Self- assessment Case History

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Disclosures: Nothing to Disclose

Learning objectives, at the end of the presentation -

the candidate should be familiar with

1. Clinical approach to isolated thrombocytopenia
2. How to diagnose hypersplenism
3. When to suspect MDS as a cause for cytopenia
4. The need for bone marrow study in cytopenia

49-year-male, asymptomatic, doing heavy manual work

- Surgery for varicose veins planned
- Routine blood tests revealed low platelet counts
- No other comorbidities, never been a smoker or alcoholic
- Did not have any significant illnesses in the past
- Referred for isolated thrombocytopenia -56 $\times 10^9$/l
- Hb – 128 g/l, WBC 4.67 $\times 10^9$/l (N-70, L-16, M-10, E2), ESR 20 mm, MCV 97 fl

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For each question you have 15 seconds.

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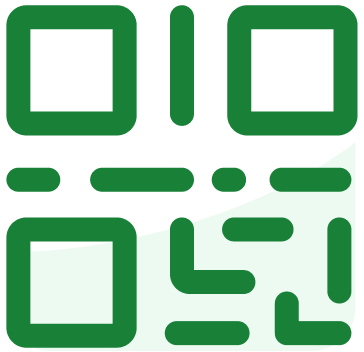

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Which is the most probable cause for the low platelet count in such a person?

a) Acute autoimmune thrombocytopenia (ITP)

b) Acute leukaemia

c) B12/folic acid deficiency

d) Liver disease

e) Myelodysplastic syndrome (MDS)

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3.31 Which is the most probable cause for the low platelet count in such a person?

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49-year-old male -Isolated thrombocytopenia

- Physical examination – overweight, body mass index (BMI) of **27.3 Kg/m^2**
- Looked healthy, with no pallor/icterus/lymphadenopathy/oedema
- Varicose veins +, No signs of chronic liver disease
- Moderate splenomegaly and mild firm hepatomegaly detected
- These were not detected during the previous evaluation
- Other systems normal

Give one most likely cause of low platelet count in this situation

a) Chronic ITP

b) Myelofibrosis

c) Pseudo thrombocytopenia

d) Hypersplenism

e) Myelodysplastic syndrome (MDS)

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3.32 Give one most likely cause of low platelet count in this situation:

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- Acute ITP is a problem of children, different clinical setting
- Acute leukemia clinical presentation, complete hemogram will be different
- Do not consider MDS if splenomegaly present, it is a diagnosis of exclusion
- Do not consider chronic ITP when there is organomegaly
- Strong possibility of liver disease + hypersplenism - if firm liver and spleen
- Pseudo-thrombocytopenia - possible but not in this scenario

Initial Investigations

- Random blood sugar- 160mg/dL, HbA1c – 6 %
- Hb – 129 g/l, (12.9g/dL): WBC 4.99 $\times 10^9$/l (N70, L16, M10, E2),
- Platelets 46 $\times 10^9$/l, MCV 98 fl, RDW 13.4%,
- Alanine aminotransferase (ALT)43 IU/l (<40);
- Aspartate amino transferase (AST) 40 IU/l (<40),
- Albumin/globulin-3.7/3.6 , ALP-Normal

Diagnosis at this stage was

Portal hypertension, hypersplenism

Chronic liver disease

Chronic active hepatitis – elevated liver enzymes

Non-alcoholic fatty liver disease in view of high BMI

Type 2 diabetes

What could be the cause for high MCV in this sceneario (98 fl)?

a) Folic acid deficiency

b) B12 deficiency

c) Liver disease

d) Hemolysis

e) All the above

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3.33 What could be the cause for high MCV in this sceneario (98 fl)?

ⓘ Start presenting to display the poll results on this slide.

