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Case Report

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Spontaneous perinephric hematoma due to acquired factor X deficiency in AL amyloidosis

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Abstract
Spontaneous perinephric hematoma (SPH) is a rare entity whose diagnosis is challenging because of its varied clinical presentation and lack of any specific etiology. We report a 34-year-old African-American male who presented with left flank pain and was found to have a large left perinephric hematoma, in the setting of undiagnosed AL amylodosis. The case illustrates that while a SPH due to the vascular angiopathy of amyloid is rare, when amyloidosis is associated with abnormal coagulation studies or bleeding at multiple sites, it should be considered because of its protean systemic manifestations and potential response to chemotherapy.

Keywords: amyloidosis; spontaneous perinephric hematoma

Background

Spontaneous perinephric hematoma (SPH) is rare and has been described in association with conditions, such as angiomyolipomata, renal cell carcinoma, renal artery aneurysm and metastatic renal melanoma [1, 2]. Due to varied clinical presentation, without any specific cause, the diagnosis of SPH is a clinical dilemma. Symptoms and natural history range from slight flank and/or abdominal pain to acute collapse. Other conditions associated with SPH include vascular disease, blood disorder and infection [2]. Imaging plays a significant role in the diagnosis and management of this potentially lethal entity [3, 4].

Since the clinical picture of SPH varies considerably depending on the degree and duration of bleeding, ruling out other etiologies which can be managed conservatively is critical. We present a case of SPH in the setting of primary amyloidosis.

Case report

A 34-year-old African-American male presented to the emergency department (ED) with a sudden onset of left flank pain, radiating to the left testicle. The medical history was significant for hypertension since the age of 14. Spontaneous splenic capsular bleeding requiring splenectomy had occurred 3 months previously, and he was being followed by hematology for post-splenectomy thrombocytosis. Of note, platelets were 513 k/μL (normal 150–400 k/μL) on admission and patient was not on Aspirin. A Computed Tomography scan of the abdomen performed in the ED showed a large left perinephric hematoma (Figure 1). A left renal angiogram showed active extravasation from the lower pole branch of the left renal artery, and gelfoam embolization was performed which resulted in the resolution of bleeding.

Acute renal failure developed within 1 day of admission, due to a combination of renal artery embolization and contrast administration (pre-embolization creatinine 1.33 mg/dL and post-embolization creatinine 1.85 mg/dL with peak of 2.28 mg/dL). It resolved rapidly over the ensuing 48 h. Subsequently, the patient developed spontaneous bilateral subconjunctival hemorrhage on Day 2 of his hospitalization, followed by gastrointestinal bleeding. His relevant laboratory studies showed the following: prolonged prothrombin time (PT) with International Normalized Ratio of 1.4 (normal 0.8–1.2) and a mixing study showed complete correction and moderately low factor X levels of 52 (normal 73–163).

Protein studies: both serum and urine immunofixation electrophoresis showed an abnormal homogenous band in the lambda region (Table 1).

A bone marrow biopsy demonstrated mild plasmacytosis (10% of total cellularity) with lambda light chain restriction and aberrant cyclin D1 expression, consistent with the presence of a plasma cell neoplasm. In addition, amyloid deposition was noted in the surrounding soft tissue, as supported by the presence of congophilic material with apple-green birefringence under polarized light (Figures 2–4).

Stomach, duodenal and splenectomy specimen biopsies also demonstrated amyloid deposition, confirmed by Congo red staining. Immunohistochemical stains showed the amyloid to be negative for amyloid A and transthyretin and positive for lambda light chain, consistent with Amyloid light chain (AL)-type amyloid (Figure 4).

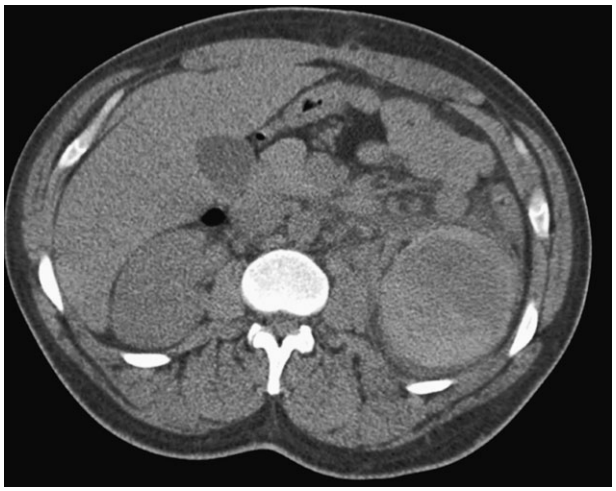

Fig. 1. CT Abdomen: left perinephric hematoma.

