Spontaneous subepithelial hemorrhage of renal pelvis and ureter (Antopol-Goldman lesion) in hemophilia A patient with inhibitor

Case report and review of the literature

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Abstract

Introduction: The Antopol-Goldman lesion (AGL), which expresses subepithelial hemorrhage in the renal pelvis, was first defined by Antopol and Goldman in 1948. The objective of this study is to report the first case of AGL in patients with congenital hemophilia and review the relevant literature.

Patient concerns: A 32-year-old male patient diagnosed with congenital hemophilia A (FVIII = 4%) with high responding inhibitors (7.4 BU) was admitted to our emergency department with gross hematuria and sudden onset flank pain.

Diagnosis: Abdominal computed tomography (CT-scan) presented a hyperdense lesion in the left ureteropelvic junction with Hounsfield Units of 56 consistent with hemorrhage.

Interventions: The patient was given 4500 IU of factor eight inhibitor bypass activity (FEIBA) intravenously twice daily for 5 days. Subsequently, 4500 IU of FEIBA was administered once a day for 2 days.

Outcomes: The patient’s complaints disappeared on the fourth day of treatment. Macroscopic and microscopic hematuria was not seen in the following days. Follow-up CT was done 3 months after discharge and showed normal left renal pelvis without hyperdenosis. Follow-up CT was performed 3 months after discharge and presented normal left renal pelvis with no hyperdense lesion.

Conclusion: Although very rare, AGL should be kept in mind in the differential diagnosis of renal pelvic hemorrhage. In the patient who has an underlying history of coagulopathy nephrectomy can be avoided when there is awareness of AGL.

Abbreviations: AGL = Antopol-Goldman lesion, APCC = activated prothrombin complex concentrate, aPTT = activated partial thromboplastin time, BU = Bethesda units, CT = computed tomography, FEIBA = factor eight inhibitor bypass activity, PT = prothrombin time, rFVIIa = recombinant activated factor VII.

Keywords: Antopol-Goldman lesion, hemophilia

1. Introduction

Antopol-Goldman Lesion (AGL), which states subepithelial hemorrhage in the renal pelvis, was first pronounced by Antopol and Goldman in 1948.[1] The first cases are diagnosed after nephrectomy because they mimic renal neoplasm.[2,3] Although this hemorrhage is extremely difficult to distinguish from the true renal pelvis tumors, the diagnosis can be established by radiologically and clinically. The patients may have with hematuria and flank pain. Conservative approach is preferred as a treatment in recent studies.[4–6]

Hemophilia A is an X-linked congenital bleeding disorder caused by factor VIII deficiency. Hematuria and renal-ureteral hemorrhage are the most common complications in hemophilia A patients.[7] Prevention or treatment of bleeding is the replacement of VIII. However, inhibitor development is the most common and most serious complication in hemophilia A patients and it occurs in up to 30% of patients with severe hemophilia A.[8] The current standard hemostatic agents for patients with inhibitor are recombinant activated factor VII (rFVIIa) and activated prothrombin complex concentrate (APCC).
To date, 39 cases have been reported due to severe factor V deficiency, overuse nonsteroidal anti-inflammatory drugs, trauma, and amyloidosis (Table 1).

Table 1
Summary of previously published cases of subepithelial pelvic hematoma (Antopol-Goldman lesion). Our present patient is the first case of hemophilia A with Antopol-Goldman lesion.

