HbA_2 Variability in Iron Deficiency and Thalassemia Trait

When HbA_2 Misleads: A Real Case of Iron Deficiency vs Beta Thalassemia Trait

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A patient presented with mild anemia:

Hemoglobin: 11.1 g/dL
MCV: 87.7 fL
MCH: 28.9 pg
MCHC: 33.0 g/dL

HPLC findings showed:
Initial HbA_2: 4.2%
Repeat HbA_2: 3.7%(Repeat was done after 2 months on request of treating doctor as outside lab reports were different)

This fluctuation raised an important diagnostic dilemma: Is this Beta Thalassemia Trait (BTT), Iron Deficiency Anemia (IDA), or a combination of both?

The Diagnostic Challenge

At first glance:
HbA_2 of 4.2% points toward BTT
A later value of 3.7% falls into a borderline zone

However, the red cell indices tell a different story:

MCV, MCH and MCHC is within normal range!
This is not typical for isolated BTT, where microcytosis is expected
This discrepancy highlights a common but critical pitfall in HPLC interpretation.

The Key Confounder: Iron Deficiency
Iron deficiency has a well-documented effect: It can suppress HbA_2 levels

So what likely happened here?
The patient may have underlying BTT
Concurrent or evolving iron deficiency altered HbA_2 values
This resulted in variation from 4.2% → 3.7%

What This Case Teaches Us?

1. HbA_2 Is Not Static
HbA_2 levels can fluctuate depending on iron status.
A single value—especially borderline—should never be interpreted in isolation.

2. CBC Correlation Is Essential
Normal red cell indices reduces the likelihood of classic BTT
Always interpret HPLC alongside red cell indices

3. Dual Pathology Is Common
In real-world practice:BTT + Iron deficiency coexist more often than we think

Recommended Approach:
✓ Evaluate iron profile (serum ferritin, iron studies)
✓ Treat iron deficiency if present
✓ Repeat HPLC after iron correction
✓ Consider family screening if suspicion persists

Common Mistake:
Labeling a patient as BTT based on a single elevated or borderline HbA_2 without evaluating iron status.

Clinical Takeaway:
"Fluctuating HbA_2 is not a laboratory error—it is often a physiological clue."

Understanding this prevents:
-Misdiagnosis
-Unnecessary lifelong labeling
-Missed identification of carriers

Conclusion:
This case reinforces the importance of integrated hematological interpretation.
As pathologists, our role goes beyond reporting values—we interpret patterns, question inconsistencies, and guide clinicians toward accurate diagnosis.

Have you encountered similar HbA_2 fluctuations in your practice?
Share your experience.

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