

## INTRODUCTION

Gastrointestinal bleeding is common in the elderly and is a frequent indication for hospitalization. More than 1% of people aged 80 years and older are hospitalized each year because of either upper or lower gastrointestinal bleeding. In the elderly, morbidity and mortality from gastrointestinal bleeding is often associated with the use of aspirin, NSAIDs, and other antiplatelet agents. Acquired inhibitors of coagulation are antibodies that either inhibit the activity or increase the clearance of a clotting factor. Factor II deficiency is rare and is found in 1 in 1-2 million people. Factor II deficiency caused by an acquired inhibitor of factor II is even rarer and only causes bleeding in extreme cases. Gastrointestinal bleeding caused by factor II inhibitor is rare, and to our knowledge, no previous case has been reported. This report emphasizes the need to consider rare causes of gastrointestinal bleeding in an otherwise common scenario.

## CASE SUMMARY

- 83-year-old female, who is on aspirin and ibuprofen, and who is not on a PPI, presented with progressive symptoms of anemia: weakness, fatigue, dizziness, and falls. These symptoms had been getting worse over the last 1 to 2 weeks.
- On physical examination, the patient's blood pressure was 140/60, heart rate was 74, and O2 saturation was 98% on room air. The patient was a well-developed woman in no apparent distress, lying comfortably in bed. She was found to have melena and multiple bruises on exam. Otherwise, her exam was unremarkable.
- On initial blood work, the hemoglobin was 6.7. EGD revealed a 0.5 cm pyloric channel ulcer, which was oozing slightly (see figure 1). Colonoscopy did not reveal a bleeding source.
- Based on these results, the initial impression was that the patient had gastrointestinal bleeding, thought to be secondary to a pyloric channel ulcer in the setting of NSAIDs and coagulopathy, possibly due to malnutrition.
- After undergoing the EGD and colonoscopy, her hemoglobin had decreased again and her INR went up to 6.6. It was very difficult to achieve hemostasis despite many units of fresh frozen plasma, red blood cells, cryoprecipitate and vitamin K. After an extensive workup, the patient was found to be factor II deficient.
- Since the patient was found to be factor II deficient, the patient was provided with factor replacement. In addition, the patient was provided with steroid pulse dosing with four days of decadron dosing, which was started on 8/30/2008. Her factor II levels increased rapidly to normal levels as a result of the steroid therapy (please see figure 2).
- After steroid therapy, the patient's hemoglobin and PT/PTT/ INR had normalized and stabilized (see Table 1). The patient also underwent a CT scan of the chest, abdomen, pelvis, which revealed no evidence of any neoplasms.
- These observations suggest that life-threatening gastrointestinal bleeding can be induced by factor II inhibitor and that immunosuppressive therapy using steroids can be successful in inhibiting the production of the autoantibody.

