

Thrombocytosis and Cancer Risk: A Practical Approach in Primary Care

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Abstract

Original Research Article

Thrombocytosis is a common abnormality encountered in primary care and is frequently attributed to reactive causes such as inflammation, infection or iron deficiency. Although it is often detected incidentally on routine blood tests, persistent or unexplained thrombocytosis warrants careful assessment. Primary-care studies have demonstrated an association between thrombocytosis and a subsequent cancer diagnosis, with notable associations reported for lung, endometrial, gastric and colorectal cancers, among others [1,2]. However, thrombocytosis is neither a diagnostic test for cancer nor a reliable means of excluding it. Instead, it should prompt clinicians to consider the whole clinical picture and arrange appropriate investigation when a reactive explanation is not evident. This is particularly important in patients with non-specific symptoms or no immediately suggestive examination findings. This article reviews the differential diagnosis of thrombocytosis, its association with cancer, a practical approach to investigation and the importance of safety-netting.

Keywords: Thrombocytosis, Cancer, Reactive causes, Platelet count, Primary care, Diagnosis.

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INTRODUCTION

The number of people diagnosed with cancer in the UK continues to grow. For the first time, the number of new cancer diagnoses each year in the UK has passed 400,000. If recent trends continue, new cases are projected to exceed half a million annually by 2040 [7].

Thrombocytosis is generally defined as a platelet count above the laboratory reference range, commonly using a threshold of $450 \times 10^9/L$. It is frequently identified incidentally during investigations in primary care. Most cases are reactive, and the platelet count may return to baseline when the underlying cause resolves. Common causes include acute or chronic infection, inflammation, iron deficiency, tissue injury, haemorrhage and malignancy. In day-to-day practice, the challenge for the GP is not simply to identify thrombocytosis, but to establish whether the abnormality has an adequate explanation and whether further investigation is warranted.

Evidence and prevalence

NICE initially updated its suspected-cancer guidance in 2015 to include raised platelet count among the features that may prompt investigation for several

cancers. This has been further revised in December 2025 [6]. The acronym LEGO-C is sometimes used to describe lung, endometrial, gastric, oesophageal and colorectal cancers associated with thrombocytosis. A large UK primary-care cohort study found that cancer was diagnosed within one year in 11.6% of men and 6.2% of women aged 40 years and over with thrombocytosis, compared with 4.1% and 2.2%, respectively, among matched patients without thrombocytosis.[2]

The study also reported that cancer risk increased with higher platelet counts and was greater when thrombocytosis was present on two occasions within six months. The reported one-year cancer incidence in patients with two raised platelet counts was 18% in men and 10% in women. Lung and colorectal cancers were among the most frequent diagnoses. Approximately one-third of patients diagnosed with lung or colorectal cancer had no other symptoms suggestive of cancer at the time, while around two-thirds had symptoms that could have prompted referral [2]. These findings support treating unexplained thrombocytosis as a diagnostic prompt, rather than as a stand-alone cancer test or screening tool [5].

For GPs, the key message is that a raised platelet count may indicate an underlying inflammatory or malignant process and should be interpreted alongside the patient's symptoms, examination findings and other investigations.

Why can cancer cause thrombocytosis?

The relationship between cancer and thrombocytosis is complex and is thought to involve inflammatory and cytokine-mediated pathways. Tumours can stimulate the production of inflammatory mediators, including interleukin-6, which promotes hepatic production of thrombopoietin and consequently, platelet production [3]. Cancer-associated inflammation can therefore lead to reactive thrombocytosis. There is also evidence that platelets interact directly with tumour cells and may contribute to tumour progression, angiogenesis and metastatic processes [3]. In patients with established cancer, thrombocytosis has been associated with more advanced disease and poorer survival. In primary care [4], however, the platelet count must be considered in the context of the patient's overall presentation.

Causes and risk factors

Reactive or primary thrombocytosis?

The initial assessment should establish whether there is an identifiable reactive cause.

Common reactive causes include:

- Acute or chronic infection
- Inflammatory disease
- Iron deficiency
- Recent surgery or tissue injury
- Significant blood loss or haemolysis
- Malignancy
- Post-splenectomy state

Iron deficiency deserves particular attention. Thrombocytosis accompanied by microcytosis should prompt assessment for iron deficiency and investigation of its underlying cause. In an older adult, for example, iron deficiency may require investigation for gastrointestinal blood loss. Similarly, a recent infection may explain a transient platelet elevation; if the count remains raised after the expected resolution of the illness, the differential diagnosis should be reconsidered. Persistent thrombocytosis without a clear reactive cause may also require assessment for a primary haematological disorder, including a myeloproliferative neoplasm.

Primary thrombocytosis

Is caused by an underlying abnormality in bone marrow function, usually due to a myeloproliferative or myelodysplastic disorder.

