Mock FRCPath Part 2 Morphology Paper Answers
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"It's just another exam, like all the rest"

SUGGESTED ANSWERS

Answers are based on the real film reports (+/- other pathology reports) for each case. Answers for questions about further investigation / management just based on my own thoughts – you may have other equally legitimate answers. This is only for practice, not definitive truth ☺

Question 1: A 40 year old receiving gemcitabine chemotherapy for pancreatic cancer presents to the acute oncology service with breathlessness and lethargy. They have had diarrhoea for the last week following the most recent chemotherapy cycle. Hb 80, Creatinine 150.

- Report the blood film (3 marks)

Thrombocytopenia
Polychromasia, red cell fragments
Vacuolated neutrophils

- State the diagnosis and differential causes (3 marks)

This is microangiopathic haemolytic anaemia (MAHA)
TTP – congenital, acquired autoimmune
HUS – E.coli shiga toxin
aHUS – congenital
Other MAHA/TTP – includes drug-induced (e.g. gemcitabine, tacrolimus), malignancy-associated (e.g. pancreatic), infections (e.g. CMV, HIV), pregnancy (HELLP, eclampsia, AFLP), allogeneic stem cell transplant, malignant hypertension, AI disease (e.g. CAPS, Lupus, Vasculitis)

- List the further tests you would request at this point (3 marks)

Prothrombin time, APPT, Fibrinogen
ADAMTS13 level
Troponin (Ass. with poor prognosis)
Haptoglobins, LDH, Reticulocyte Count, Direct Antiglobulin Test (Haemolysis screen)

Question 2: A 65 year old has an annual review at his GP surgery. He is a nursing home resident following a severe road traffic collision five years previously. Hb 120, Plt 550, WBC 15.

- Report the blood film (3 marks)

Thrombocytosis
Target cells, Howell jolly bodies
Normal neutrophils

- State the cause of your findings (1 mark)

Hyposplenism (?splenectomy at time of RTC)

- Regarding the cause of this patient's abnormal blood film, what prophylactic measures should be offered to the patient at their annual review, and why? (3 marks)

Consider vaccination schedule in accordance with Green Book guidance. i.e. Offer annual influenza vaccine and should be due 5-year pneumococcal booster
Consider prophylactic antibiotics against encapsulated bacteria (e.g. pneumococcus, Neisseria) with e.g. Phenoxymethylpenicillin.

Question 3: A 60 year old woman presents to the emergency department with a progressive history of breathlessness and lethargy. Chest X-ray reveals bilateral pleural effusions and cardiomegaly.

- Report the blood film (3 marks)

Normal platelets
Normal red cells
Eosinophilia

- Provide a differential diagnosis for the blood film finding(s). Include examples of primary haematological causes. (5 marks)

Idiopathic (Idiopathic hypereosinophilia syndrome)
Primary clonal – Gene re-arrangements including, for example, FIP1L1, PDGFRA, PDGFRB
Secondary – Allergic, Drugs, Parasites and tropical infections, Autoimmune disease, Malignancy,
Reactive (e.g. Loffler's Syndrome) etc etc etc

- State your initial investigation and management of this patient in the first instance (3 marks)

Steroids, e.g. methylprednisolone 1mg/kg/day with allopurinol, gastro and bone protection
Consider empirical ivermectin if relevant travel history
ECG, Echocardiogram (?pericardial effusion)
Serum tryptase
Others – stool for parasites, autoantibody screens etc

Question 4: A two year old boy presents generally unwell with a fever that has not responded to antibiotics. Hb 42, WBC 260.

- Report the blood film (3 marks)

Thrombocytopenia
Red cells unremarkable
Neutropenia
Majority of nucleated cells are blasts – small to medium sized, very high NC ratio, nucleoli.

- Immunophenotyping of the peripheral blood was reported as follows: CD19+, CD79a+, CD9+, HLA-DR+, TdT+, CD13-, CD33-, CD10-, CD20-, CD34-. What is the diagnosis? (3 marks)

Pro-B Cell Acute Lymphoblastic Leukaemia

- Fluorescent in situ hybridisation (FISH) of the peripheral blood identified re-arrangement of KMT2A (MLL) (11q23). Give four examples of high/poor risk stratifying features in this patient's illness (4 marks)

Age >40/55/65
WBC >30 (B-ALL) or >100 (T-ALL)
>4 weeks to reach CR
t(9;22) BCR-ABL1 (Philidelphia chromosome, "Ph+")
t(1;19) *PBX-E2A*
t(4;11) *MLL-AFA4*
Hypodiploidy (e.g. del(6q), del(7p), del(17p), -7)
NOTCH1 unmutated
Complex Karyotype (5 or more clonal abnormalities)