He was given tips on weight reduction, After 5 Kg weight reduction - liver enzymes normalized, sugar normalized

Platelet remained low

- On follow up after a year, he had developed pancytopenia
- Hb 90 g/l (9 g/dL), WBC 3.6 $\times 10^9$/l
- Platelet count 50 $\times 10^9$/l
- Direct Coombs test negative - Reticulocyte count was 3%

What is your most appropriate clinical diagnosis at this stage?

a) Aplastic anaemia
b) MDS
c) Myelofibrosis
d) Hypersplenism
e) B12 deficiency

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3.34 What is your most appropriate clinical diagnosis at this stage?

ⓘ Start presenting to display the poll results on this slide.

- Do not entertain aplastic anemia and MDS when there is splenomegaly
- Myelofibrosis - possible if there is no evidence of hypersplenism and bone marrow shows fibrosis
- B12 deficiency cannot explain other findings in the patient, there is evidence of liver disease
- Is a bone marrow study indicated or not?

Bone marrow study is to look for which abnormality?

a) Myelofibrosis

b) Infiltrative disorders

c) Tuberculosis or leishmaniasis (LD bodies)

d) Features of MDS

e) All the above

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3.35 Bone marrow study is to look for which abnormality?

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Other investigations

- Bone marrow trephine biopsy - reported as normal
- Ultrasound (USG) of abdomen - moderate splenomegaly and coarsening of hepatic echoes
- Upper gastrointestinal (GI) endoscopy showed grade 3 oesophageal varices
- Confirmed portal hypertension - hypersplenism

Course of disease

- Referred for splenectomy
- Anaesthetist suggested a repeat haematology consultation
- Underwent a repeat bone marrow study
- It was reported as consistent with MDS

Will you accept MDS as a definite diagnosis in this patient?

Why a diagnosis of MDS is not acceptable?

- Younger age – primary MDS unlikely
- Splenomegaly doesn't fit into primary MDS
- MDS should be a diagnosis of exclusion
- Rule out all causes of cytopenia & suspect MDS as a last possibility
- In that context, a bone marrow report of MDS can be accepted as MDS

What are mimics of MDS?

a) Autoimmune disorders/vasculitic disorders/ SLE

b) Human immunodeficiency virus (HIV) infection

c) B12 deficiency

d) Secondary dysplasia due to neoplasia

e) All the above

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3.36 What are mimics of MDS?

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Course of disease

- After reported as MDS, surgery was cancelled, discharged as MDS.
- In course of time, pancytopenia further worsened
- He came back for review - moderate splenomegaly persisting.
- Hb 92 g/l (9g/dL) , WBC 1.89 $\times 10^9$/l (N57, L40, E3),
- Platelets – 50 $\times 10^9$/l , ESR 4 mm/h

Other Investigations

- Activated partial thromboplastic time (aPTT) 43 sec (normal 31 sec)
- B12 levels normal
- Antinuclear activity (ANA)-profile negative , lupus anticoagulant – negative
- Reticulocyte count - 2% , peripheral film - normal
- Hepatitis B surface antigen, hepatitis C, human immunodeficiency virus1 and 2 – negative,
- Serum ferritin, transferrin saturation were within normal limits
- Alpha fetoprotein – negative.

Course of disease

- Patient & relatives briefed on need for splenectomy, despite diagnosis of MDS
- Splenectomy and splenic histology done on 16/12/2019
- Second post-operative day, Hb went up to123 g/l, haematocrit (HCT 34%)
- WBC was 22.88 × 10^9/l (N57, L40, E3), platelet count -105 x 10^9/l

on 5th post-operative day

Hb - 121 g/l, HCT 34%, WBC 13.76 × 10^9/l (N66, L17, M9), Platelet -260x10^9/l

Course of disease

- Given folic acid and Injection of B12 (cyanocobalamin)
- No treatment on the lines of MDS was given
- Prompt improvement in blood cell counts post-splenectomy
- Favouring a functioning bone marrow - proof against MDS
- The lesson - MDS should be a diagnosis of exclusion
- Bone marrow biopsy is to look for alternative causes of pancytopenia

Comment on the wrong trends

- Gone through at least three doctors initially
- Splenomegaly and firm liver not picked up
- No one had examined the abdomen
- These days history and physical examination are grossly neglected
- Instead, depend on USG abdomen for splenomegaly/hepatomegaly

MDS – When to suspect?

