EUROPEAN HEMATOLOGY ASSOCIATION

EHA-TSH Hematology Tutorial on Immune Hematological Disorders

Self-assessment Case – Immune Thrombocytopenia

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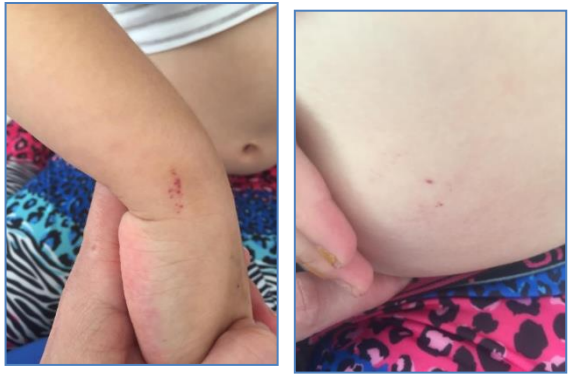
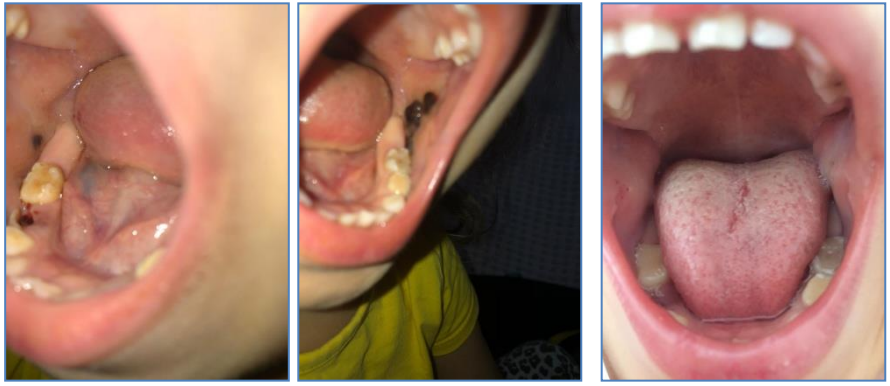
Introduction

- A six-year-old Caucasian girl presented with petechiae in emergency room
- Acute onset symptoms
- Had influenza three weeks before
- No history of fever, loss of weight, night sweats
- Past medical history: unremarkable
- No consanguinity

Physical examination

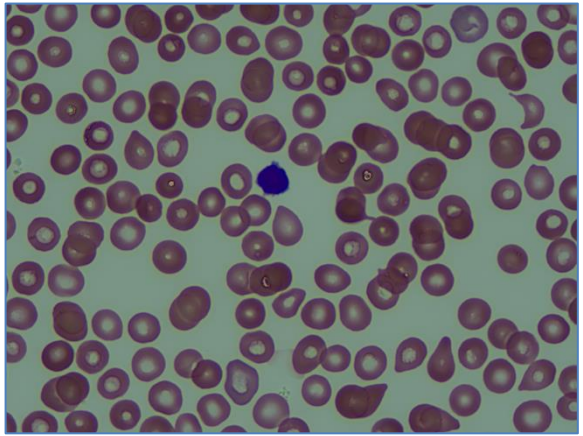
- Organomegaly not present
- Enlarged lymph nodes not detected
- Dysmorphic appearance not detected





Blood count and film

- WBC 5.3 × 10^9/l
- RBC 4.5 × 10^{12}/l
- Hb 130 g/l
- Hct 0.36
- MCV 81.4 fl
- Platelets 3 × 10^9/l



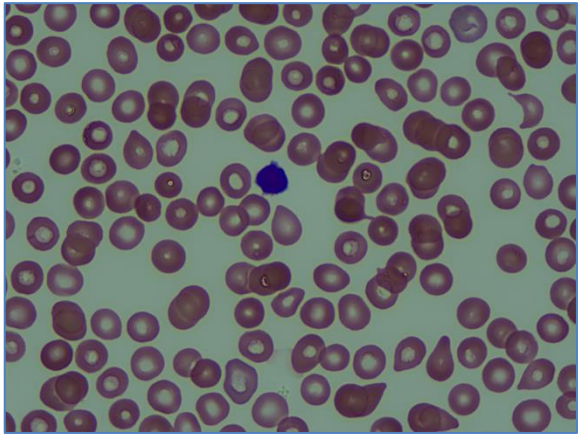
Q1) What is most likely diagnosis?

1. Acute leukemia
2. Immune Thrombocytopenia
3. Hemolytic uremic syndrome
4. Fanconi aplastic anemia
5. Pseudothrombocytopenia

Blood film

The blood film showed

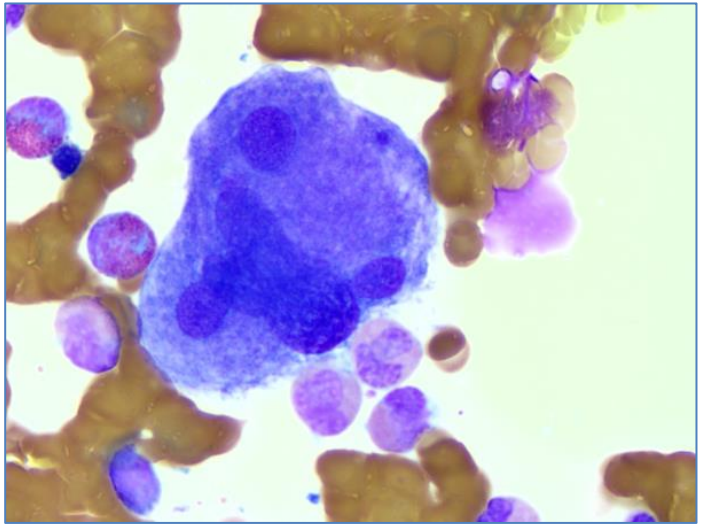
- Normochromic normocytic erythrocytes
- No atypical lymphocytes
- No prominent signs of intravascular hemolysis
- No platelets



Q2)Which of the tests is not required for further investigation?