## DATA/IMAGES

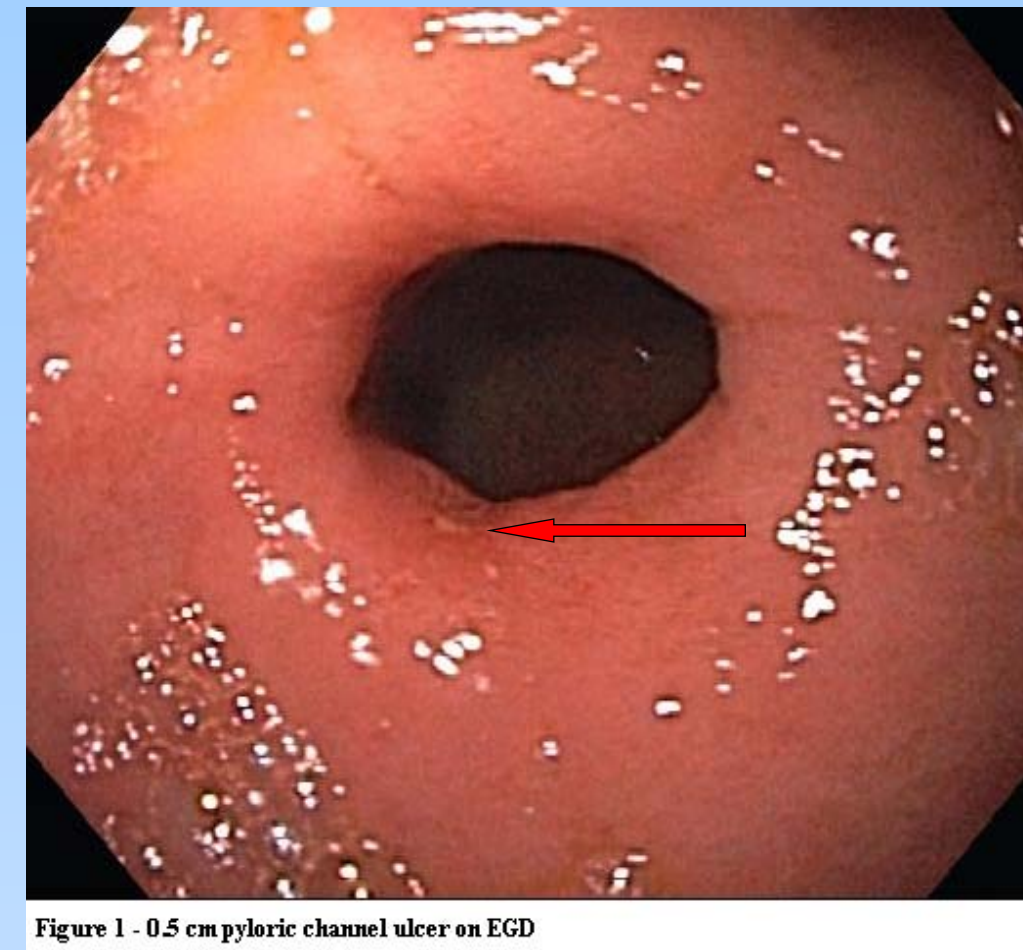


Figure 1 - 0.5 cm pyloric channel ulcer on EGD

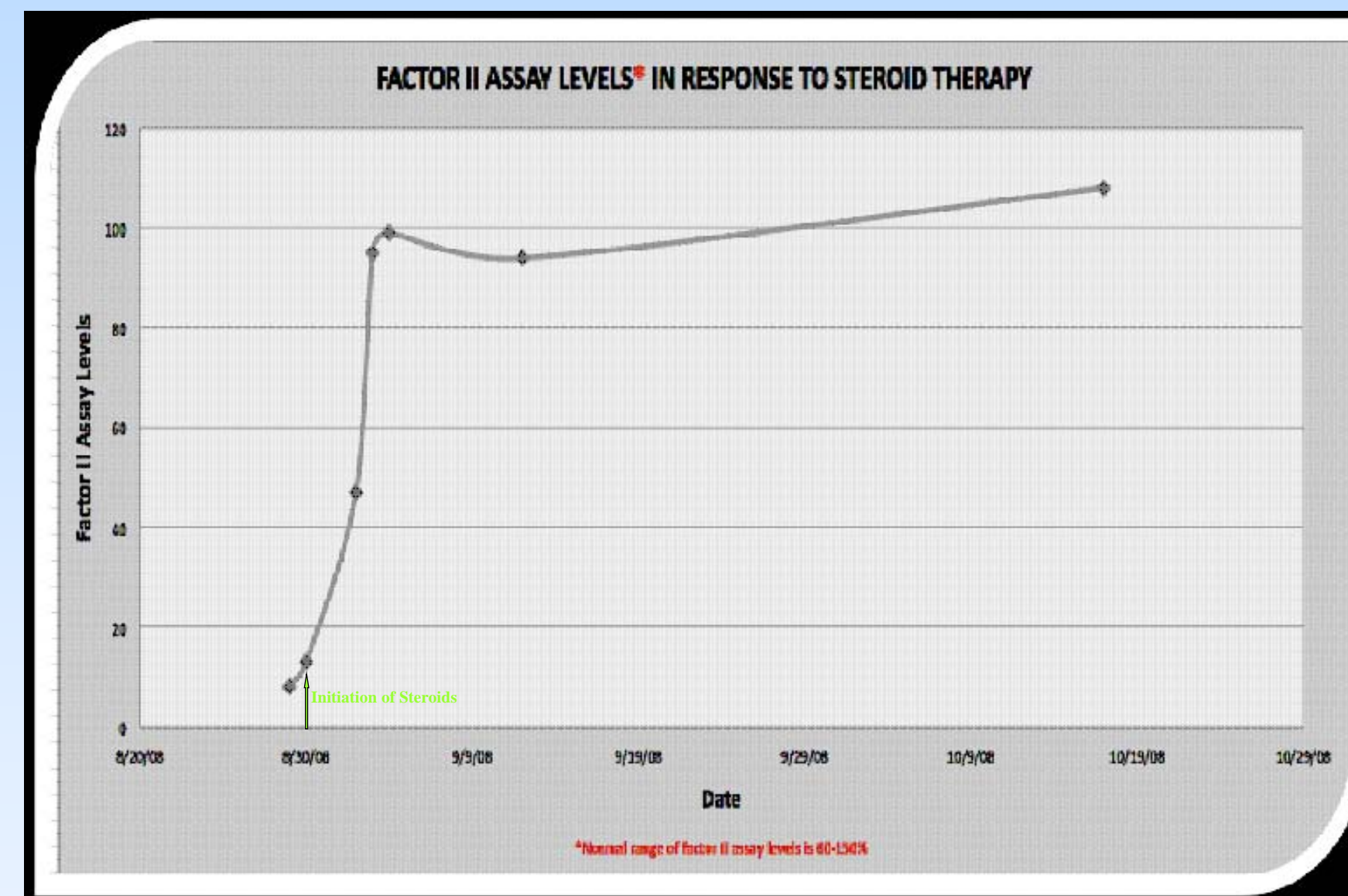


Figure 2 - Factor II Levels in Response to Steroid Therapy

DRAW DATE	DRAW TIME	PT (sec)	PTT (sec)	INR	Platelets
4/10/2001	23:15	12.6	27.0	1.0	205,000
8/24/2008	20:00	20.0	43.0	2.3	223,000
8/28/2008	06:10	36.7	95.0	6.6	247,000
8/28/2008	09:00	18.9	40.0	2.1	247,000
8/28/2008	16:45	26.5	62.0	3.7	227,000
8/29/2008	01:45	24.3	57.0	3.2	151,000
8/29/2008	05:55	24.9	51.0	3.4	160,000
8/29/2008	09:30	15.3	32.0	1.5	145,000
8/29/2008	17:07	11.6	32.0	0.9	150,000
8/30/2008	00:00	16.0	43.0	1.6	156,000
8/30/2008	05:00	18.5	55.0	2.0	155,000
8/30/2008	20:30	22.0	50.0	2.7	184,000
8/31/2008	08:00	20.4	45.0	2.4	168,000
9/1/2008	18:50	16.1	32.0	1.6	166,000
9/1/2008	07:02	16.1	28.0	1.6	182,000
9/2/2008	08:14	12.1	24.0	1.0	201,000
9/3/2008	06:00	14.0	22.0	1.3	224,000
9/4/2008	07:32	13.9	23.0	1.2	270,000
9/5/2008	06:00	13.5	24.0	1.2	278,000

