Case - Hematuria and uroepithelial thickening

Anticoagulation-induced suburothelial hemorrhage

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INTRODUCTION

Antopol and Goldman discovered lesions mimicking renal neoplasms in seven patients who had undergone nephrectomies as a result, and subsequently named them Antopol-Goldman lesions (AGL).[1]

AGL is a subepithelial hemorrhage typically affecting the renal pelvis,[1,2] and usually presents as hematuria and flank pain, most commonly in the elderly.[1-6] Since AGL masquerades as renal neoplasms, it was mainly diagnosed histologically from specimens collected after nephrectomies.[3] With the advent of advanced imaging modalities and diagnostic tools, such as flexible ureteroscopy, nephrectomies are avoided, and patients are treated conservatively.[3,5,7,8]

In this report, we present the case of a 52-year-old female with AGL occurring in the context of supratherapeutic international normalized ratio (INR) level secondary to warfarin therapy. We demonstrate that conservative management by temporary cessation of warfarin and optimizing anticoagulant dosing led to the full resolution of symptoms.

CASE REPORT

A 52-year-old female presented to the emergency department (ED) with painless gross hematuria persisting for three days, accompanied by mild left lower quadrant (LLQ) pain radiating from the left flank. Her medical history was significant for hypertension and a mechanical mitral valve replacement performed two months prior for severe mitral regurgitation. She was maintained on warfarin for anticoagulation, alongside metoprolol and aspirin.

Two days prior to the ED presentation, she attended a routine hematology clinic visit, where her INR was found to be 4.6 (therapeutic target for mechanical mitral valves: 3.0–3.5[9]). In response, the hematologist advised holding her next warfarin dose; however, by that time, she had already been experiencing gross hematuria for one day. Despite the temporary discontinuation of warfarin, her hematuria persisted and was followed by worse LLQ pain, prompting her presentation to the ED the following day.

On initial assessment, her vital signs were stable. Physical examination was unremarkable except for mild LLQ tenderness without costovertebral angle tenderness or peritoneal signs. Given the ongoing hematuria, warfarin was temporarily withheld, while her other medications were continued. Laboratory investigations, including a complete blood count, coagulation profile, comprehensive metabolic panel, liver function tests, urinalysis, and urine culture, were performed.

Pertinent findings included an INR of 4.09, which had decreased from 4.6 but remained above the therapeutic range, numerous red blood cells on urinalysis, and the presence of leukocyte esterase. The urine culture was negative for bacterial growth, and hemoglobin remained stable at 122 g/L (reference range 120–160 g/L). A multiphasic computed tomography (CT) urogram was performed on the day of admission (approximately three days after symptom onset), revealing non-enhancing hyperdense suburothelial collections (Hounsfield unit 25) extending from the left renal collecting system to the mid-ureter, with associated left pelviectasis (Figures 1A, 1B). The radiologist interpreted these findings as consistent with suburothelial hemorrhage, raising suspicion for an AGL attributed to supratherapeutic anticoagulation. Notably, a contrast-enhanced CT scan of the abdomen and pelvis from one month prior had shown no abnormalities in the kidneys or ureters.

The patient remained hemodynamically stable throughout her hospitalization. Withholding one additional dose of warfarin resulted in the resolution of hematuria and LLQ pain. She was advised to continue holding warfarin for two additional days following discharge before resuming at a reduced dose of 5 mg daily (previously 7 mg on Fridays and 5 mg on other

KEY MESSAGES

- Supratherapeutic warfarin therapy is a risk factor for Antopol-Goldman lesion occurrence.
- Diagnosis relies on imaging, typically CT urogram, showing suburothelial hemorrhage.
- Conservative management is effective in stable patients without concerning features.
- Followup may include cystoscopy, repeat imaging, and INR monitoring based on individual risk.

days). Invasive diagnostic procedures, such as ureteroscopy or retrograde pyelography, were not pursued, given the patient's hemodynamic stability, absence of hydronephrosis or suspicious enhancing masses, and the radiologist's diagnostic impression. Outpatient followup was arranged in urology for cystoscopic evaluation of the lower urinary tract, along with urine cytology, as well as a followup CT scan to ensure resolution of findings. Additionally, she was scheduled for hematology followup for warfarin titration.

At her most recent followup, her symptoms had completely resolved, she remained asymptomatic, and her INR had stabilized at 2.57. The cystoscopic evaluation did not reveal any lower urinary tract pathologies, and the urine cytology was normal. The followup CT scan also showed complete resolution of the suburothelial hemorrhage (Figures 1C, 1D).