1. Direct coombs’ test
2. Bone marrow aspiration
3. Viral markers
4. Quantitatives levels of immunoglobulins
5. Anti-platelet antibodies

Bone marrow aspirate



Q3) What do you expect bone marrow aspiration to show?

1. Striking increase in erythropoiesis
2. Aplasia in all lineages
3. Abnormal cytogenetic analysis
4. Clonality
5. Normocellularity without dysplasia, increased/ normal number of megakaryocytes

Treatment

- Steroid was given
  - Platelets 95 × 10^9/l

Q4)It is recommended to use steroids for less then….

1. Seven days
2. Ten days
3. 14 days
4. One month
5. Three months

Follow- up

– Platelets declined: $<10 \times 10^9$/l within one week after steroid therapy

–The patient was hospitalized several times for severe thrombocytopenia and mucosal bleeding

Q5) By definition newly diagnosed ITP covers?

1. The first month from diagnosis
2. The first three months from diagnosis
3. The first six months from diagnosis
4. The first year from diagnosis
5. The two years from diagnosis

Follow-up

- No sustained response to short period of steroids, IVIG, anti Rh immunoglobulin therapies
- Eltrombopag was started
- Methylprednisolone (1-2mg/kg) was continued

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Q6) Eltrombopag is started. The target platelet count is?

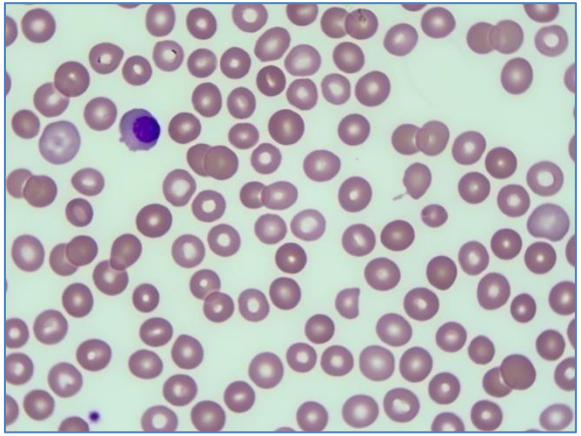
1. $20 \times 10^9/l$
2. $30\text{-}50 \times 10^9/l$
3. $50\text{-}150 \times 10^9/l$
4. $150\text{-}250 \times 10^9/l$
5. $>250 \times 10^9/l$

Follow up

- No response to eltrombopag within one month
- Cessation of eltrombopag

Follow up

- The patient developed Evan's syndrome
- Then she developed Hashimoto thyroiditis
- Double negative T cell ratio was 6%
- Genetic analysis for immune deficiency is being performed



Follow up

- Mycophenolate mofetil was started
- Platelets: 80 × 10^9/l in two weeks
- Platelets: 250 × 10^9/l in four weeks
- Evan's syndrome regressed
- The patient has been taking mycophenolate mofetil for five months
- Methylprednisolone was ceased slowly in three months
- Laboratory results on last visit: Hb: 118 g/l, WBC: 6.0 × 10^9/l, platelets: 560 × 10^9/l

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Discussion

ITP is a diagnosis of exclusion

- Acute leukemia
- Infection
- Autoimmune diseases
- Immune deficiency syndromes
- Medication
- Bone marrow failure syndromes
- Microangiopathic hemolytic anemia
- Congenital thrombocytopenia
- Hypersplenism

Corticosteroids: type, dosage, and duration

- At the recommended doses, the panel of experts suggests prednisone rather than dexamethasone
- Prednisone:
  - A short course of ≤ 7 day
  - Dosage of 2–4 mg/kg/day (maximum 120 mg/day) for 5–7 days
- Dexamethasone: Dosage of 0.6 mg/kg/day (maximum 40 mg/day) for 4 days

Terminology: duration from diagnosis

- Newly diagnosed: 0-3 months
- Persistent: 3-12 months
- Chronic: >12 months

Eltrombopag : dose adjustments

Recommended starting dose:*

50 mg once daily for children aged 6–17 years

25 mg once daily for children aged 1–5 years

Wait 2 weeks

<50 ×10⁹/l	≥50 ×10⁹/l to ≤ 150×10⁹/l	>150 ×10⁹/l to ≤250 ×10⁹/l	>250 ×10⁹/l
Increase dose by 25 mg to a maximum of 75 mg/day† Reassess in 2 weeks	**Maintain** dose at 50 mg/day	**Decrease** dose to 25 mg/day Reassess in 2 weeks	**Stop** and increase the frequency of platelet monitoring to twice weekly. Once the platelet count is <100 x10⁹/l, reinitiate therapy at 25 mg

References

1. Neunert C, Lim W, Crowther M, *et al*. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood.* 2011;117(16):4190-4207.
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3. Provan D, Arnold DM, Bussel JB, *et al*. Blood Advances. 2019;3:3780-3817
4. Neunert C, Terrell DR, Arnold DM, et al. Blood Advances. 2019;3:3829-66.
5. Eltrombopag Local Summary of product characteristics (SmPC),