Table 1.

Serum component	Result	Normal range
IgG	1100 mg/dL	717–1411 mg/dL
IgA	114 mg/dL	78–391 mg/dL
IgM	44 mg/dL (low)	53–334 mg/dL
Kappa	761 mg/dL	534–1267 mg/dL
Lambda	414 mg/dL	253–653 mg/dL
Kappa/lambda ratio	1.84	1–3

IgG = Immunoglobulin G; IgA = Immunoglobulin A; IgM = Immunoglobulin M; mg/dL = Milligrams per Deciliter

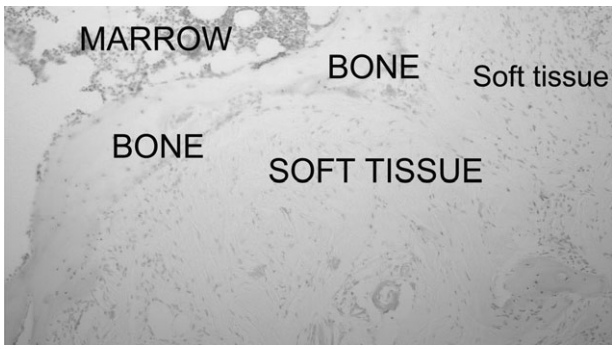

Fig. 2. Pathology.

Conclusions

SPH is a clinical entity that poses a diagnostic and therapeutic challenge. SPH due to vascular angiopathy of amyloidosis is rare. However, when associated with abnormal coagulation studies or bleeding at multiple sites, amyloidosis should be considered because of its protean systemic manifestations and potential response to chemotherapy [2]. Of the major causes reported, tumors accounted for 57–63% of cases (benign in 24–33% and malignant in 30–33%), vascular disease (such as polyarteritis nodosa) for 18–26% and infection for 7–10% [2].

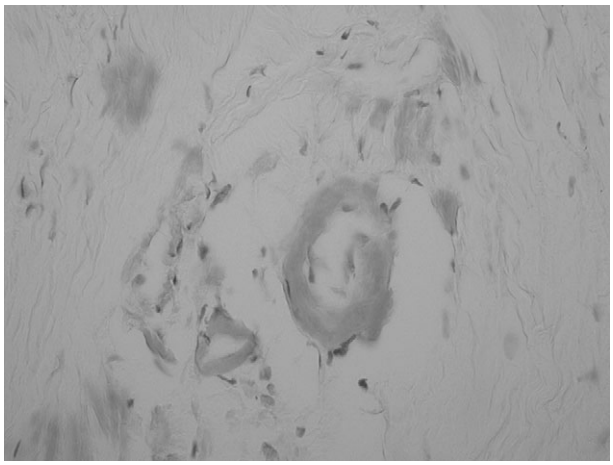

Fig. 3. Pathology.

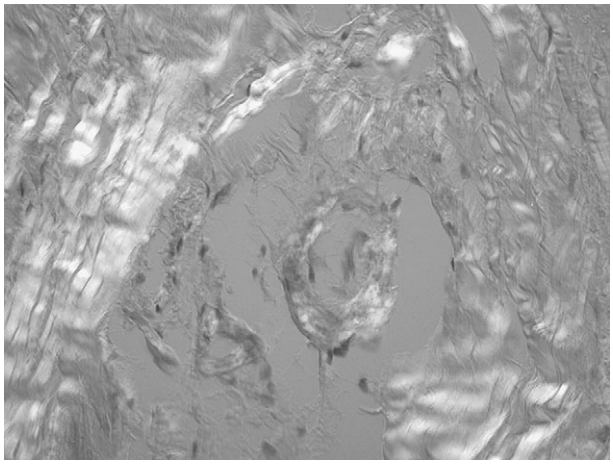

Fig. 4. Pathology.

AL amylodosis is a rare cause of SPH. Acquired hemostatic abnormalities, including factor Xa deficiency, hyperfibrinolysis and platelet dysfunction, can be regarded as important pathogenetic factors in AL amyloidosis. This patient's bleeding diathesis likely resulted from perivascular/vascular amyloid deposition and factor Xa deficiency [5–7]. Pathology demonstrated amyloid infiltration of blood vessels, which leads to amyloid angiopathy with increased vascular wall fragility and impaired vasoconstriction [8]. In the literature, the mechanisms attributed to factor X deficiency in the setting of amylodosis is thought to be due to binding of factor Xa on amyloid fibrils primarily in the liver and spleen and decreased synthesis of coagulation factors in patients with advanced liver disease due to the infiltrative process [5].

