eha

Case 1

eha

65 year old male

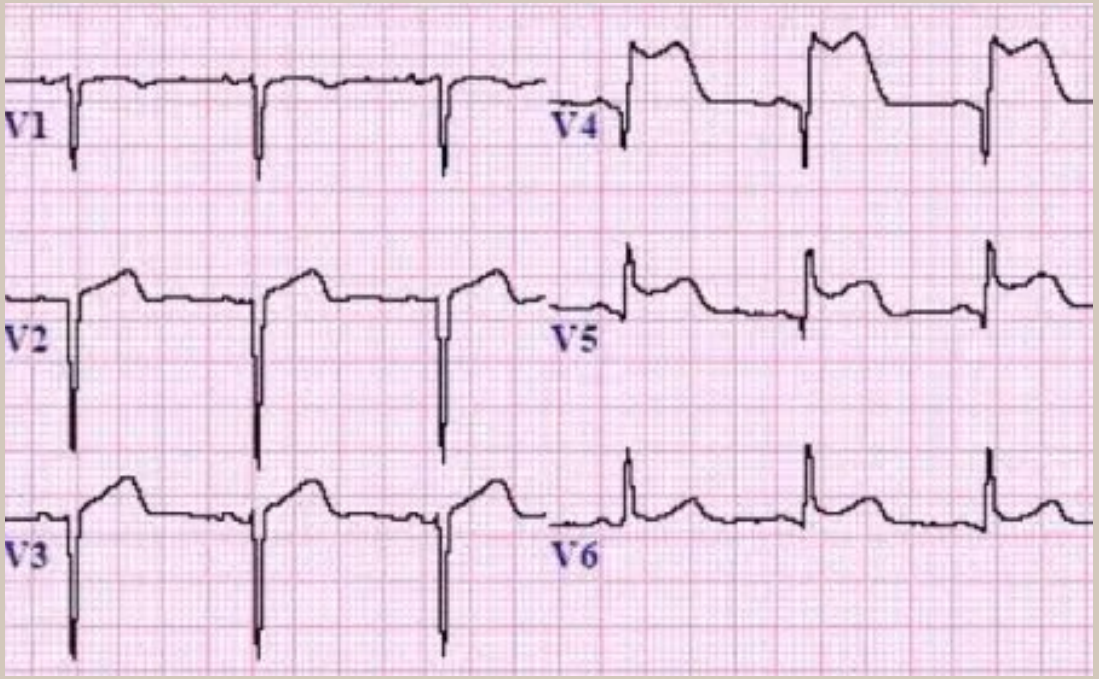
- Presented to A&E with central chest pain
- Radiation to back and shortness of breath

Past medical history: Hypertension, autoimmune thyroiditis, severe depression

Medication: amlodipine, levothyroxine

Social history: Non-smoker; no excess alcohol consumption

On examination: Spleen palpable 3cm below costal margin



Dr P. Harrington, GSTT

eha

Investigations:

FBC: Hb 184 g/L, MCV 88, HCT 58%, WBC 14.2x10^9/L, Neut 12.1x10^9/L, Pt 1223x10^9/L

Blood film: Packed with increased red cells, marked thrombocytosis, confirmed with large platelet aggregates, normal maturation to neutrophils