| References                     | Sex/age, y | Side | Hematuria | Possible etiology | Treatment          |
|--------------------------------|------------|------|-----------|-------------------|--------------------|
| Antopol and Goldman[1]         | M/25       | R    | Microscopic | Trauma            | Nephrectomy        |
|                                | F/58       | L    | Macroscopic | NA                | Nephrectomy        |
|                                | M/53       | R    | Macroscopic | NA                | Nephrectomy        |
|                                | F/33       | R    | Macroscopic | Dysfunctional ureter | Nephrectomy        |
|                                | F/30       | R    | Macroscopic | Duplicate ureter  | Nephrectomy        |
|                                | F/35       | R    | Macroscopic | Trauma            | Nephrectomy        |
|                                | F/39       | R    | Macroscopic | Vascular dysfunction | Nephrectomy        |
| Labay and Orkin[12]            | F/42       | R    | Macroscopic | NA                | Nephrectomy        |
|                                | M/67       | L    | Macroscopic | Fetal lobulation  | Nephrectomy        |
|                                | F/42       | L    | Macroscopic | NA                | Partial nephrectomy |
| Viamonte et al[13]             | M/53       | L    | Macroscopic | Anticoagulative treatment | Nephrectomy        |
|                                | F/67       | L    | Macroscopic | NA                | Nephrectomy        |
| Levitt et al[14]               | F/45       | R    | Macroscopic | Analgesic abuse   | Partial nephrectomy |
| Oza et al[15]                  | F/26       | R    | Macroscopic | NA                | Nephrectomy        |
| Kim et al[16]                  | F/55       | L    | Macroscopic | NA                | Nephrectomy        |
| Iczkowski et al[17]            | M/46       | L    | Macroscopic | NA                | Nephrectomy        |
|                                | F/24       | R    | Macroscopic | NA                | Nephrectomy        |
|                                | F/40       | R    | Macroscopic | NA                | Nephrectomy        |
|                                | F/84       | R    | Macroscopic | Pelvic calcification | Nephrectomy        |
|                                | F/43       | L    | Macroscopic | NA                | Nephrectomy        |
| Demirkan et al[17]             | M/60       | R    | Microscopic | Analgesic abuse   | Nephrectomy        |
| Vilar Pastor et al[18]         | F/56       | L    | Macroscopic | Renal biopsy      | Nephrectomy        |
|                                | M/69       | R    | Macroscopic | NA                | Nephrectomy        |
|                                | M/22       | L    | Macroscopic | NA                | Nephrectomy        |
|                                | F/46       | L    | Macroscopic | NA                | Nephrectomy        |
| Rodriguez Alonso et al[19]     | M/32       | L    | Macroscopic | Trauma            | Conservative approach |
| Duffau et al[20]               | M/26       | L    | Macroscopic | NA                | Conservative approach |
| Ortiz Gorriz and Campana Gutiérrez[21] | NA | NA | NA | Anticoagulative treatment | Nephrectomy        |
| Cardón et al[22]               | M/72       | L    | Macroscopic | NA                | Conservative approach |
| Eccher et al[23]               | M/77       | L    | Macroscopic | Amyloidosis       | Nephrectomy        |
| Yapanoglu et al[24]            | F/36       | L    | Macroscopic | NA                | Nephrectomy        |
| Chan et al[9]                  | F/0        | R    | No         | NA                | Conservative approach |
| Branchereau et al[25]          | M/43       | R + L| Macroscopic | Severe factor V deficiency | Arterial embolization |
| Sánchez Zalabardo et al[26]    | F/86       | R    | Macroscopic | NA                | Nephrectomy        |
| Aguilar-García and Vargas-Serrano[24] | F/43 | L    | No         | NA                | Conservative approach |
| Attya et al[27]                | M/60       | R    | Macroscopic | NA                | Conservative approach |
| Seker et al[28]                | M/75       | R    | Macroscopic | Thrombocytopenia  | Conservative approach |
| Jelvandzam and et al[29]       | NA/7       | R    | Macroscopic | Induction chemotherapy | Conservative approach |
| Present case                   | M/32       | L    | Macroscopic | Hemophilia        | Conservative approach |

AGL = Antopol-Goldman lesion, F = female, L = left, M = male, NA = not available, R = right.

To date, 39 cases have been reported due to severe factor V deficiency, overuse nonsteroidal anti-inflammatory drugs, trauma, and amyloidosis (Table 1). However, AGL had never been reported in any hemophilia patient. Therefore, the purpose of this study is to report the first case ever of AGL in a patient with congenital hemophilia and to review the relevant literature.

2. Case report

The patient has provided written informed consent for publication of the case.

