

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 compatibles 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

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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).

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/57	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 ^[3]	M/46	M	Microscopic	NA	Pelvis plastic	
	M/56	R	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
	Villar Pastor et al ^[18]	F/56	L	Macroscopic	Renal biopsy	Nephrectomy
		M/69	R	Macroscopic	NA	Nephrectomy
M/22		L	Microscopic	NA	Nephrectomy	
F/46		L	Microscopic	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 Gorraiz and Campaña Gutiérrez ^[21]	NA	NA	NA	Anticoagulative treatment	Nephrectomy	
Cardin et al ^[10]	M/72	L	Macroscopic	NA	Conservative approach	
Eccher et al ^[2]	M/77	L	Macroscopic	Amyloidosis	Nephrectomy	
Yapanoglu et al ^[22]	F/36	L	Macroscopic	NA	Nephrectomy	
Chan et al ^[9]	F/0	R	No	NA	Conservative approach	
Branchereau et al ^[11]	M/43	R + L	Macroscopic	Severe factor V deficiency	Arterial embolization	
Sánchez Zalabardo et al ^[23]	F/86	R	Macroscopic	NA	Nephrectomy	
Aguilar-García and Vargas-Serrano ^[24]	F/43	L	No	NA	Conservative approach	
Altay et al ^[4]	M/80	R	Macroscopic	NA	Conservative approach	
Şeker et al ^[5]	M/75	R	Macroscopic	Thrombocytopenia	Conservative approach	
Jeevanandham et al ^[6]	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).^[1–6,9–24] 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 presented 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 APCC are administered. During the disease, significant hemorrhages such as psoas hematoma and hemarthrosis 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 shown a hyperdense lesion in the left ureteropelvic junction with Hounsfield Units of 56 compatibles with hemorrhage (Fig. 1).

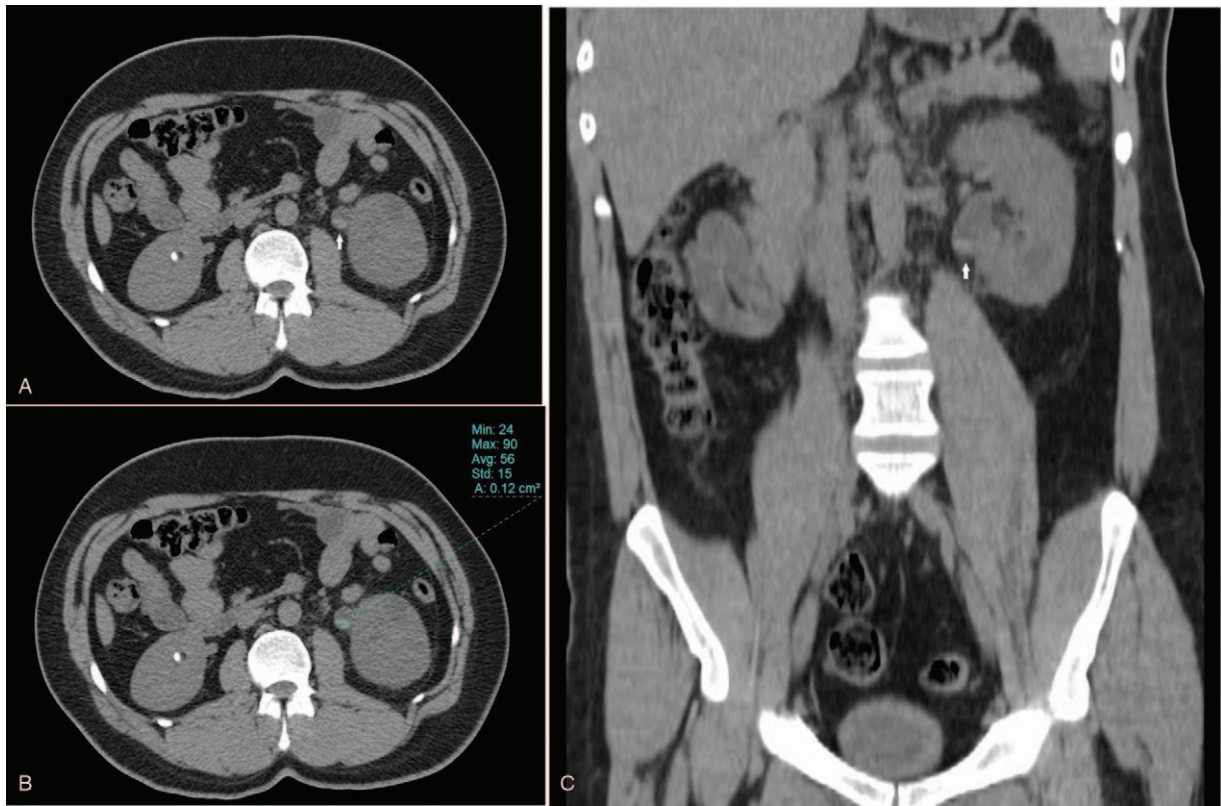


Figure 1. Axial (A, B) and coronal reformatted (C) unenhanced computed tomography (CT) images demonstrate hyperdense lesion in the left ureteropelvic junction (arrows). There is also small stone in the right kidney.