JAK2 **V617F:** Detected, variant allele frequency 64%

Ultrasound abdomen: spleen 16.6cm in maximal diameters

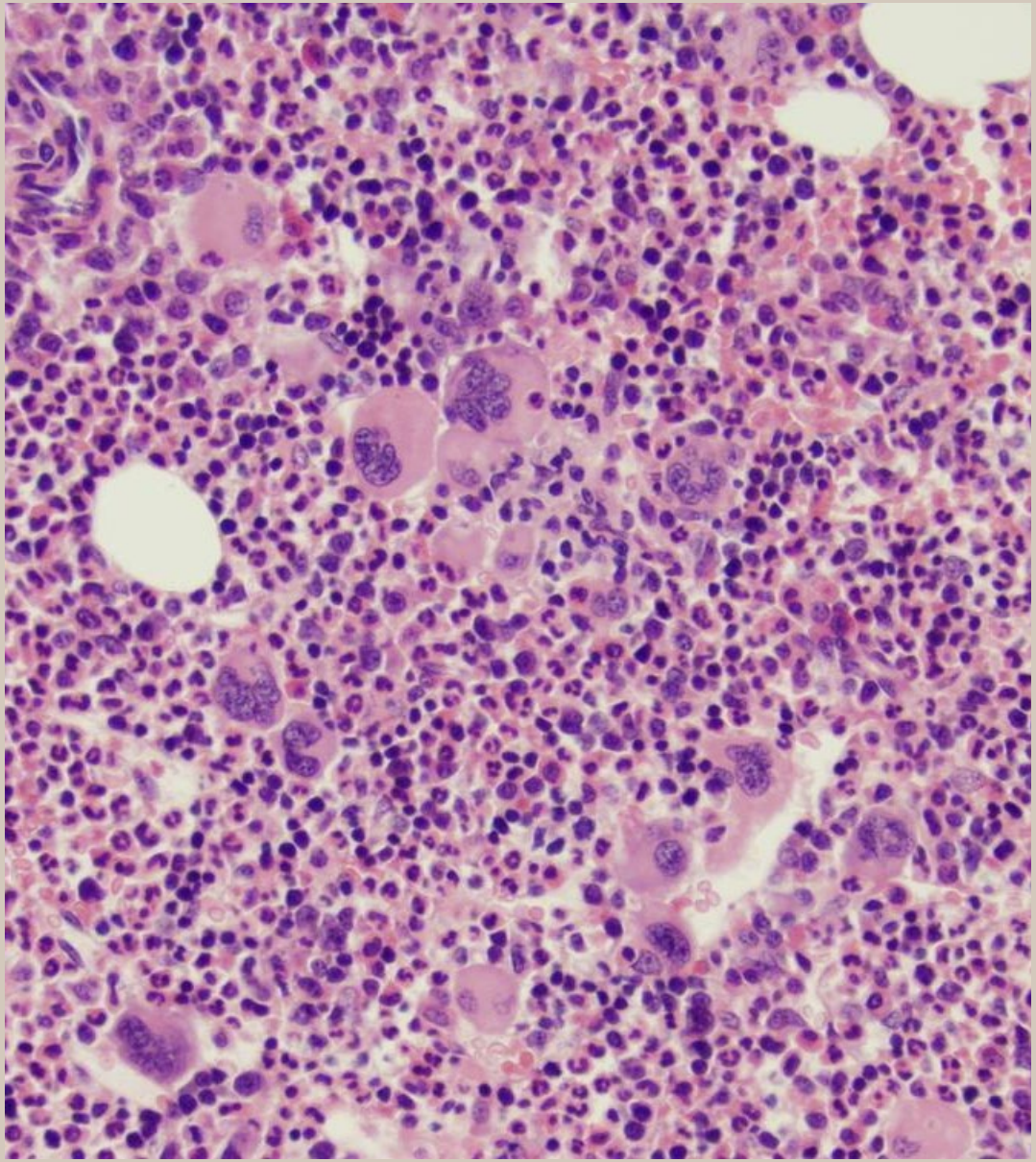
Bone marrow Trephine:

Hypercellular marrow with 90% cellularity

Expanded erythroid series, panmyelosis.

Megakaryocytes appear increased and mature without atypical features

No increase in precursors



October 2024, Dr P. Harrington GSTT

eha

Question 1: What is the likely Diagnosis?

a. Chronic myeloid leukemia

b. Essential Thrombocythemia

c. Polycythemia vera

d. Primary myelofibrosis

e. Post ET myelofibrosis

eha

Question 1: What is the likely Diagnosis?

a. Chronic myeloid leukemia

b. Essential Thrombocythemia

c. Polycythemia vera

d. Primary myelofibrosis

e. Post ET myelofibrosis

eha

Question 2: Diagnostic Criteria for PV

Which of the following is major criterion as per WHO 5th Edition 2022?

a. *CALR* mutation

b. Subnormal Epo level

c. Megakaryocyte atypia

d. Elevated Hb >160g/l

e. *JAK2* exon 12 mutation

eha

Question 2: Diagnostic Criteria for PV

Which of the following is major criterion as per WHO 5th Edition 2022?

a. *CALR* mutation

b. Subnormal Epo level

c. Megakaryocyte atypia

d. Elevated Hb >160g/l

e. *JAK2* exon 12 mutation

eha

Management:

Patient taken for urgent PCI

Dual antiplatelet therapy initiated with aspirin and ticagrelor

Diagnosis of PV confirmed

WHO 2022[1]
Major criteria: • Elevated Hb (>16.5 g/dL in males; >16.0 g/dL in females) or elevated HCT (>49% in males; >48% in females) • BM biopsy: hypercellularity with trilineage grown (panmyelosis), including erythroid, granulocytic and megakaryocytic proliferation with pleomorphic, mature megakaryocytes • *JAK2* or *JAK2* exon 12 mutation **Minor:** • Subnormal EPO level

eha

Question 3: What is appropriate initial management?

a. Pegylated interferon alpha

b. Hydroxycarbamide

c. Ruxolitinib

d. Plateletpheresis

e. Imatinib

eha

Question 3: What is appropriate initial management?

a. Pegylated interferon alpha

b. Hydroxycarbamide

c. Ruxolitinib

d. Plateletpheresis

e. Imatinib

eha

Clinical course:

After 12 months: Established on hydroxycarbamide, 2g OD.

