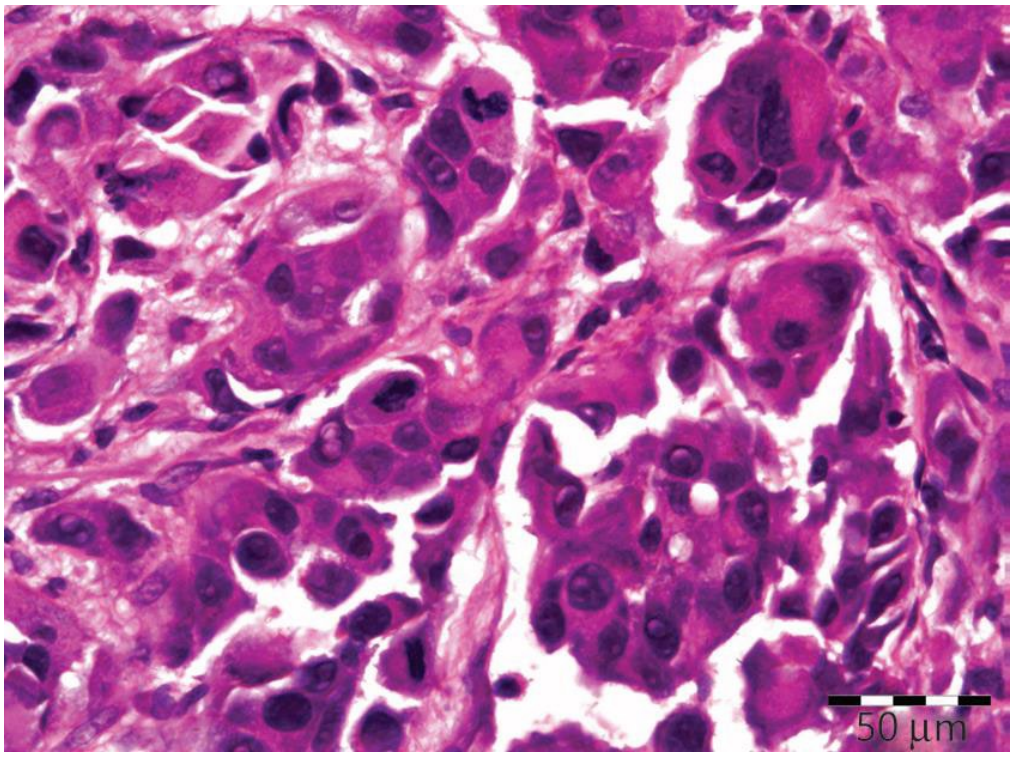


FIGURE 2 High Power – HE Stained Section



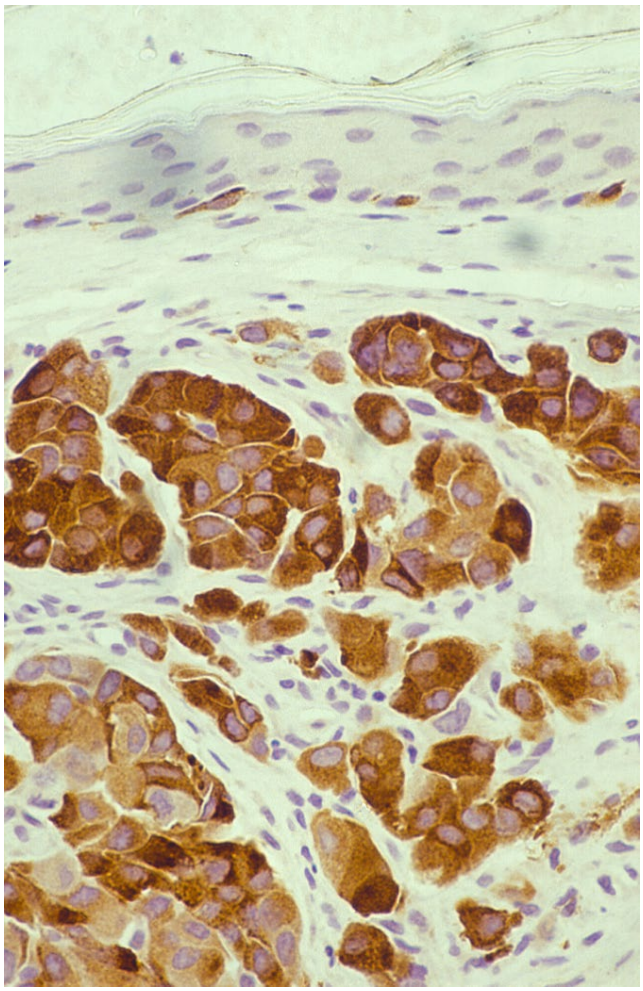
b. Describe the features seen within the low and high power HE stained sections (10 marks)