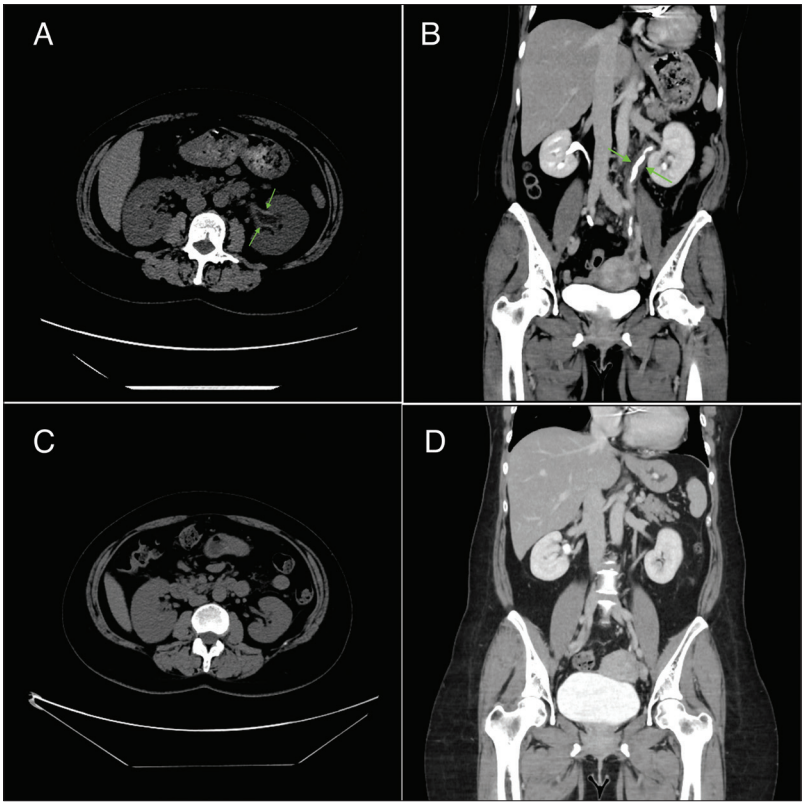

Figure 1. Multiphasic computed tomography urogram showing a left-sided Antopol Goldman lesion and its interval resolution. The axial non-contrast and coronal delayed excretory-phased images demonstrate hyperdense suburothelial collections along the left renal pelvis and proximal ureter as shown by the arrows (panels A & B), which showed complete resolution on followup imaging (panels C & D).

DISCUSSION

Subepithelial hemorrhage of the urothelium, also known as AGL,[1] is a rare condition with less than 60 cases reported in the literature. It classically affects the renal pelvis[1,2] and presents as flank pain and hematuria mostly in the elderly.[1-6] Previously, AGL was diagnosed histologically post-partial or -radical nephrectomies due to its radiographic resemblance to renal neoplasms (e.g., evidence of filling defects on CT imaging).[7] Today, improvements in imaging modalities and increased awareness of AGL have largely eradicated unnecessary nephrectomies, and AGL is mainly diagnosed radiologically.[3,10]

Cardin et al demonstrated for the first time that AGL can be managed conservatively with followups in patients with coagulopathies or anticoagulant use and unremarkable ureterorenoscopic examinations.[5] Similarly, Gayer and colleagues conservatively managed AGL in seven patients by correcting their coagulopathies or discontinuing anticoagulants, leading to full symptom resolution.[10] Despite the modern adoption of such conservative approaches, complications such as refractory hematuria requiring selective arterial embolization[10] and emphysematous pyelonephritis requiring urgent nephrectomy[4] should not be missed. Moreover, although the etiology of AGL remains poorly understood, it has been associated with trauma, hypertension, diabetes, amyloidosis, and coagulopathies.[3,5,6] Of note, anticoagulant use is a common feature of several reported cases of AGL.[6,7,11-15]

In our report, we present the case of a 52-year-old female patient who presented to the ED complaining of left flank pain and hematuria, who was on warfarin therapy due to a prior mitral valve replacement. Laboratory investigation indicated an elevated INR (4.09), which is higher than the acceptable upper limit of 3.5 for mechanical mitral valves.[9] A CT urogram showed suburothelial hemorrhage extending from the left renal collecting system to the proximal ureter. The extension of the hemorrhage to the level of the proxi-

mal ureter is an interesting and uncommon finding in our case, as AGL typically affects the renal pelvis.[1]

Nevertheless, our findings are consistent with previous reports where AGL was attributed to anticoagulant use and/or elevated INR levels.[7,12-15] Importantly, the resolution of hematuria with cessation of warfarin further reinforces the utility of conservative management, especially in patients on anticoagulant therapy.

While there are no clear followup guidelines or recommendations, cystoscopy of the lower urinary tract, outpatient assessment of underlying factors, such as coagulopathies or hypertension, or CT imaging can be considered; however, with the resolution of symptoms and the absence of worrisome malignant features, followups may be of little value.

CONCLUSIONS

With less than 60 cases reported to date, suburothelial hemorrhage is an uncommon presentation associated with certain risk factors. Here, we present the case of a suburothelial hemorrhage secondary to supratherapeutic warfarin dosing and show that its discontinuation leads to full symptom resolution. Our report further demonstrates that AGL can be managed conservatively by correcting underlying contributing factors, such as an unoptimized anticoagulant dosage. Further followup with cystoscopy, repeat CT imaging, and outpatient assessment of risk factors can be considered depending on the patient profile and the presence of malignant features.

COMPETING INTERESTS: Dr. Rompré-Brodeur has participated in advisory boards for Knight, Tersera, and Tolmar; and has been a speakers' bureau member for Abbvie, Merck, Novartis, Tersera, and Tolmar. The remaining authors do not report any competing personal or financial interests related to this work.

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