- Above 50 years
- Absence of constitutional symptoms & organomegaly
- Cellular marrow/occasionally hypoplastic
- Dysplastic changes in marrow-- BUT
- Exclude B12 deficiency, infections like HIV/autoimmune disorders/SLE

67 Male Diagnosed as MDS

- On protein pump inhibitor (PPI), metformin x 5 years
- Angina after stressful situation
- Hb 66 g/l (6.6g/dL), WBC 4.5 $\times 10^9$/l, platelet 100 $\times 10^9$/l
- Elective angioplasty was done
- Packed cells before angioplasty
- Dual antiplatelets started

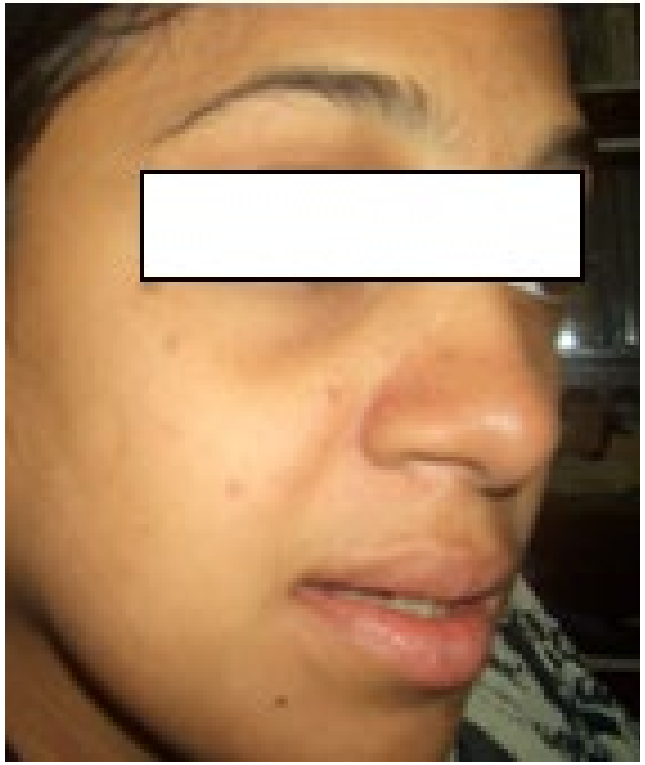
- BM erythroid hyperplasia, dysplastic
- Cytogenetics monosomy 5
- Loss of Y chromosome, confirmed MDS
- Two months after, severe melena
- Hb fell to 35 g/l (3.5g/dL)
- At this point he was brought to us

67 Male -was it MDS ?

- Dietary history - no meat intake, fruits rarely --B12, folate deficiency suspected
- Knuckle hyperpigmentation +, MCV 100fl
- B12 level – 623 pg/ ml(187-883pg/ml)
- Normal levels will not rule out B12 deficiency
- Dysplastic changes are seen in B12 deficiency also
- On injection B12, and folic acid---- Hb 115 g/l, WBC 6.2 $\times 10^9$/l , Plt-167 x10^9/l
- Seven year follow up , still normal on B12, folic acid and proper diet