c. From the histological microscopic description above what deductions can be made about the microscopic appearance of these lesions and what other features would you expect to see? (10 marks)

d. To evaluate the differential classification of the lesions what panel of markers would you use to help delineate carcinoma from lymphoma from melanoma and what special stains may be useful with classifying carcinoma and melanoma? (15 marks)

e. All the markers for lymphoma and carcinoma were NEGATIVE. However, S100 protein and Melan A (See Figure 3) and anti-tyrosinase were strongly positive. What does this suggest is the nature of this metastatic multifocal tumour deposits? Justify your answer. (10 marks)

FIGURE 3 - Melan A



f. Name some other areas where S100 protein is used in a diagnostic setting. (10 marks)

g. Recently a new antibody derived from cells from the neural crest and has shown improved selectivity and sensitivity for typing tumours derived from tissue from this site. What is the name of this new antibody? (10 marks)

Following these investigations, the patient was found to have a primary pigmented lesion on the nail bed of the right big toe. The toe was removed and primary diagnosis was made with accompanying assessment of tumour clearance on the margins.

h. A direct measurement of the depth of tumour invasion into the dermis was measured using an eye piece graticule in mm, what is this assessment called and how does it help the clinician when discussing the subsequent treatment with the patient? (10 marks)

The patient was treated for all lesions identified and was reviewed 6 months later. No further associated pathology was identified but screening for a molecular assay was recommended.

i. Name the molecular assay and describe what information this will provide for the clinician. (10 marks)

UNSEEN CASE STUDIES

2.

A 57-year-old farmer presented with kidney failure. All routine blood tests and kidney function tests were performed. These were all found to be abnormal. Most notably there was increased levels of creatinine following a glomerular filtration rate (GFR) assessment indicating renal dysfunction. Urine analysis provided evidence of proteinuria with elevated albumin levels. A renal core biopsy was performed. In addition, CT and MRI scans were requested.

a. Describe how you would fix, dissect and subsequently process the renal core biopsy specimen. (20 marks)

On histological evaluation there were significant deposits of immunoglobulin and amyloid found within the Bowman's Capsules and glomerular structures

b. List the panel of tinctorial and immunocytochemical / immunoflouresence and electron microscopic tests that would be performed in such an investigation and explain what information is provided by each. (20 marks)

Widespread amyloid deposits were seen within the glomeruli (**FIGURE 1**). Ultra- structural transmission electron microscope analysis revealed fine fibrillary amyloid fibres (**FIGURE 2**).

FIGURE 1: Amyloid deposits within the glomerulus (Congo Red)

