Managing Unexplained Thrombocytosis and Associated Cancer Risk in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

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Key Information

- Thrombocytosis is generally defined as a raised platelet count >450x10⁹/l
- Thrombocytosis is a common incidental finding in around 2% of those aged ≥40 years attending primary care
- Reassuringly, 80–90% of thrombocytosis is reactive (secondary to acute blood loss, infection, or inflammation) and the majority of cases resolve within 3 months.

'Think Cancer'

- Although most cases are reactive, NICE's NG12 *Suspected Cancer: Recognition and Referral* (2023) and the *Scottish Referral Guidelines for Suspected Cancer* (2019) illustrate that unexplained thrombocytosis is a risk marker for some solid tumour malignancies
  - thrombocytosis is associated with a 1-year cancer incidence of 11.6% and 6.2% in males and females respectively, well exceeding the standard 3% threshold warranting investigation for underlying malignancy
- However, thrombocytosis should not be used as a standalone diagnostic or screening test for cancer, or to rule out cancer
  - unexplained thrombocytosis should prompt us to **'think cancer'**
- The Scottish referral guideline includes thrombocytosis in the investigation criteria for **LEGO-C** cancers: **L**ung, **E**ndometrial, **G**astric, **O**esophageal, and **C**olorectal
- NG12 includes thrombocytosis in the investigation criteria for **LEGO** cancers: **L**ung, **E**ndometrial, **G**astric, and **O**esophageal.

Recommended Actions After an Incidental Finding of a High Blood Platelet Count

- Consider possible causes: infection, inflammation, blood loss (including menstrual), myeloproliferative disorders (e.g. PRV, CML, essential thrombocythaemia), and malignancy
- Based on clinical examination and suspected diagnosis, arrange necessary investigations
- Review FBC and repeat if likely underlying reversible cause present (remember: 80–90% of cases are reactive thrombocytosis and the majority of cases resolve within 3 months)
- **Consider urgent Haematology referral if platelet count >1000x10⁹/l**, or 600–1000x10⁹/l with associated:
  - recent thrombosis
  - abnormal bleeding
  - age >60 years
  - other significantly abnormal FBC indices
  - neurological symptoms (Neurology referral may be warranted)
- Consider routine Haematology referral if two platelet counts >600x10⁹/l in 4–6 weeks, or if platelet count >450x10⁹/l for >3 months, and an alternative cause has not been identified.

If thrombocytosis is unexplained or not resolving: **check ferritin, CRP, and blood film, in addition to more detailed history taking and examination, to elicit any red flags**.

Unexplained thrombocytosis should prompt us to **'think cancer'**

Use clinical judgement to guide next most appropriate steps.

- Consider a JAK-2 gene mutation test (if available locally) and Haematology referral to exclude myeloproliferative disorders
  - JAK-2 is a genetic mutation that may be present in people with essential thrombocythaemia and can indicate a diagnosis of PRV
- Consider a referral for unexplained symptoms of cancer (if available locally).

- Carry out safety netting (consider weight diary)
  - NG12 recommends considering a review for people with symptoms associated with increased cancer risk but who do not meet referral criteria
  - this review could be planned within a timeframe agreed with the patient, or initiated by the patient if they continue to be concerned, new symptoms develop, or their symptoms worsen, persist, or recur
- Check for resolution of thrombocytosis according to the condition being suspected and/or treated—repeat FBC after 4–12 weeks (remember: most cases resolve within 3 months).

Exclude LEGO-C cancers

L: Consider an urgent CXR (to be performed within 2 weeks)—if normal, consider alternative diagnoses, including other cancers

E: Consider direct-access pelvic USS in women aged ≥55 years with unexplained vaginal discharge or visible haematuria

G/O: Consider direct-access UGIE if aged ≥55 years and associated UGI symptoms and/or weight loss (use clinical judgement to determine urgency of referral)

C: Consider qFIT (if available locally) or urgent lower GI investigations (see Indications for qFIT/Colorectal Cancer Referral)

- refer urgently using a suspected cancer pathway referral if qFIT >10 mcg/g.

Indications for qFIT/Colorectal Cancer Referral

NICE Guidance

- Abdominal mass
- Change in bowel habit
- IDA
- Age ≥40 years with unexplained weight loss and abdominal pain
- Age <50 years with rectal bleeding and abdominal pain or weight loss
- Age ≥50 years with rectal bleeding, abdominal pain, or weight loss
- Age ≥60 years with any anaemia.

NHS Scotland Guidance

- Bleeding (repeated rectal bleeding without an anal cause, or blood mixed with the stool)
- Persistent change in bowel habit (for >4 weeks, especially if looser stools)
- Mass (unexplained abdominal, or palpable ano-rectal)
- Pain (abdominal pain with weight loss)
- IDA (unexplained).

Abbreviations
CML=chronic myeloid leukaemia; **CRP**=C-reactive protein; **CXR**=chest X-ray; **FBC**=full blood count; **GI**=gastrointestinal; **IDA**=iron deficiency anaemia; **JAK-2**=Janus kinase 2; **LEGO-C**=Lung, Endometrial, Gastric, Oesophageal, Colorectal; **NG**=NICE Guideline; **PRV**=polycythaemia rubra vera; **qFIT**=quantitative faecal immunochemical test; **UGI**=upper gastrointestinal; **UGIE**=upper gastrointestinal endoscopy; **USS**=ultrasound scan

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