Question 5: An 80 year old gentleman attending the renal low clearance clinic. The blood film has been examined previously and shown similar findings. WBC 3.4, Hb 121

- Report the blood film (3 marks)

Platelets clumped
Red cell anisopoikilocytosis, elliptocytes, echinocytes
Normal white cells

- State the likely diagnosis and the site of the causative red cell defect (3 marks)

Hereditary elliptocytosis
Glycophorin 4.1 complex within red cell membrane

- Briefly describe two potentially diagnostic tests for this group of red cell disorders (5 marks)

SDS-PAGE - Sodium dodecyl sulfate-polyacrylamide gel electrophoresis
Gel electrophoresis of red cell membrane proteins
Identifies and quantifies membrane contents
HE & HPP --> Reduced protein 4.2 (and reduced a-spectrin in HPP)
Eosin-5-Maleimide (EMA) Binding Test
Fluorescent test using flow cytometry
Reference ranges need to be established within each laboratory
Band 3 is the main binding site for EMA --> HS cells will show reduced binding
i.e. normal ratio seen in HE
Also: Osmotic fragility test, Acid glycerol lysis time, Osmotic deformability test

Question 6: A six year old child presents to the emergency department with a three day history of fever, lethargy, back pain and jaundice. She had recently recovered from an upper respiratory tract infection.

- Report the blood film (3 marks)

Normal platelets
Red cell spherocytosis, polychromasia, NRBC
Neutrophil leucocytosis. Myelocytes

- Further results: Bilirubin 60. Blood group O Rh D positive. Direct antiglobulin test – IgG 4+, C3d 2+. List the differential diagnosis (3 marks)

Autoimmune haemolytic anaemia (warm / mixed)
Paroxysmal cold haemoglobinuria
Delayed haemolytic transfusion reaction

- Describe the principles of the Donath-Landsteiner test (5 marks)

Principle: Biphasic IgG anti-P antibody binding at low temp but causing complement lysis as temperature rises.
Method: Patient serum sample left to clot at 37 degrees
Pt serum : 50% suspension of washed O P+ red cells in a ratio of 9:1
Chill at 0 degrees for one hour. Then 37 degrees for 30 minutes
Centrifuge and examine for lysis – presence of lysis positive for D-L antibodies
Use positive and negative controls

Question 7: A 64 year old man is referred by his GP with a four month history of progressive lethargy and easy bruising. WBC 2.6, Hb 98, Plt 57.

- Report the bone marrow aspirate. A quantified differential is not required. (5 marks)

Particulate, hypercellular bone marrow aspirate.
Granulopoeisis is left-shifted with increased numbers of blasts/promonocytes. These are medium to large cells, many with bilobed or cleft nuceli, fine nucelar chromatin and prominent nucleoli.
Dyserythropoeisis – bilobed forms, ragged cytoplasm
Megakaryocyte dysplasia – separation of nuclear lobes
Conclusion: Trilineage dysplasia. MDS or Acute leukaemia depending on blast percentage

- Subsequent results: Flow cytometry identified myeloid blasts in this bone marrow aspirate. List a typical immunophenotype that might be expected for myeloid blasts (3 marks)

CD34+, HLA-DR+ (immature markers)
CD13+, CD33+, CD117+ (myeloid markers)
CD10-, CD20-, CD2-, CD3- (example negative lymphoid markers)

- List the additional tests you would request on this bone marrow biopsy, and very briefly justify each (4 marks)

FISH – exclude specific re-arrangements, e.g. t(15;17), and to assess for dysplasia
Molecular – prognostication, therapeutic options e.g. FLT3 mutation status & identification of marker of measurable residual disease (MRD)
Karyotype – prognostication
Trephine – alternative method for blast % and immunohistochemistry (not essential).

Question 8: A 25 year old presents to the emergency department with severe, bilateral leg pain. Hb 60, Plt 500, WBC 12

- Report the blood film (3 marks)

Thrombocytosis
Red cell anisopoikilocytosis, sickle cells, polychromasia, NRBC, Howell jolly bodies
Mild neutrophil leukocytosis

- State the likely diagnosis and the pathogenic mutation responsible (3 marks)

Sickle cell anaemia, HbSS. Point mutation in Beta globin gene. (A for C at codon 6)

- The patient's haemoglobin is 20g/l below normal baseline and decision is made to offer top up red cell transfusion. State the preferred red cell specification for transfusion of this patient (5 marks)

ABO, full Rh and Kell matched, HbS negative, <10 days old, crossmatch compatible at 37 degrees.