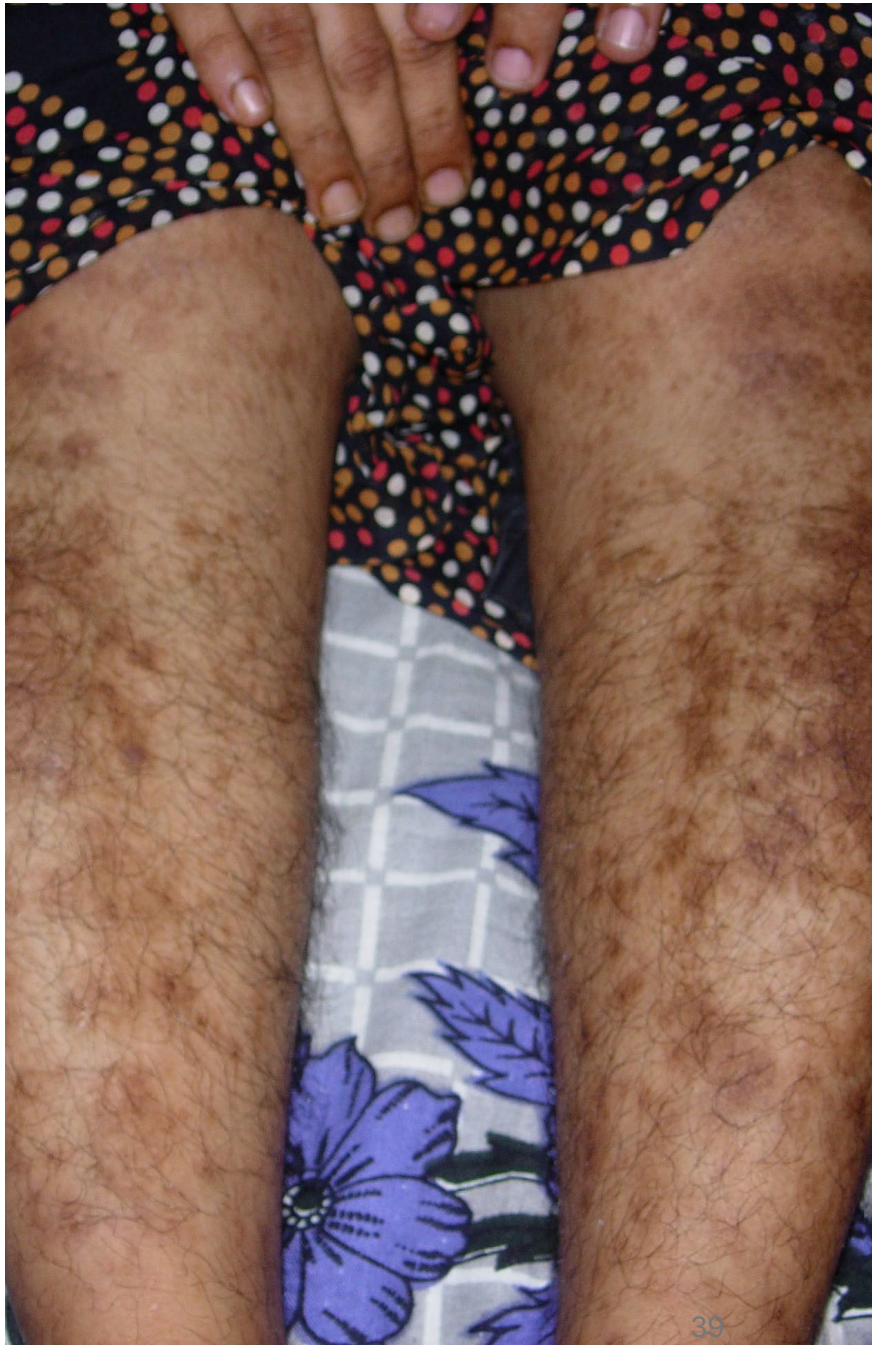
24-year-old female- diagnosed as MDS after BM biopsy