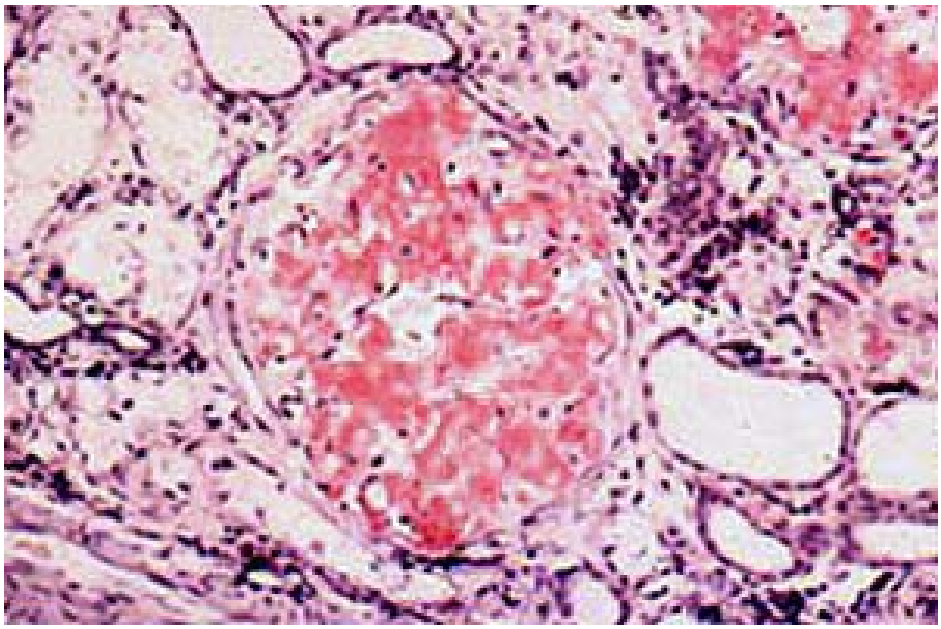
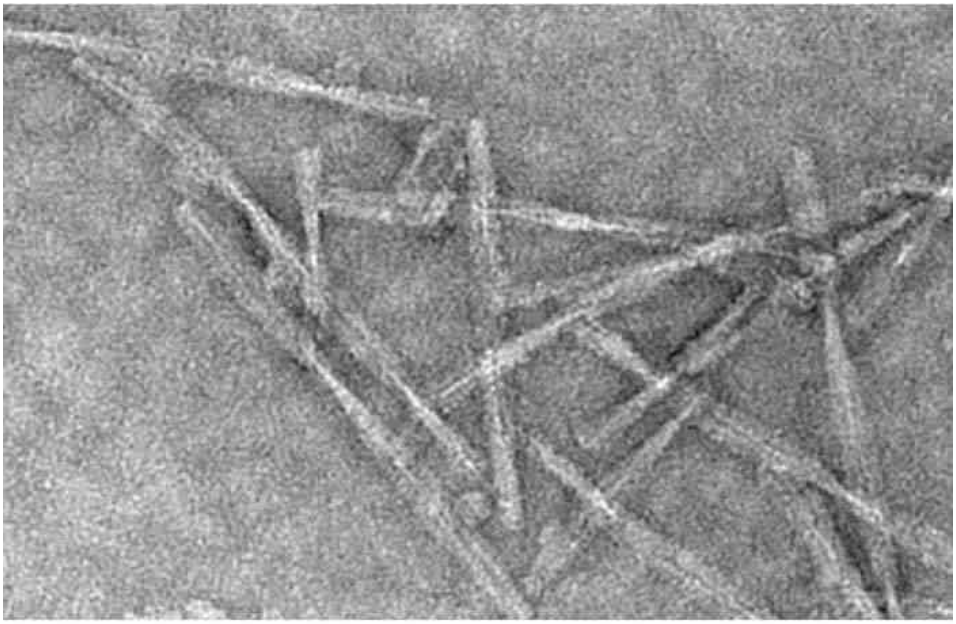


FIGURE 2: Transmission electron microscopy image of amyloid fibres



c. Describe and explain the structure of amyloid fibres and the nature of the amyloid deposits. (10 marks)

Additional scans CT and NMR revealed abnormal lytic lesions within the skull (**pepper pot** appearance) (**FIGURE 3**) and also within the long bones of both arms and legs.

FIGURE 3: CT scan revealing 'Pepper Pot' lytic lesions within the skull

d. What do the images suggest about the patients underlying condition? (10 marks)

Blood tests revealed a neoplastic proliferation of cells that also produced high levels of immunoglobulins with heavy chains: IgG (52%), IgA (21%), IgM (12%). High levels of light chains for predominantly kappa were also detected in urine also known as Bence Jones proteins. Frozen section analysis of swollen nodular lesions in skin and several other organs revealed numerous angulated crystal deposits.

e. What is the likely nature of these crystalloid deposits? (10 marks)

f. In light of all the collective findings above what is the favoured diagnosis and give an example of some subtypes (10 marks)

Subsequent further Immunocytochemical tests were requested to evaluate the crystalloid deposits and surrounding large cells with characteristic 'clock face' chromatin patterns within the nucleus.

g. What are the cells described as having the clock face chromatin pattern and what other morphological features do these cells exhibit? (10 marks)

h. What immunocytochemical investigations would be requested to clarify the immunophenotype of these cells? (10 marks)

3.
A 85-year-old male patient who formally worked in the building manufacturing industry who had a smoking habit of 30 cigarettes a day for over 50 years presents with haemoptysis and shortness of breath at his GP. A referral is made to the local hospital where the respiratory care team requested an initial chest x-ray and some cytological tests.

a. Critically review the most likely cytological investigations that would be performed on this patient. (10 marks)

b. The cellular material was then centrifuged and a cell block prepared. Comment and critically assess how best to maximise the cellular yield from such a procedure? (10 marks)

The x ray revealed a medium sized mass on the upper aspect of his left lung some distance from the central bronchus. Following the cytological investigations a lung biopsy was requested. The findings from HE's performed on the blocks from the biopsy are seen below (**FIGURES 1** and **2**).