Table 1 Coagulation Panel and Response to Steroid Therapy

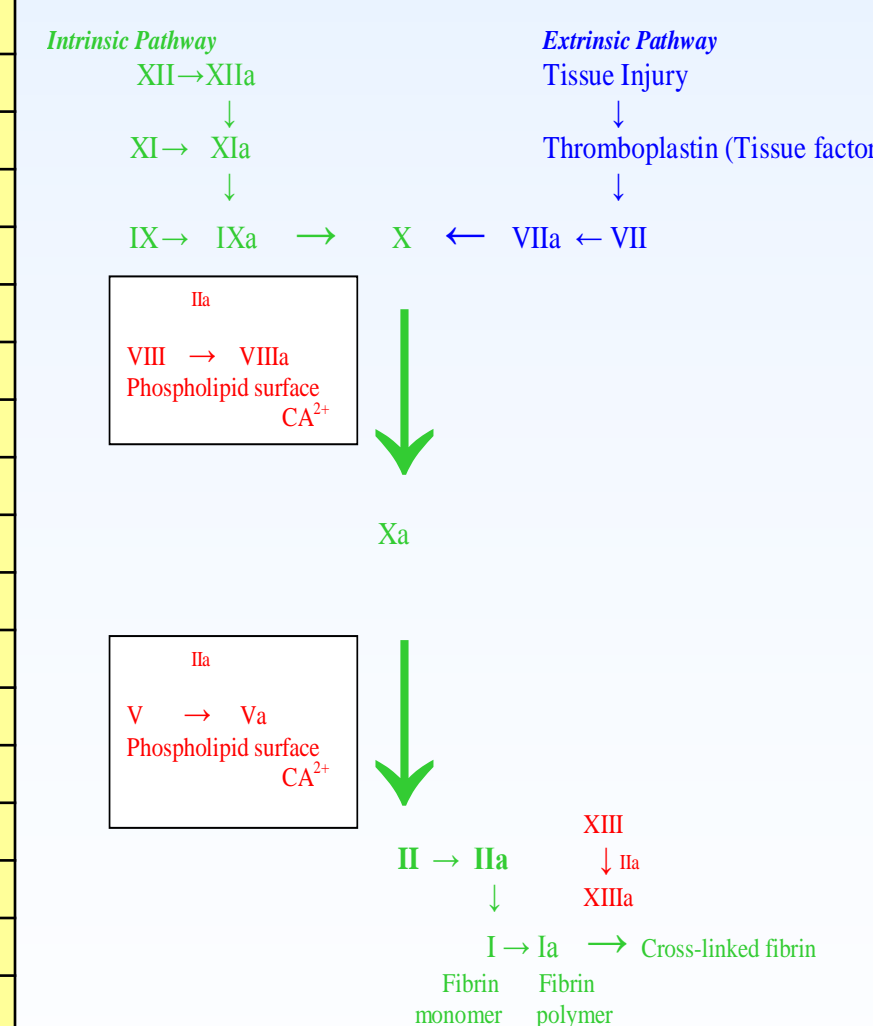


Figure 3 Coagulation Cascade

## DISCUSSION

- The overwhelming majority (95 to 97 percent) of all the inherited deficiencies of coagulation factors is comprised of the X-linked inherited coagulation disorders, which include hemophilia A and B (factor VIII and IX deficiency, respectively), and von Willebrand disease. Deficiencies of the rest of the coagulation factors, including factors II, V, VII, X, XI, and XIII, are rare and are transmitted as autosomal recessive disorders. Their prevalence ranges from 1 in 500,000 to 1 in 2 million.
- Diagnosis of any of the recessively inherited factor deficiencies can be made by checking a prothrombin time (PT) and activated partial thromboplastin time (aPTT). The specific factor assays are only indicated when the PT and/or PTT are severely prolonged.
- Acquired inhibitors of coagulation are antibodies that react or cross react with clotting factors or components used in coagulation screening tests (phospholipids) and thereby inhibit the activity or increase the clearance of clotting factors.
- Factor II (prothrombin) is a vitamin K dependent glycoprotein. It is synthesized in the liver and is posttranslationally modified in a vitamin K-dependent reaction that converts ten glutamic acids on prothrombin to gamma-carboxyglutamic acid (Gla); Gla residues, in the presence of calcium, promote the binding of thrombin (activated factor II or factor IIa) to phospholipid bilayers (please see figure 3).
- Acquired causes of prothrombin deficiency include vitamin K deficiency, warfarin therapy, liver disease, and antiprothrombin antibodies associated with lupus anticoagulant. In general, the lower the factor II levels, the more severe the bleeding. However it is difficult to ascertain this correlation, since there are so few cases reported in the literature.
- The reported cases of bleeding include easy bruising, mucosal bleeding, surgical bleeding, trauma-related bleeding, hemarthroses, and intracranial hemorrhage.
- *Alamelu et al.* reported a case of acquired prothrombin deficiency in a patient with follicular lymphoma and stated that there had only been one other case report of this prior to theirs in 2008. The authors reported that following diagnosis of lymphoma, treatment with chemotherapy resulted in an improvement in prothrombin levels with a corresponding fall in antiprothrombin levels. Thus, they postulated that the lymphoproliferative malignancy was responsible for the antiprothrombin antibody and that treatment of the underlying malignancy made the antibody disappear.
- To our knowledge, prior to our case report, no other cases of gastrointestinal bleeding secondary to prothrombin deficiency or inhibitor have been reported in the literature.

## REFERENCES

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