Higher Specialist Diploma

Cellular Pathology

Examination 2018

Paper 3

Discipline-specific questions

120 minutes

Attempt 3 out of 6 questions

Instructions to candidates

1. Record your candidate number, qualification title and where appropriate the discipline and examination paper number 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 answer on a new page
4. Write on one side of the answer sheet only
5. Each question is worth 100 marks
1. Critically review and appraise the histological investigative performed on bone marrow trephine biopsies.

2. Critically assess the term clinical governance in the modern cellular pathology laboratory.

3. Discuss and critically appraise the impact of liquid base cytology technology on the of gynaecological cytopathology.

4. Discuss the importance of the growing role of biomedical scientists in performing histological dissection.

5. Critically review the impact of automated platforms within cellular pathology.

6. Discuss the interrelationship between histopathology and molecular analysis in the diagnosis and management of non-small cell lung cancer.
Higher Specialist Diploma

Cellular Pathology

Examination 2018

Paper 4

Case studies

120 minutes

Attempt all case studies

Instructions to candidates

1. Record your candidate number, qualification title and where appropriate the discipline and examination paper number 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 answer on a new page
4. Write on one side of the answer sheet only
5. Each case study is worth 100 marks
1. 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 the procedures that would be followed to perform tissue dissection, fixation and preparation of a renal core biopsy (20 marks)

On histological evaluation of the renal core biopsy there was found to be significant deposits of immunoglobulin and amyloid within the Bowman’s Capsules and glomerular structures

b. Explain the investigative tinctorial and immunocytochemical/ immunofluoresence and electron microscopic tests that would be performed in such an investigation. (20 marks)

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

Figure 1: Amyloid deposits within the glomerulus (Congo Red)
c. Describe and explain the structure of amyloid fibres and the nature of the amyloid deposits.

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.
d. Explain what these findings may 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)

Unseen Case Studies

2.
A 55 year old female presented at her GP surgery with a soft mass in her right breast. She was referred for mammography and this confirmed the presence of a 1.5 cm diameter lesion. A core biopsy was taken and processed for FFPE histopathological analysis.

a. Describe how a core biopsy is taken and its optimal preparation for histopathological analysis. (10 marks)

b. Outline why histological assessment is required over cytology for the definitive diagnosis of breast disease. (5 marks)

Morphological and immunocytochemical analysis was undertaken on sections of the core biopsy. The results indicated the presence of invasive ductal carcinoma.

c. What are the key morphological features of invasive ductal carcinoma and how can immunocytochemistry assist in distinguishing between this and ductal carcinoma in situ? (10 marks)

Immunocytochemistry of additional sections of the core biopsy was undertaken for hormone receptor status, HER2 and Ki67.
d. Explain how the results of this further immunocytochemical assessment serve as predictive and prognostic indicators. (15 marks)

The results of this immunocytochemical assessment were as follows:
- Oestrogen receptor; positive (Quickscore, 7).
- Progesterone receptor; negative.
- HER2: negative.
- Ki67; high proliferation index.

e. What is the potential significance of diagnosis and immunocytochemical profile for the patient’s treatment? (10 marks)

The patient’s diagnosis and immunocytochemical profile were presented at the next MDT. At this meeting it was agreed that resection of the tumour and intraoperative sentinel lymph node assessment should be offered to the patient.

f. Describe the rationale for intraoperative sentinel lymph node assessment, principles of methods available and the advantages and limitations of each. (20 marks)

The patient consented to surgery. Sentinel lymph node assessment was positive and a radical mastectomy including the removal of axillary chain lymph nodes was undertaken. The mastectomy specimen and lymph node chain were sent for FFPE histopathology.

g. How should the tumour and lymph nodes be prepared for and histopathologically assessed? (15 marks)

The profile of the tumour in the resection specimen was identical to the core biopsy and, in addition to the sentinel lymph node, tumour cells were identified in two additional lymph nodes. At a subsequent MDT these findings were reviewed and it was recommended that OncotypeDX gene expression test should be undertaken using a portion of the resection specimen.

h. Describe the OncotypeDX gene expression test and explain why it was recommended for this patient. (15 marks)
3. A 59-year-old male patient presents with the following symptoms: abdominal pain, a mass or swelling in the abdomen, nausea, vomiting, a feeling of being full after eating only a small amount of food and weight loss with associated problems swallowing. He undergoes a gastric resection and a fresh specimen is received in the laboratory. The specimen is suspected clinically to have a differential diagnosis of lymphoma/stromal tumour/carcinoma/carcinoid. On slicing, a firm white tumour is seen which does not appear to invade the epithelium.

a. Discuss how the specimen should be sampled, fixed and dissected. (15 marks)

b. Comment on how the differential diagnosis is affected by there being no epithelial involvement on gross investigation. (10 marks)

The pathologist suspects a GIST tumour.

c. Discuss the features of various cell types responsible for GIST tumours. (15 marks)

d. Discuss and describe which immunocytochemistry markers may be used to assist in the confirmation of this diagnosis. (20 marks)

e. Discuss the factors that determine staging of these tumours. (10 marks)

f. Briefly discuss other tumours that would have been included in the original differential diagnosis and what markers could have been used to delineate these? (20 marks)

g. The case is seen to make a good control for future tests. What information would you need to collect relating to this specimen in order to validate the control material for diagnostic use so as to conform to ISO 15189 standards? (10 marks)