Question 9: An 85 year old is admitted to critical care with acute kidney injury and sepsis of presumed urinary tract source. Hb 97, WBC 23, Plt 133, Cr 500

- Report the bone marrow aspirate. A quantified differential is not required. (5 marks)

Particulate, hypercellular bone marrow aspirate
Trilineage haematopoesis present
Plasma cell numbers increased. Some atypical forms, e.g. bi-lobed

- State the remaining tests you would request to complete this patient's initial workup (3 marks)

Bone profile (calcium), serum protein electrophoresis, serum free light chains
Beta-2-microglobulin, Albumin (ISS Staging)
Skeletal survey (CT/MRI/PET-CT)
Immunophenotyping, cytogenetics, trephine histology
(Other suitable answers that come to mind: Urine culture, Urinary ACR, Urinary bence jones protein, LDH, USS renal tract, Congo red staining)

- Give one example each from the standard risk and high risk cytogenetic risk groups (2 marks)

Standard – t(11;14), t(6;14), Hyperdiploidy
High – t(4;14), t(14;16), t(14;20), 17p-, 1p-, 1q+

Question 10: A 67 year old man attends clinic and reports worsening breathlessness and feeling dizzy on standing. Hb 67, WBC 137

- Report the blood film (3 marks)

Thrombocytopenia
Red cell anisocytosis
Leukocytosis. Small, mature lymphocytes with clumped nuclear chromatin. Smear cells

- Immunophenotyping of this peripheral blood sample is as follows: CD5+, CD23+, CD43+, CD200+, FMC7-, Cyclin D1-, CD2-, CD3-. State the additional tests you would arrange prior to starting treatment for this patient (5 marks)

Reitc, DAT, U&E, LFT, Immunoglobulins, Hep B/C, HIV
CT Staging
BM biopsy, inc. molecular + cytogenetics: specifically TP53 mutation status, IGHV mutation

- State the potential indications for starting treatment in patients with this condition (5 marks)

Lymphocyte doubling time <6 months (provided starting Lymph count >30)
Lymphocyte count increased >50% in 2 months
Progressive marrow failure
Massive (>6cm below costal margin) splenomegaly
Massive (>10cm) lymph nodes
Autoimmune anaemia / thrombocytopenia not controlled by standard therapy
Constitutional symptoms: Wt loss >10% in 6 months, fatigue (PS 2 or worse), Fever >38 for 2 wks, night sweats for >1 month.

Question 11: A 75 year old presents with a 6 month history of weight loss, early satiety and recurrent infections. His spleen is palpable 7cm below the costal margin. WBC 36, Hb 128, Plt 84, Neut 27, Monocytes 7.9

- Report the blood film (3 marks)

Thrombocytopenia, plt anisocytosis
Red cell acanthocytes
Leukocytosis. Left shifted, toxic, dysplastic neutrophils. Monocytosis, atypical forms.

- List your differential diagnosis (3 marks)

MDS/MPN Overlap syndrome – e.g. CMML
MDS
Drug effect – e.g. GCSF + chemotherapy

- State the WHO 2016 criteria for a diagnosis of chronic myelomonocytic leukaemia (3 marks)

Persistent peripheral blood monocytosis (>1x10e9/l), with monocytes >10% of WBC
<20% blasts (myeloblasts, monoblasts and promonocytes) in PB and BM
Dysplasia in one or more lineages (can be absent if other criteria are met)
Not meeting the criteria for CML, Myelofibrosis, PV or ET
(If eosinophilia present, exclude PDGFRA, PDGFRB or FGFR1 rearrangements or PCM1-JAK2)

Or: the monocytosis has persisted for minimum of 3 months and all other causes of monocytosis excluded

(Additional: Flow of PB shows the subset of classical monocytes (CD14+,CD16-) is >94% of total monocytes)

Question 12: 66 year old man referred to clinic after a recent hospital admission with severe pneumonia and prolonged recovery post-discharge. WBC 1.7, Hb 91, Monocytes 0.06

- Report the blood film (3 marks)

Thrombocytopenia
Red cell tear drops. Occasional NRBC
Neutropenia. Monocytopenia. Lymphocytes with increased volume of granular cytoplasm.

- Immunophenotyping of the abnormal cell population is as follows: CD19+, CD20+, CD11c+, CD25+, CD103+, CD5-, CD23-, CD38-. What genetic mutation would be expected to be detected? (2 marks)

BRAF V600E

- Summarise your first line management of this patient (3 marks)

Chemotherapy: Purine analogues, e.g. cladribine or pentostatin
Supportive: Requires irradiated blood products. Aciclovir + Co-trimoxazole prophylaxis