EHA-TSH Hematology Tutorial on Immune Hematological Disorders

Tutored Clinical Case

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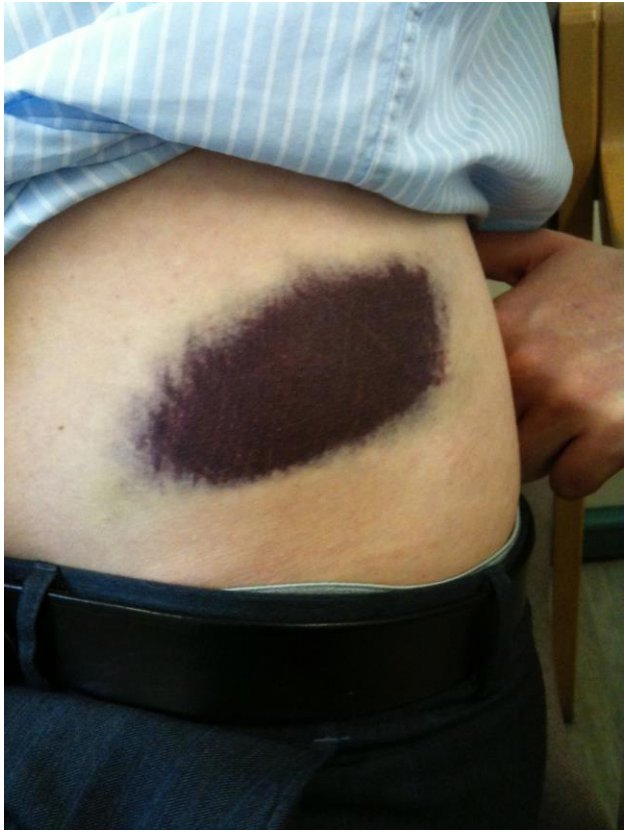
June 25-26, 2021

Clinical history

- 23-year-old male medical student
- Previously fit and well
- Noticed bruising when playing rugby
- Recent onset extreme fatigue (finals exams soon)
- **Past medical history**: unremarkable
- **Medication**: nil
- **Social history**: non-smoker, social alcohol (beer)
- **Family history**: mother type 2 diabetes

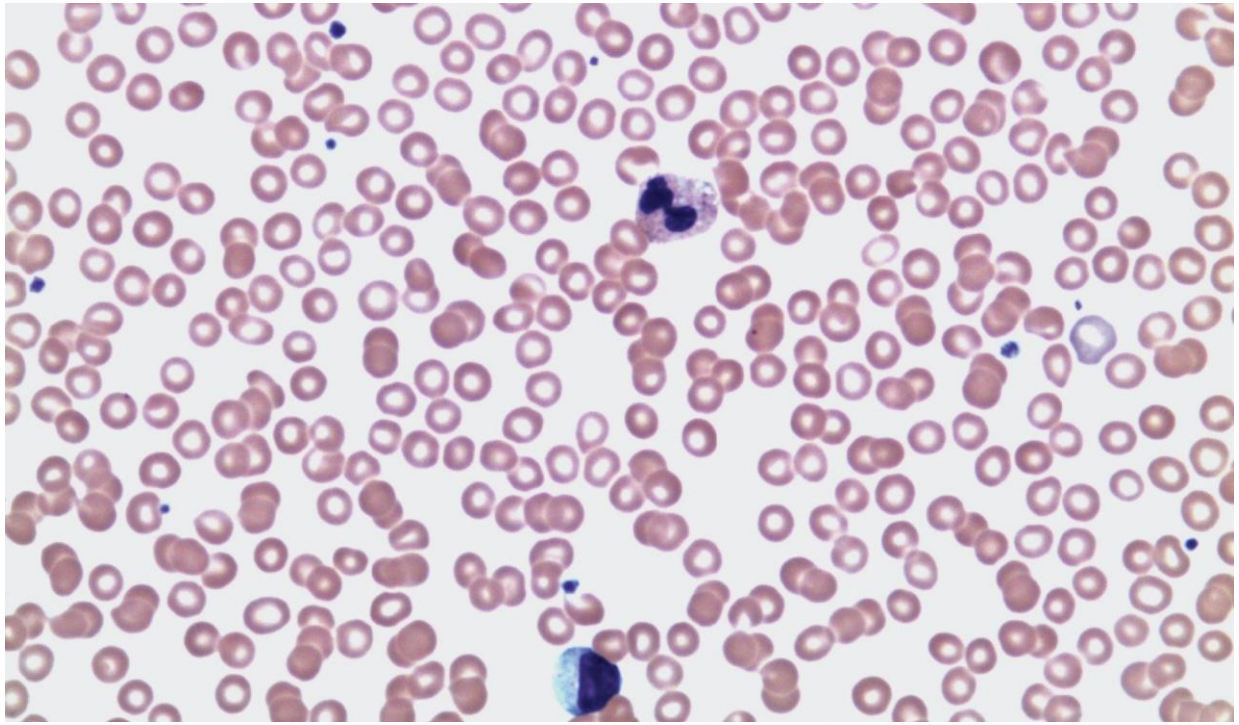


On examination

Investigations

- Investigated according to International Consensus Report
- Hb 143g/l, WBC 6.4 × 10^9/l, platelets 3 × 10^9/l
- Renal and liver function normal
- IgG, A, M normal
- Blood Group O Rh(D) Pos
- HIV, HBV, HCV negative
- *H. pylori* not checked

Provan D, *et al. Blood Advances* **3**, 3780-3817 (2019)



Blood film

Treatment

- Discussed with patient, standard first line: corticosteroids
- Prednisolone 1mg/kg/day for 2 weeks
- **Day 4**: platelets 46 × 10^9/l
- **Day 7**: platelets 162 × 10^9/l