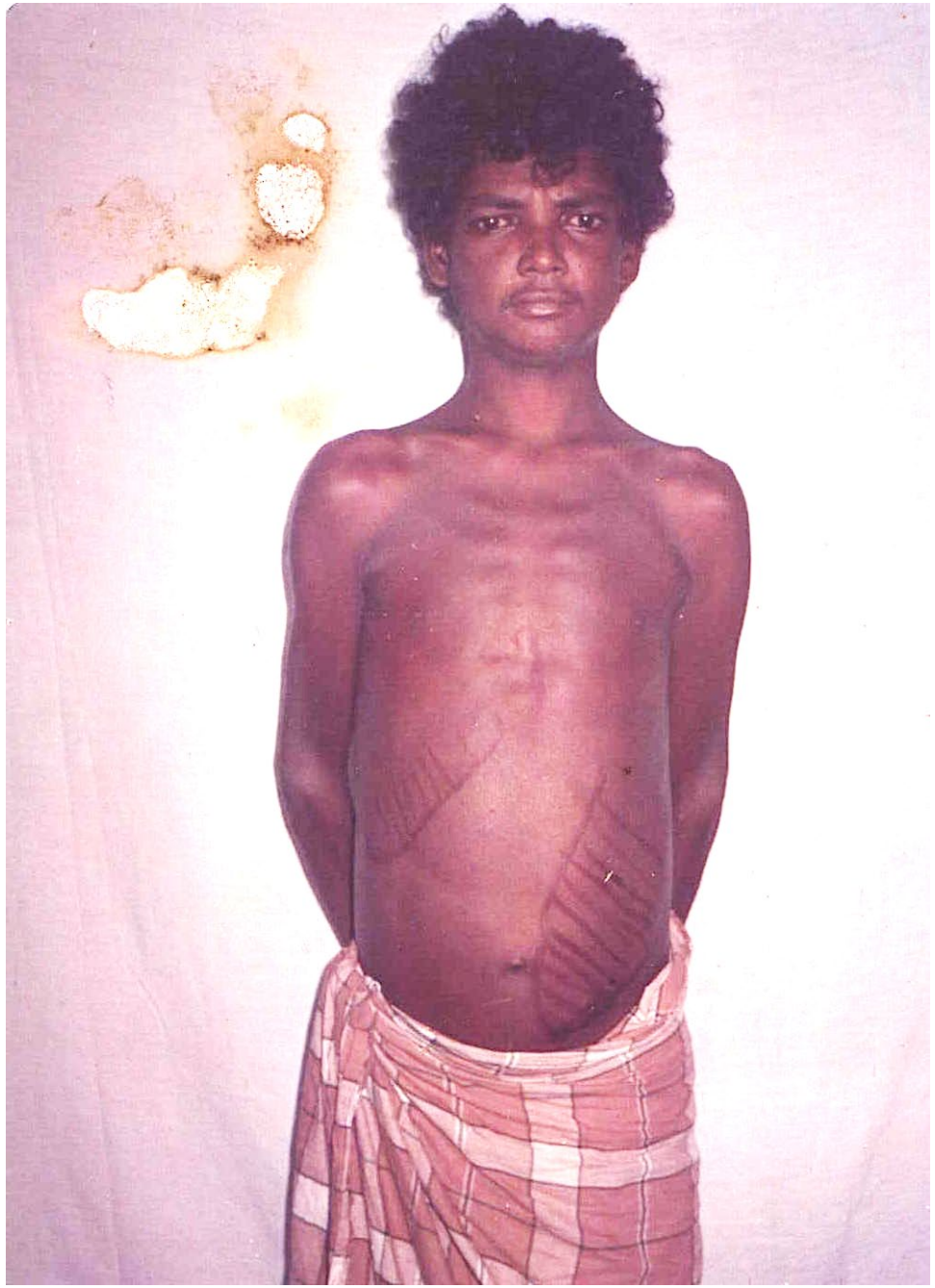
- Recurrent parotitis, dryness of mouth noted
- ESR -120 mm/h, SLE considered
- ANA and anti-double stranded (Ds) DNA were positive
- BM study - not needed here
- Younger individuals – suspect secondary dysplasia



48 F- Splenomegaly& Pancytopenia

- Hypersplenism was the diagnosis
- Hb 42 g/l, WBC 2.4 $\times 10^9$/l
- N60 L40, Platelet 18 $\times 10^9$/l
- Myelofibrosis on bone marrow ? Primary myelofibrosis suspected
- Skin lesions noted – healed vasculitis
- ANA/Anti-Ds DNA positive- SLE





- First Kala Azar in Kerala- 1988
- Pancytopenia and massive spleen
- Diagnosed as portal hypertension- non cirrhotic portal fibrosis (NCPF)
- Bone marrow showed Leishman Donovan bodies