FIGURE 1: **HE Low power**

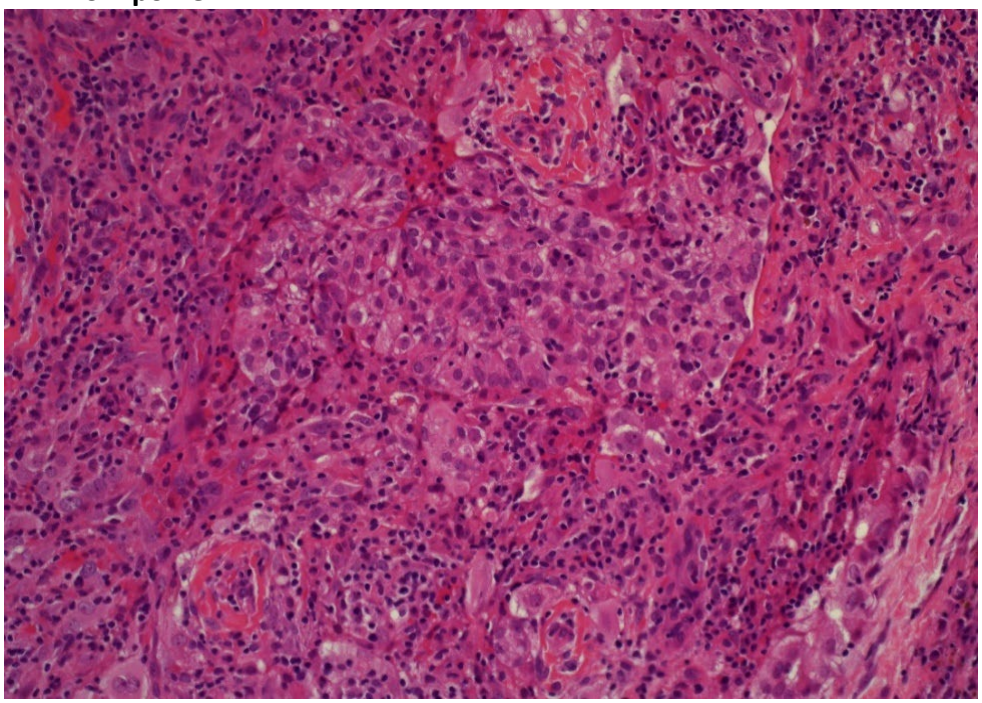
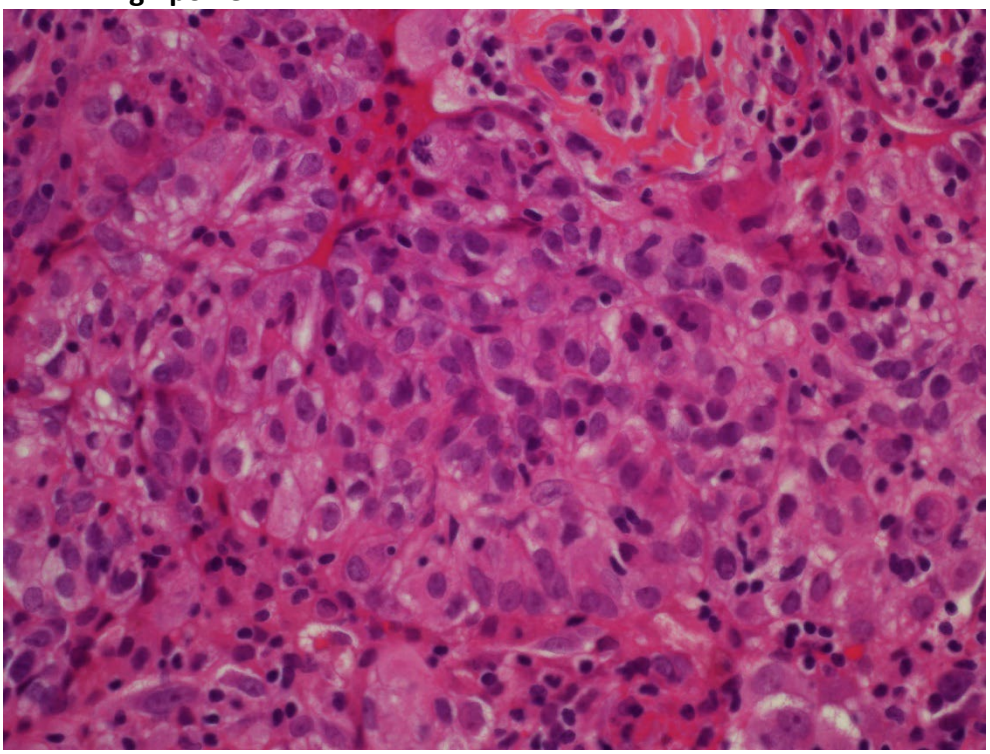