- Maintained platelets > 100 × 10^9/l until prednisolone tapered to 15mg/day

Treatment

- **Week 6**: platelets 37 × 10^9/l
- **Week 8**: platelets 11 × 10^9/l
- Petechiae, mild bruising

Investigations

- **Should we have done a bone marrow**?
- No, not necessary

- No atypical features
- Investigations showed isolated thrombocytopenia only
- Other diagnoses highly unlikely

Bone marrow

- **When?**
- Systemic symptoms, abnormal signs
- Fail initial treatment
- Other cytopenias
- Pre-splenectomy (maybe)
- → Age: not a factor

- Aspirate ± biopsy
- Flow and cytogenetics to be considered

Provan D, *et al. Blood Advances* **3**, 3780-3817 (2019)
Comont T *et al. Blood Advances* **4**, 2136-2137 (2020)

Treatment options

- Failed first line therapy (85% patients do)
- Should we watch-and-wait?
  - Fit young man, no comorbidities, platelets >10 × 10^9/l
- Add second line (subsequent) treatment
  - Rituximab?
  - Mycophenolate?
  - Thrombopoietin receptor agonist (TPA-RA)?
  - Something else?

Pros and cons

- **Rituximab**
  - Long term response rate only ~20%
  - Immune suppressant
  - Inhibits response to COVID-19 vaccine
  - Avoid
- **Mycophenolate**
  - Slow time to response
  - Moderate efficacy
  - Immune suppression
  - Avoid

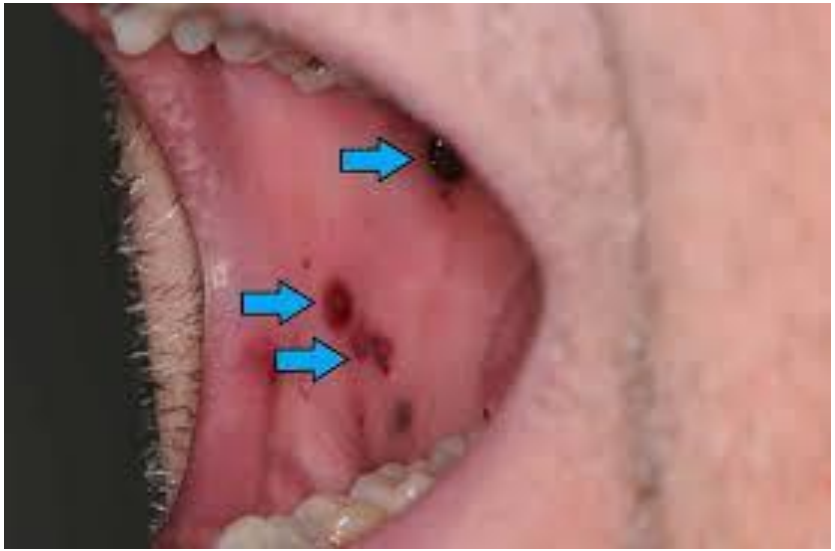
2nd line treatment

- Started romiplostim 3µg/kg weekly
- **By 2 weeks**: platelets 14 × 10^9/l
- Dose increased to 5µg/kg weekly
- **By 4 weeks**: platelets 86 × 10^9/l
- Continued 5µg/kg weekly
- **Week 8**: platelets 93 × 10^9/l

- Well, fatigue much improved

2nd line treatment

- After 6 months:
- Fatigue recurred
- Noticed petechiae on shins and more bruising
- Blood blisters in mouth (buccal mucosa)



Picture from cureus.com

Review on haematology ward

- Confirmed bruising & blood blisters
- Blood count:
  - Platelets 2 × 10^9/l
  - Rest of FBC normal
  - Bloods otherwise normal

- Was still receiving romiplostim 5µg/kg weekly

Relapse management plan

- Watch-and-wait is not an option (wet + dry purpura)
- Patient refuses to take another long course of corticosteroids

- Treatment:
  - IVIg 1g/kg × 1 day + dexamethasone 20mg/d × 4
- Day 7: platelets 120 × 10^9/l
- Feels well
- Day 14: platelets 35 × 10^9/l

TPO-RA switching

- Romiplostim switched to eltrombopag
- 50mg/day orally
- Day 14: platelets 90 × 10^9/l
- Day 30: platelets 87 × 10^9/l
- Day 74: platelets 95 × 10^9/l

- Remains well on eltrombopag 50mg/day
- Liver function normal, no signs of bone marrow fibrosis

Key points

- Response to corticosteroids & IVIg helps confirm diagnosis
  - Failure to respond suggests another diagnosis

- Long courses of corticosteroids cause problems
  - Avoid using for >8 weeks
  - Don’t recycle steroids (repeat courses)

Provan D, *et al. Blood Advances* **3**, 3780-3817 (2019)

Key points

- IVIg is indicated if there is wet purpura
  - Otherwise corticosteroids are used alone

Provan D, *et al. Blood Advances* **3**, 3780-3817 (2019)

Key points

- TPO-RAs have high efficacy (≥80%) with no immune suppression

- But patients can lose response to a TPO-RA
- Switching TPO-RAs works in ~60% cases

Provan D, *et al. Blood Advances* **3**, 3780-3817 (2019)

Switching TPO-R agonists

- Retrospective pilot
- 46 patients
- Switched due to: lack of efficacy; platelet count fluctuations; side-effects; patient preference
- 50–80% responded on switching (both directions)

- Switching beneficial if fail to respond or side-effects

Khellaf M et al. Haematologica 2013;98:881–7

Key points

- Avoid immune suppression during pandemic

Pavord S et al. Brit J Haem (May 2020)