Full recovery from anterior MI, cardiac function normalized.

Ongoing requirement for venesection, 450ml, every 2 months to maintain HCT <0.45%

Development of leg ulcers, not responsive to medical management

MI, myocardial infarction

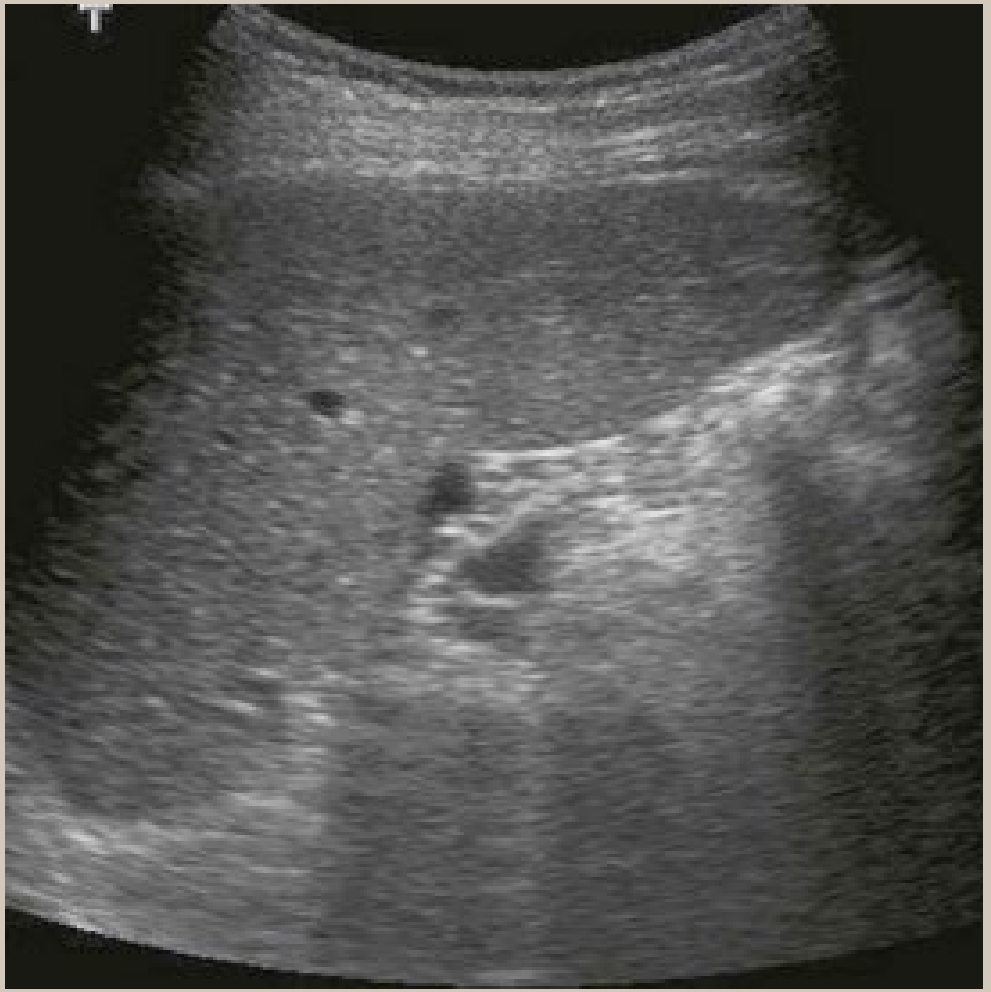
eha

Investigations:

FBC: HB 154 g/l , MCV 87, HCT 48%, WBC 11.4 x10^9/l, Plt 460 x10^9/l

JAK2 **V617F:** Variant allele frequency 74%

US abdomen: spleen increased in size, 19.4cm maximal diameter



US, ultrasound

eha

Question 4: What are the features of hydroxycarbamide resistance

ELN Consensus Criteria:

After >3 months at maximal tolerated dose or dosage of 2000mg/day

a. Development of leg ulcers

b. Platelet >600 $x10^9/l$

c. HCT >0.5%

d. White cell count >10 $x10^9/l$

eha

Question 4: What are the features of hydroxycarbamide resistance

ELN Consensus Criteria:

After >3 months at maximal tolerated dose or dosage of 2000mg/day

a. Development of leg ulcers

b. Platelet >600 $x10^9/l$

c. HCT >0.5%

d. White cell count >10 $x10^9/l$

eha

Question 5: What is the most appropriate second line management?

a. Continue Hydroxycarbamide

b. Pegylated interferon alpha

c. Ruxolitinib

d. Rusfertide

e. Allogeneic stem cell transplantation

eha

Question 5: What is the most appropriate second line management?

a. Continue Hydroxycarbamide

b. Pegylated interferon alpha

c. Ruxolitinib

d. Rusfertide

e. Allogeneic stem cell transplantation

eha

Clinical course:

Patient started on ruxolitinib, 10mg twice daily.

After 12 months: No further venesection required

Gradual healing of leg ulcers observed

Annual screening for increased risk of non-melanomatous skin cancer

Annual vaccines to include: Covid-19, seasonal flu, varicella zoster

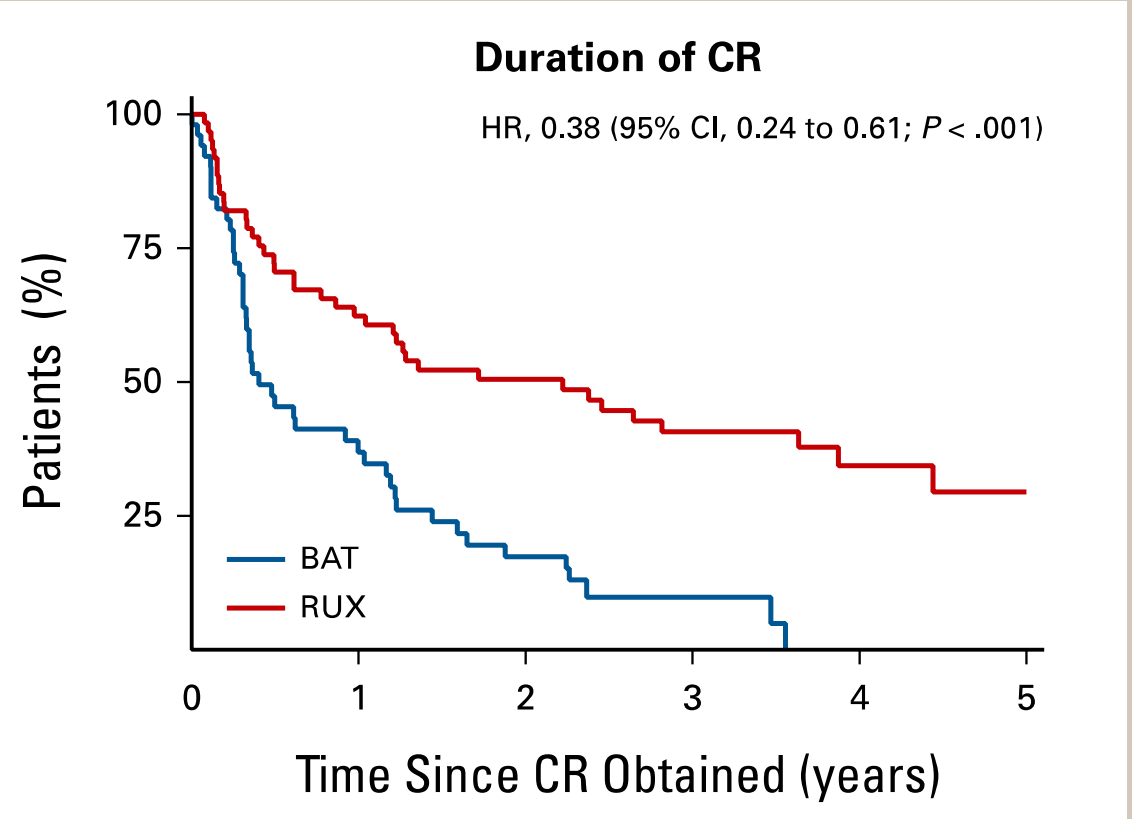
eha

Investigations:

FBC: Hb 110 g/l, HCT 0.39%, WBC 6.7x10^9/l, Neut 3.4x10^9/l, Plt 231x10^9/l

Repeat *JAK2* V617F: 52% VAF

US abdomen - spleen 12.6 cm in maximal diameter (>35% reduction in spleen volume)



eha

Question 6: Which of the following is a high risk feature of PV for myelofibrotic transformation

a. White cell count >15x10^9/l

b. Platelet count >1000x10^9/l

c. Lower *JAK2* V617F VAF

d. Prior Hydroxycarbamide treatment

eha

Question 6: Which of the following is a high risk feature of PV for myelofibrotic transformation

a. White cell count >15x10^9/l

b. Platelet count >1000x10^9/l

c. Lower *JAK2* V617F VAF

d. Prior Hydroxycarbamide treatment

eha

Case 2

eha

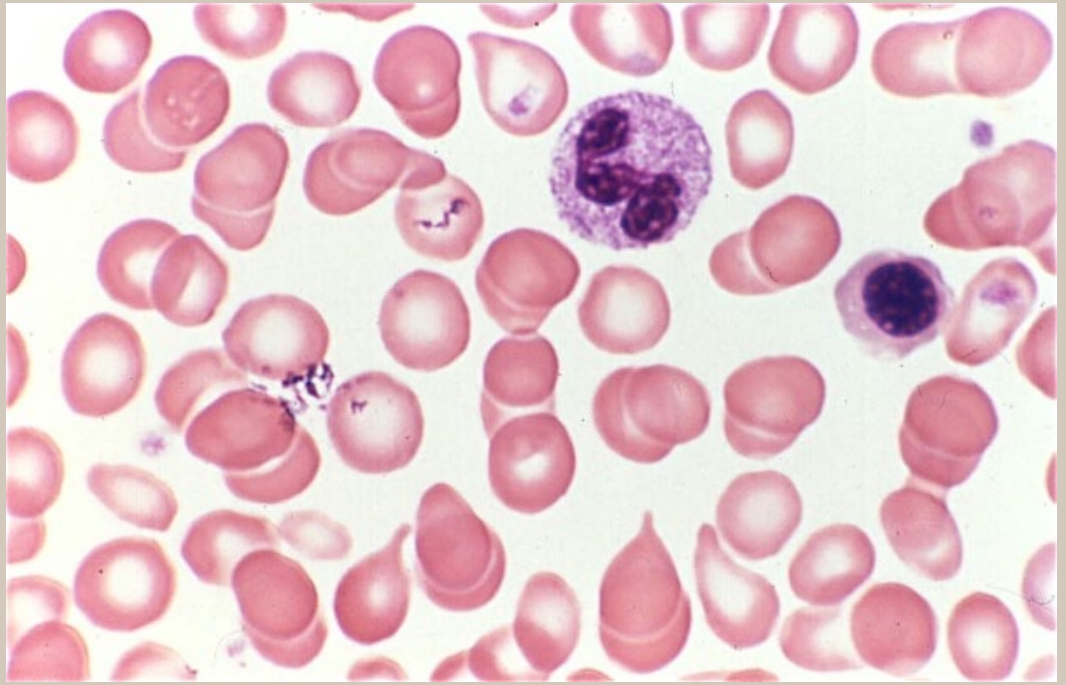
65-year-old woman diagnosed with Essential Thrombocythemia in 2015

CAL-R type 1 identified

No prior history of thrombosis

Management with hydroxycarbamide 500mg OD with complete hematologic response

3 years after diagnosis – seen in clinic complaining of abdominal pain.



Investigations:

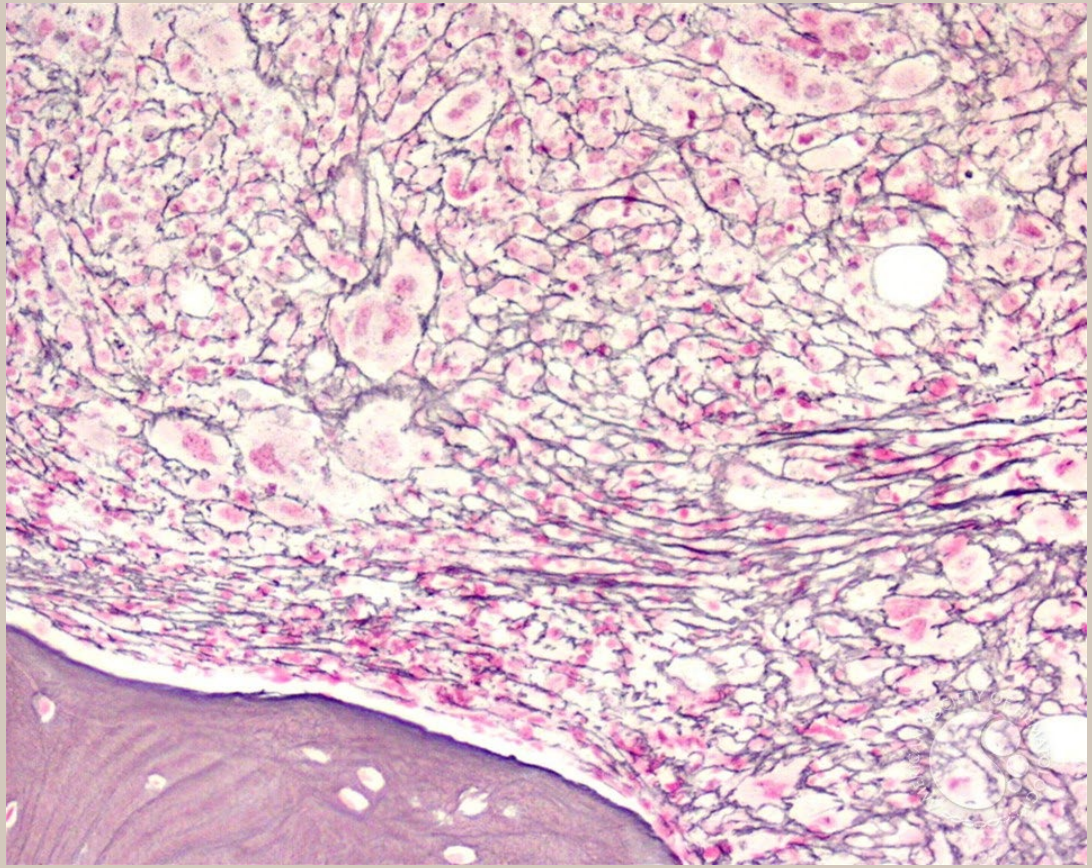
FBC:

Hb 114 g/l, MCV 102 fl, HCT 0.31%, WBC 14.1x10^9/l, Plt 120x10^9/l

Bone marrow biopsy: extensive fibrosis with clustered megakaryocytes

Reticulin stain shows grade 3 fibrosis

US abdomen: spleen 21cm in maximal diameter



eha

Question 1: Which of the following is associated with increased risk of myelofibrotic progression in ET?

a. *CALR* type 2

b. *JAK2* VAF >30%

c. *MPL*

d. Female sex

e. Age >50 years

eha

Question 1: Which of the following is associated with increased risk of myelofibrotic progression in ET?

a. *CALR* type 2

b. *JAK2* VAF >30%

c. *MPL*

d. Female sex

e. Age >50 years

eha

Question 2: Which of the following is a major or minor criteria for post ET myelofibrosis?

a. Platelet >1500x10^9/l

b. Increased serum lactate dehydrogenase

c. WBC >10x10^9/l

d. *JAK2* VAF >35%

e. Dysplastic blood film

eha

Question 2: Which of the following is a major or minor criteria for post ET myelofibrosis?

a. Platelet >1500

b. Increased serum lactate dehydrogenase

c. WBC >10x10^9/l

d. *JAK2* VAF >35%

e. Dysplastic blood film

Clinical Course:

DIPPS plus: Intermediate 1

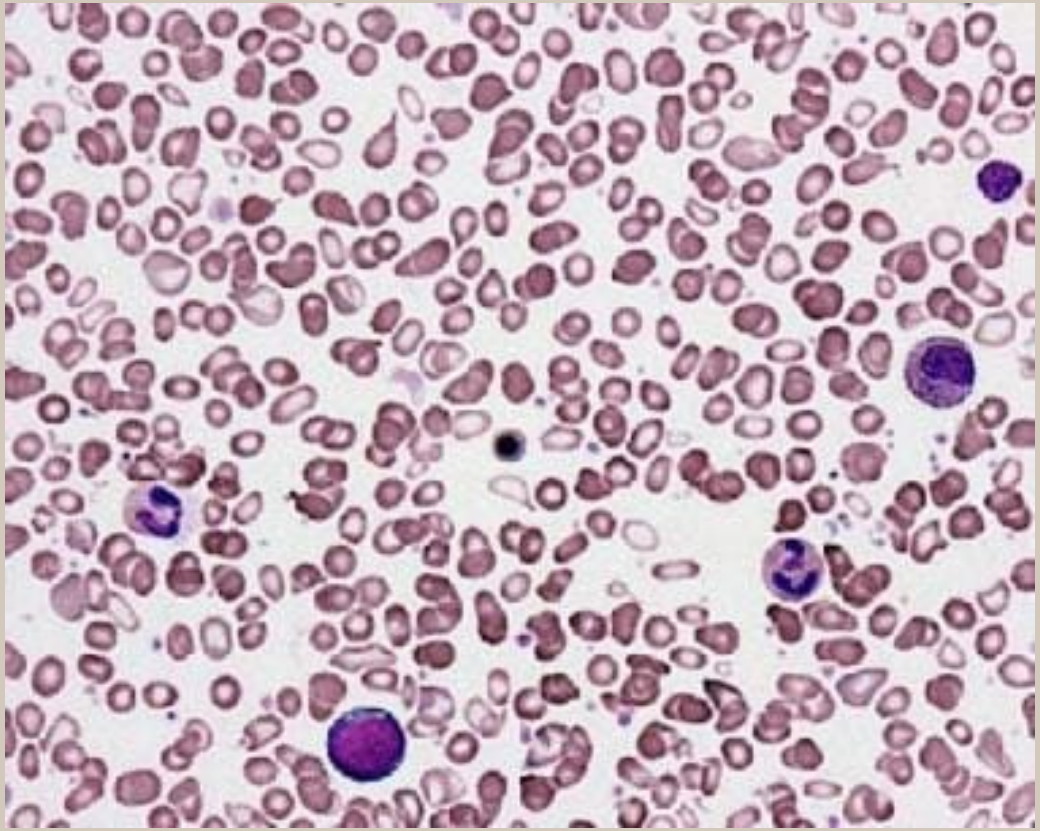
Management: active surveillance

Close monitoring with clinic review every 3 months

Ongoing symptom burden from splenomegaly – spleen now 24cm

MPN 10 TSS: 42

Repeat blood film: myeloid blasts: 2%



October 2024, Dr P. Harrington GSTT

eha

Question 3: Which of the following is an adverse risk factor in the DIPPS Plus prognostic score?

a. Age >60

b. WBC >20x10^9/l

c. Platelets <100x10^9/l

d. +9 on cytogenetics

e. ASXL1 mutation

eha

Question 3: Which of the following is an adverse risk factor in the DIPPS Plus prognostic score?

a. Age >60

b. WBC >20x10^9/l

c. Platelets <100x10^9/l

d. +9 on cytogenetics

e. ASXL1 mutation

eha

Question 4: Most appropriate treatment option at this point?

a. Hydroxycarbamide

b. Pegylated interferon

c. Splenectomy

d. Allogeneic stem cell transplantation

e. Ruxolitinib

eha

Question 4: Most appropriate treatment option at this point?