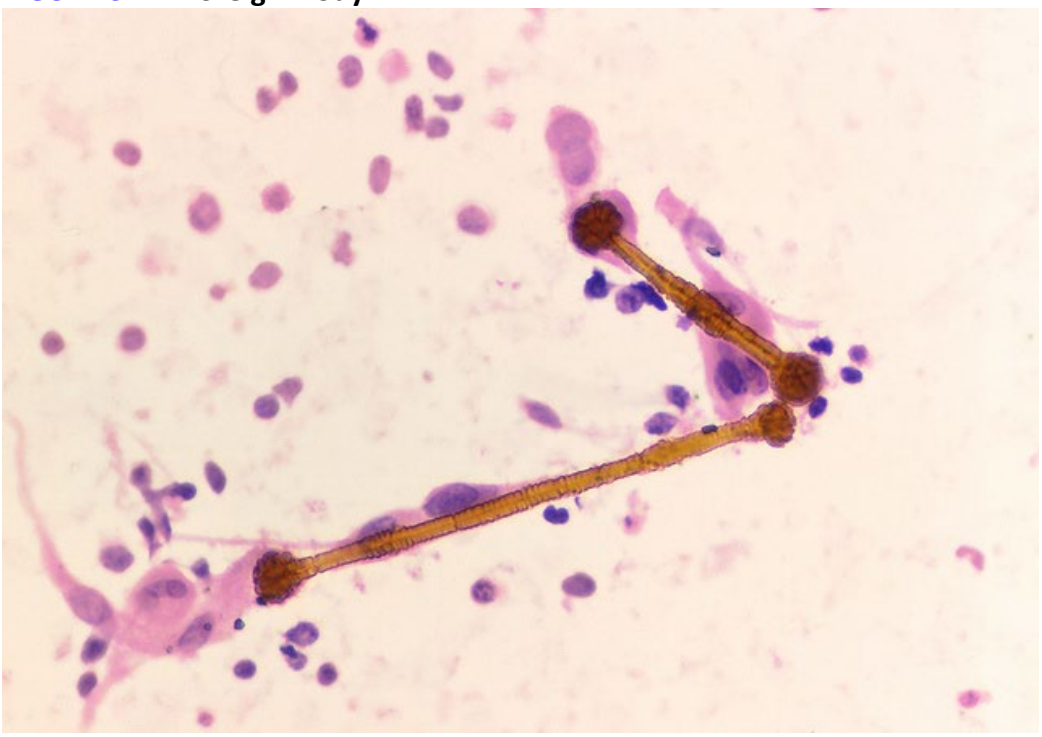
FIGURE 2: **HE High power**



c. Describe and discuss the structural and nuclear features of the atypical cells seen.
(20 marks)

On review of this material an unexpected foreign body was identified (**FIGURE 3**).

FIGURE 3: **HE Foreign Body**



d. Describe what name is given to this foreign body and explain its appearance. Critically evaluate what special stains can be used to highlight it? Diagnostically what form of lung cancer may this finding often support? (20 marks)

e. Discuss and appraise what immunocytochemical markers would you employ to support a diagnosis. (20 marks)

f. Explain the value of PD1 / PDL1 investigations in selected patients with lung cancer. Critically review what these investigations are and how they elicit an effect in terms of treatment for patients with lung cancer. (20 marks)