- Polycythaemia vera
- Chronic myeloid leukaemia
- Essential thrombocythaemia

- Primary myelofibrosis
- Myelodysplastic syndromes

When should cancer be considered?

The association between thrombocytosis and cancer is clinically important because patients do not necessarily present with classical cancer symptoms. The UK primary-care study found particularly notable associations with lung and colorectal cancers; approximately one-third of patients with these cancers and thrombocytosis had no other symptoms suggestive of malignancy at the time.[2] A systematic review also found an association between thrombocytosis and a range of cancers, concluding that it may be useful as an early marker in primary care.[1]

Thrombocytosis should therefore be regarded as a risk marker and a potential diagnostic clue, particularly in patients with otherwise non-specific symptoms. It is not diagnostic of cancer, and a normal platelet count does not exclude malignancy.

Clinical assessment and investigation

Which cancers are associated with thrombocytosis?

Thrombocytosis does not point to one specific cancer, and presentations vary according to the underlying disease. The LEGO-C mnemonic (lung, endometrial, gastric, oesophageal and colorectal) can help clinicians remember cancer sites and structure the assessment:

A practical approach

Investigations should be guided by the patient's symptoms, examination and risk factors rather than by the platelet count alone. The following framework is intended as a prompt for clinical judgement and should be checked against current local pathways and NICE guidance.

Step 1: Assess for symptoms and signs

Review the platelet trend and assess for a reactive cause. Ask about relevant symptoms and investigate or refer through the appropriate pathway when indicated.

- **Lung:** cough, haemoptysis or relevant smoking history—consider pulmonary pathology and appropriate imaging.
- **Endometrial:** postmenopausal bleeding or unexplained vaginal discharge—consider gynaecological pathology.
- **Gastric:** upper abdominal pain, nausea, vomiting, weight loss, reflux or dyspepsia—consider upper gastrointestinal pathology and the need for endoscopy.
- **Oesophageal:** dysphagia or relevant persistent upper gastrointestinal symptoms—consider oesophageal pathology.
- **Colorectal:** weight loss, altered bowel habit, rectal bleeding or iron deficiency—consider colorectal pathology.

Step 2: Consider investigation when no clear cause is found

If no relevant symptoms are identified and thrombocytosis remains unexplained, consider investigations in line with current guidance and the patient's overall risk. NICE recommends considering an urgent direct-access chest X-ray to assess for lung cancer in adults aged 40 years and over with a platelet count >450 [6]. In males and post-menopausal females with unexplained iron deficiency anaemia, FIT testing may be appropriate where indicated by symptoms, risk factors and the applicable pathway.

Step 3: Arrange follow-up and reassessment

If initial assessment is reassuring and no cause is identified, arrange repeat blood testing at an appropriate interval and document a clear follow-up plan. If the platelet count remains raised, increases, or new symptoms develop, reassess the patient and consider further investigation, including an appropriate non-specific symptom or cancer pathway where indicated. Also remember other causes of thrombocytosis, including chronic inflammation, infection and myeloproliferative disorders. Routine haematology referral is recommended if there is a persistent or progressive unexplained platelet count over $450 \times 10^9/L$.

