Subtle blood loss can be associated with a lack of response to testosterone replacement therapy

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Introduction

As testosterone replacement therapy (TRT) becomes more widely accepted, more practitioners will need to be familiar with associated adverse events. We present a case that highlights the need for frequent monitoring of patients on TRT.

Methods

Case Report:

History:

A 45-year-old man being treated with testosterone replacement therapy for the past year presents for follow-up. Despite an increase in dose 3 months ago, he noted more fatigue over this time period. He felt that his fatigue had been completely alleviated in the past with therapy. The patient denied any orthopnea, paroxysmal nocturnal dyspnea or weight gain. He denied any abdominal pain, hematochezia or melena.

Physical Exam :

Unremarkable

BP: 124/80 HR: 78 Wt: 192 lbs

Labs/Studies:

Total testosterone: 634 ng/dL

Calculated free testosterone: 22 ng/dL

Estrogen: 31 pg/mL

Hemoglobin: 14.5 g/dL (prior Hgb 16.7 g/dL)

Hematocrit: 45 % (prior Hct 50.5 %)

MCV: 73 fL (prior MCV 85 fL)

RESULTS

Upon further questioning, the patient admitted to daily use of diclofenac (a NSAID) for 5-6 months. The patient subsequently underwent upper gastrointestinal endoscopy which revealed gastric ulcers consistent with NSAID use. After cessation of NSAIDs, his follow-up 3 months later showed a Hemoglobin of 16.1 g/dL and Hematocrit 50.8%, and his fatigue had resolved.

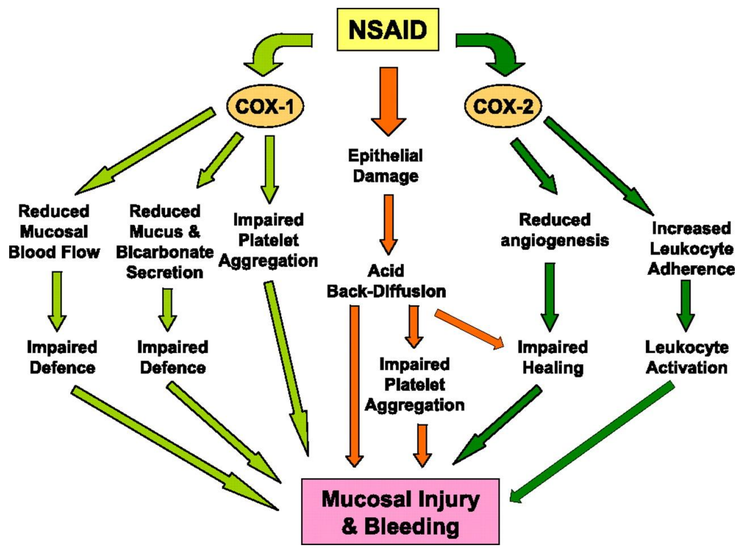

Figure 1. Pathogenesis of NSAID-induced gastric injury and bleeding. NSAIDs induce injury/bleeding via three key pathways: inhibition of cyclooxygenase (COX)-1 activity, inhibition of COX-2 activity, and direct cytotoxic effects on the epithelium.

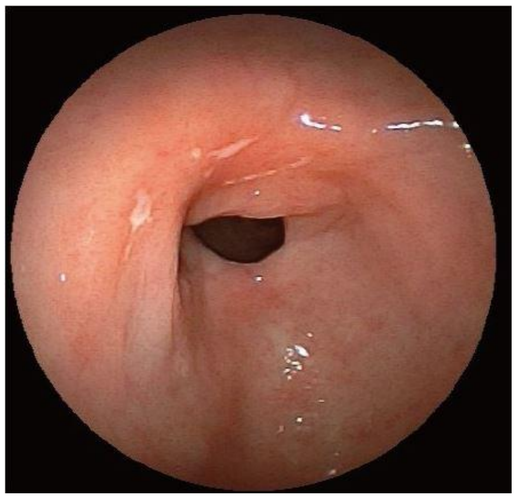

Figure 2. NSAID induced gastric ulcer

DISCUSSI0N

When a patient on TRT develops worsening of previously alleviated symptoms, an increase in dose will often be the first action but may not solve the patient's problem. Careful attention to blood work may reveal an alternative diagnosis.

In this case, the patient had an occult bleed resulting in a microcytosis yet no anemia, with a seemingly "normal" Hgb/Hct. The stimulatory effects of testosterone on erythropoiesis were able to mask the blood loss by maintaining a "normal" Hgb/Hct level. Testosterone stimulates erythropoietic action in the marrow, and a knowledge of the adverse events related to TRT helped identify an occult bleed in this case.

NSAID related GI complications are one of the most common drug-related side effects. With their widespread use, they are seen as safe and often patients fail to mention them as a drug they are taking. This case highlights the clinical importance of follow up on patients on TRT. It also highlights the importance of routine medication reconciliation.

Reference: Wallace, J. Prostaglandins, NSAIDs, and Gastric Mucosal Protection: Why Doesn't the Stomach Digest Itself? Physiological Reviews Oct 2008, 88 (4) 1547-1565; **DOI:**10.1152/physrev.00004.2008

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