Thirty-two-year-old male patient with a history of severe hemophilia A was admitted to the emergency department with gross hematuria and sudden onset of side pain. His medical history was unremarkable except for hemophilia A. He was diagnosed at 1 month old and since then, he begins to administer factor VIII concentrates. However, 20 years after diagnosis, inhibitors were detected. Treatment with factor VIII concentrates is discontinued. Instead, rFVIIa and APC are administered. During the disease, significant hemorrhages such as psoas hematoma and hemorrhathrosis were observed. He had no history of trauma or use of anticoagulant or anti-aggregant agents. The patient was transferred to the hematology service. Physical inspection exposed tenderness was present on the left flank and lower abdominal quadrant, whereas other systemic evaluations were normal. In addition, his vital signs were within normal ranges. Preliminary laboratory results comprised a normal complete blood count, including platelets, prolonged activated partial thromboplastin time (aPTT), and prolonged prothrombin time (PT). FVIII had significantly reduced activity (4%; normal range, 60%–150%), and FVIII inhibitor had a high titer (7.4 Bethesda units [BU]/mL; normal range, 0–0.6 BU/mL). Abdominal computed tomography (CT) scan without intravenous contrast media showed a hyperdense lesion in the left ureteropelvic junction with Hounsfield Units of 56 compatibles with hemorrhage (Fig. 1).
To control his bleeding, the patient was given 4500 IU of factor eight inhibitor bypass activity (FEIBA) intravenously twice daily for 5 days. He was given intravenous tramadol 100mg/day for severe pain. The patient’s complaints disappeared on the fourth day of treatment. The patient had no macroscopic and microscopic hematuria in the following days. Subsequently, 4500 IU FEIBA was administered once daily for 2 days and the patient was discharged from the hospital. Follow-up CT was done 3 months after discharge and showed normal left renal pelvis with no hyperdense lesion which confirmed the radiological diagnosis of AGL (Fig. 2). Although prophylactic treatment was not applied to the patient, no recurrence was observed at 1-year follow-up.

3. Discussion
AGL is a benign hemorrhagic lesion that is rarely seen with clinical appearance and imaging results that can mimic the tumor of the renal collection system. Although it can be seen in all age group, it is more common in the elderly. However, 1 neonatal

Figure 1. Axial (A, B) and coronal reformatted (C) unenhanced computed tomography (CT) images demonstrate hyperdense lesion in the left ureteropelvic junction (arrows). There is also small stone in the right kidney.

Figure 2. Computed tomography (CT) without intravenous contrast media shows complete resolution of the lesion at follow-up 3 months after discharge.
activity.\textsuperscript{[25]} Hematuria is a frequent manifestation of hemophilia. Beck and Evans\textsuperscript{[26]} showed that 66% of hemophilia patient had a history of hematuria. Chakarova et al\textsuperscript{[27]} reported that during a 5-year follow-up of patients with hemophilia hematuria was found in approximately 25% of patients. Hematuria in hemophiliacs usually responds to conservative therapies and self-limited, some cases of severe hematuria have been reported which require cystectomy.\textsuperscript{[28]} Although the etiology of hematuria in hemophilia disease is often uncertain, it could be related to an underlying coagulation deficiency. In our case, there were no predisposing factors that would cause bleeding other than Hemophilia A, and the patient responded well to bypassing agents, suggesting that AGL was potentially associated with hemophilia A. Although spontaneous intramural hemorrhage of the ureter in hemophilia patients is a rare condition and has been stated in only 2 earlier cases not de...
[23] Sánchez Zalabardo D, De Pablo Cárdenas A, Fuertes Zárate A. Antopol–Goldman lesion: a rare clinical entity in the differential diagnosis of macroscopic hematuria. Arch Esp Urol 2012;65:238–62.
[24] Aguilar-García JJ, Vargas-Serrano R. Subepithelial pelvic hematoma. Actas Urol Esp 2012;36:620–3.
[25] White GC, Rosendaal F, Aledort LM, et al. Definitions in hemophilia—recommendation of the scientific subcommittee on factor VIII and factor IX of the scientific and standardization committee of the international society on thrombosis and haemostasis. Thromb Haemost 2001; 85:560.

[26] Beck P, Evans KT. Renal abnormalities in patients with haemophilia and Christmas disease. Clin Radiol 1972;23:349–54.
[27] Chakarova P, Sukarova E, Chakarov R, et al. Renal changes in haemophilia A. Trakia J Sci 2005;3:52–5.
[28] Washino S, Hirai M, Kobayashi Y, et al. Heavy hematuria are requiring cystectomy in a patient with hemophilia A: a case report and literature review. BMC Urol 2015;15:64.
[29] Kierbas I. Ultrasound and computed tomography findings of spontaneous intramural hemorrhage of renal pelvis and ureter in patient with hemophilia A. Urology 2008;72:1030–2.