a. Hydroxycarbamide

b. Pegylated interferon

c. Splenectomy

d. Allogeneic stem cell transplantation

e. Ruxolitinib

eha

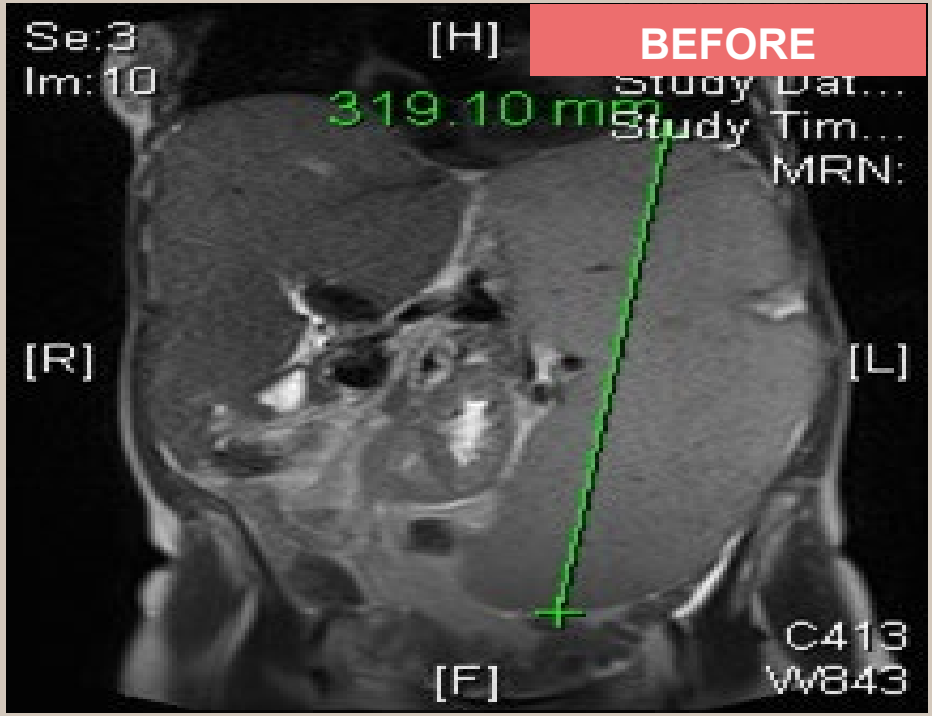
Clinical Course

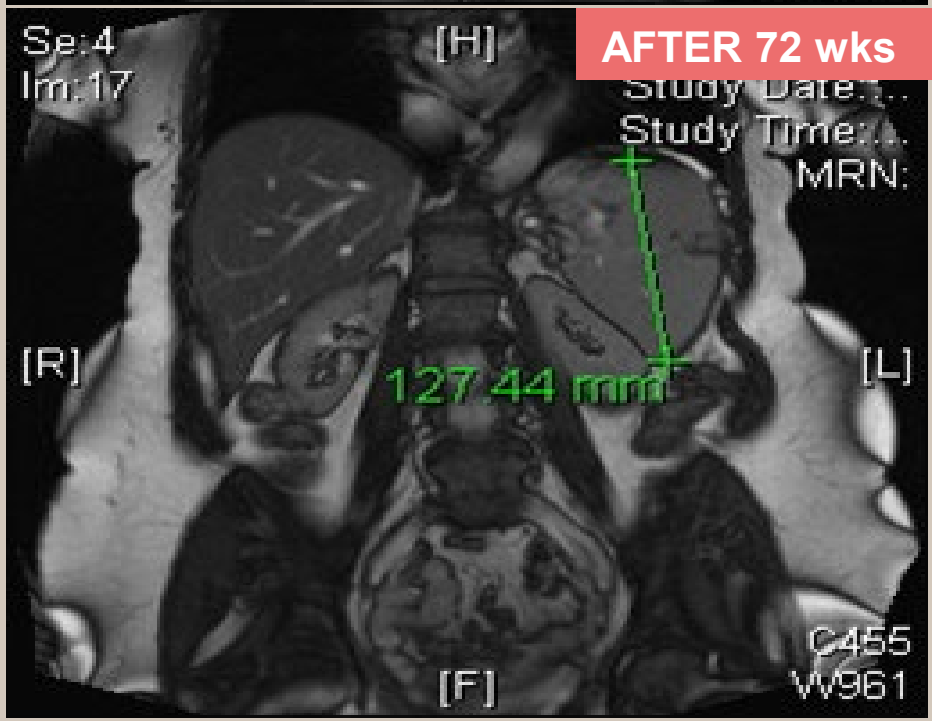
Patient started ruxolitinib 15mg twice daily

Dose up-titrated to maximal dose of 25mg BD

After 12 months: Spleen reduced to 12.7cm

MPN-10 TSS: 18





eha

Investigations

FBC: Hb 82g/l, MCV 81 fl, WBC 16.1x10^9/l, Neut 12.3x10^9/l, Plt 125x10^9/l

Blood film: 1% blasts

Serum Epo: 520 IU/L

Myeloid gene panel analysed: no additional mutations

MIPPS 70 v2 score: Low Risk

MPN 10 TSS: 28

rHuEPo added and uptitrated to 40,000 IU weekly

eha

Question 5: Which of the following is an adverse risk factor in the MIPPS 70 plus version 2 prognostic score?

a. Age >60

b. WCC >20x10^9/l

c. Blasts >1%

d. Absence of *CALR* type 1

e. U2AF1 s34 mutation

eha

Question 5: Which of the following is an adverse risk factor in the MIPPS 70 plus version 2 prognostic score?

a. Age >60

b. WCC >20x10^9/l

c. Blasts >1%

d. Absence of *CALR* type 1

e. U2AF1 s34 mutation

eha

Question 6: What is the most appropriate treatment option at this point

a. Fedratinib

b. Ruxolitinib and danazol

c. Increased dosage rHuEpo

d. Momelotinib

e. Allogeneic stem cell transplant

eha

Question 6: What is the most appropriate treatment option at this point

a. Fedratinib

b. Ruxolitinib and danazol

c. Increased dosage rHuEpo

d. Momelotinib

e. Allogeneic stem cell transplant

eha

Clinical Course

Momelotinib started 200mg OD

After 3 months:

FBC: Hb 108 g/l, MCV 81 fl, WBC 12.3x10^9/l, Plt 623x10^9/l

No further PRC transfusion required.

Notable improvement in fatigue

MPN 10 TSS: 16

rHuEpo reduced and discontinued 6 months following initiation

eha

Clinical Course

Patient developed heightened sensation and paraesthesia in stocking distribution

Nerve conduction studies confirmed axonal peripheral neuropathy

Momelotinib dosage reduced to 150mg daily

Hematologic response maintained with no PRC transfusion requirements

Notable reduction in peripheral neuropathy with dose modification burden