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

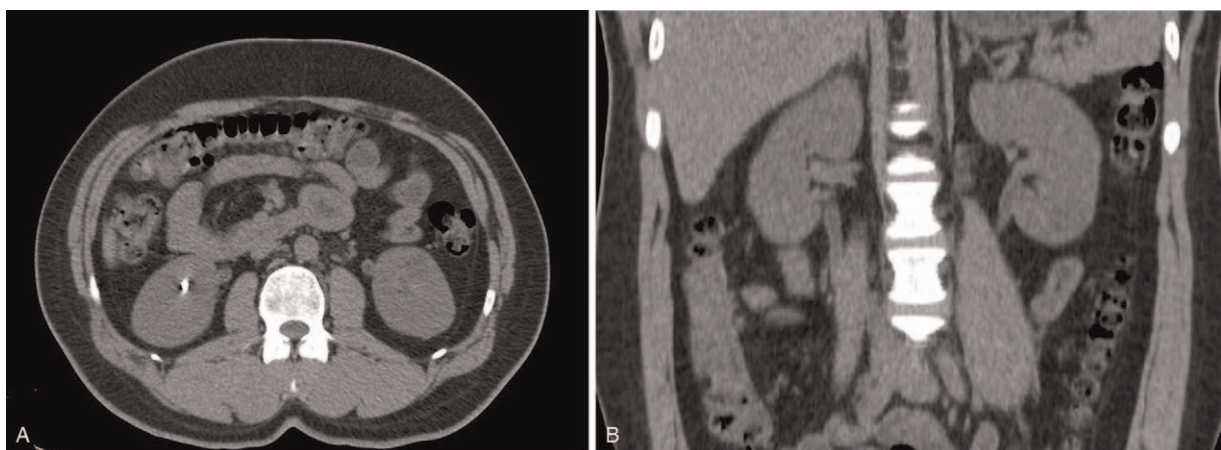


Figure 2. Computed tomography (CT) without intravenous contrast media shows complete resolution of the lesion at follow-up 3 months after discharge.

case and 12 cases under 35 years of age have also been reported.^[19] The most common clinical appearance of suburothelial pelvic hemorrhage is macroscopic hematuria and acute side pain as in our patient.^[4] Although the etiopathogenesis is unclear in most of the previously reported cases, there are 39 cases of AGL in the literature due to various possible conditions related to the etiology of AGL, including trauma, congenital malformations (bifid pelvis, fetal lobulation, aberrant vessels, and ureteral insertion abnormalities), hypertension, excessive analgesic use, anticoagulant treatment, severe factor V deficiency, amyloidosis, thrombocytopenia, and induction chemotherapy (Table 1). None of these factors were present in our case. Sixteen patients were male, 21 were female and for 2 patients the sex was not reported. The median age was 43 years (0–86 years). Thirty-one cases presented with macroscopic hematuria (%81).

Hemophilia A is classified as severe (<1% factor activity), moderate (1–5% factor activity), and mild (>5% factor activity).^[25] Hematuria is a frequent manifestation of hemophilia. Beck and Evans^[26] showed that 66% of hemophilia patient had a history of hematuria. Chakarova et al^[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.^[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 defined as AGL,^[7,29] no AGL was reported in hemophilia patients.

Until 2008, most patients were diagnosed with AGL after nephrectomy. First, Cardin et al^[10] reported a conservative approach case with subepithelial hematoma. In a case, because hematuria could not be managed conservatively, selective arterial embolization was applied.^[11] Recurrent cases of AGL have not been observed in patients managed conservatively in the literature. APCC and rFVIIa remain the mainstays for the treatment of bleeding in hemophilia patients with inhibitors. In our case, 4500 IU of FEIBA intravenously twice daily for 5 days was begun. The patient's macroscopic hematuria responded within 5 days and the frequency of FEIBA reduced once a day. During the follow-up period, abdominal CT at 3 months showed that the lesion had disappeared. We did not give long-term FEIBA prophylaxis and no bleeding episode was observed at a 1-year follow up. However, a single case may not be sufficient for long-term treatment plan. As the reported cases increase in the literature, treatment strategies may change. In the patient who has an underlying history of coagulopathy, nephrectomy can be avoided when there is awareness of AGL.

To our knowledge, this is the first case report of AGL in a patient with hemophilia A. Although rarely seen, AGL should be considered in the differential diagnosis of renal pelvic hemorrhage.

Author contributions

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