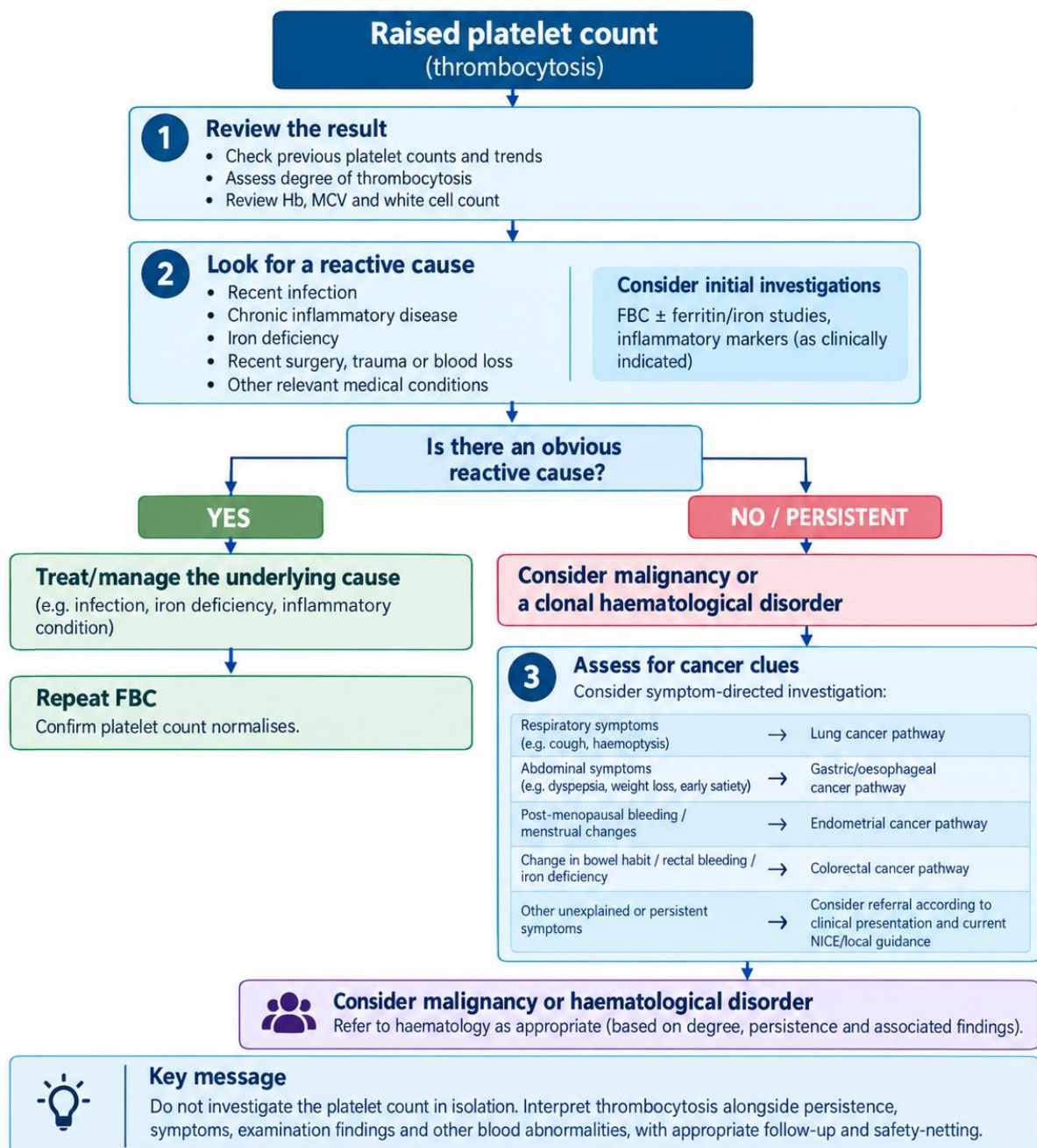


Figure 1. Practical primary-care approach to thrombocytosis.

The importance of safety-netting

One of the greatest risks when investigating thrombocytosis is false reassurance. A patient may have a plausible reactive explanation at the initial assessment, but persistent elevation or evolving symptoms may mean that the original explanation is no longer sufficient. Safety-netting should therefore be explicit and documented. This is particularly important because cancer symptoms can evolve over time and the significance of a blood test result depends on the clinical context in which it is interpreted.

Patients should understand:

- What abnormality has been identified
- What is currently thought to be causing it
- What investigations are being arranged
- What symptoms should prompt further review
- When repeat blood tests are required
- Who they should contact if symptoms persist or worsen

DISCUSSION

Thrombocytosis occupies an important position in primary care: it is common and often reactive, yet it can also provide an early clue to serious disease. Evidence supports an association between thrombocytosis and several malignancies, but a raised platelet count does not mean that a patient has cancer, and investigation should not be driven by the platelet count alone. A useful approach is to identify common reactive causes, assess whether the explanation adequately accounts for the abnormality, consider the patient's age, symptoms, examination findings and other laboratory results, and investigate through the most appropriate clinical pathway.

The distinction between a diagnostic marker and a diagnostic clue is important. Thrombocytosis does not have sufficient specificity to function as a stand-alone cancer test. Nevertheless, when considered alongside symptoms or other abnormalities, it can contribute meaningful information to the diagnostic process. In primary care, a full blood count may have been requested for one reason while an abnormal platelet count provides an additional piece of information that changes the clinical picture. The aim is not to investigate every raised platelet count aggressively, but to avoid overlooking persistent or unexplained thrombocytosis.

CONCLUSION

Thrombocytosis is a common finding in primary care and is frequently reactive. However, persistent or unexplained thrombocytosis should prompt clinicians to consider malignancy alongside other possible causes. The key message for GPs is to take the platelet count seriously without investigating it in isolation. A structured assessment that considers platelet trends, reactive causes, symptoms, examination findings

and accompanying blood abnormalities can help identify patients who need further investigation while reducing unnecessary testing. Thrombocytosis should be viewed not as a diagnosis, but as a potential early warning signal within the broader clinical picture.

1. Key points

- Most thrombocytosis in primary care is reactive, but persistent or unexplained elevation needs reassessment and interpretation alongside symptoms, examination findings and other investigations.
- Thrombocytosis is associated with an increased risk of a subsequent cancer diagnosis, particularly lung and colorectal cancer.
- The platelet count is a diagnostic clue, not a stand-alone cancer test; a normal count does not exclude cancer.
- Arranging routine haematology referral if there is a persistent or progressive unexplained platelet count over $450 \times 10^9/L$.

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