This phenomenon of abnormal bleeding was noted in 94 cases (28%), and the coagulation screen was abnormal in 172 cases (51%). The most common abnormalities were prolongation of the thrombin time (108 cases, 32%) and PT: 82 cases, 24% [9]. Of 368 consecutive patients with systemic AL amyloidosis evaluated at Boston Medical

Center, 32 patients (8.7%) had factor X levels <50% of normal. Eighteen of these patients (56%) had bleeding complications, which were more frequent and severe in the 12 patients <25% of normal; two episodes were fatal [6].

The patient was started on bortezomib and dexamethasone and showed signs of improvement. He underwent cardiac evaluation including cardiac Magnetic Resonance Imaging 1 month after chemotherapy was initiated. The results were consistent with cardiac involvement by amyloidosis (ejection fraction = 63%, basal inferoseptum 1.9 cm). Notably, however, serum troponin T levels had been normal, and the previous elevation of B-type natriuretic peptide had resolved. Serum-free light chains normalized 4 weeks after initiation of chemotherapy, and the last serum and urine immunofixation studies demonstrated no detectable monoclonal protein, consistent with ongoing hematological remission. Improvement in his plasma factor X level suggested a reduction in the overall abundance of amyloid. Thus, aggressive treatment of the underlying plasma cell neoplasm in AL amyloidosis can lead to the amelioration of amyloid-related factor X deficiency [6, 8]. Factor X normally has a long half-life (40 h). Because there is no factor X concentrate available, fresh frozen plasma would have to be used for bleeding episodes until the underlying disease can be controlled. Such temporary replacement is feasible although the response may be short-lived because of amyloid binding to factor X after factor X enters the circulation.

Overall, the patient did very well on therapy with bortezomib and steroids. The main question is whether we could improve his long-term prognosis through high-dose chemotherapy and autologous stem cell transplantation given the cardiac involvement, a particularly fatal complication of amyloidosis. The largest series to date included 312 patients who received high-dose melphalan (100–200 mg/m^2) followed by autologous stem cell transplantation [10]. Patients with cardiac amyloid (ejection fraction of ≥40%) had worse survival than those without cardiac involvement (1.6 versus 6.4 years, respectively), but 10 of 58 patients did show a cardiac response (decrease of ≥2 mm in a thickened intraventricular septum) following transplantation. It is conceivable that treatment with newer agents such as bortezomib may produce long-term outcomes that compare favorably with transplant-based approaches, but currently available data are insufficient to reach this conclusion. For these reasons, we favored pursuing an autologous stem cell transplant as part of his management strategy [6].

Conflict of interest statement. None declared.

References

1. Bosniak MA. Spontaneous subcapsular and perirenal hematomas. *Radiology* 1989; 172: 601–602
2. Zhang JQ, Fieling JR, Zou KH. Etiology of spontaneous perirenal haemorrhage: a meta-analysis. *J Urol* 2002; 167: 1593–1596
3. Polkey HJ, Vynalek WJ. Spontaneous no-traumatic perirenal and renal hematomas. An experimental and clinical study. *Arch Surg* 1933; 26: 196–202
4. Mc Dougal WS, Kursh ED, Persky L. Spontaneous rupture of the kidney with perirenal hematoma. *J Urol* 1975; 114: 181–184
5. Furie B, Greene E, Furie BC. Syndrome of acquired factor X deficiency and systemic amyloidosis in vivo studies of the metabolic fate of factor X. *N Engl J Med* 1977; 297: 81–85
6. Choufani EB, Sanchorawala V, Ernst T *et al.* Acquired factor X deficiency in patients with amyloid light-chain amyloidosis: incidence, bleeding manifestations, and response to high-dose chemotherapy. *Blood* 2001; 97: 1885–1887
7. Thompson CA, Kyle R, Gertz M *et al.* Systemic AL amyloidosis with acquired factor X deficiency: a study of perioperative bleeding risk and treatment outcomes in 60 patients. *Am J Hematol* 2010; 85: 171–173
8. Yood RA, Skinner M, Rubinow A *et al.* Bleeding manifestations in 100 patients with amyloidosis. *JAMA* 1983; 249: 1322–1324
9. Mumford AD, O'Donnell J, Gillmore JD *et al.* Bleeding symptoms and coagulation abnormalities in 337 patients with AL-amyloidosis. *Br J Hematol* 2000; 110: 454–460
10. Skinner M, Sanchorawala V, Seldin DC *et al.* High-dose melphalan and autologous stem-cell transplantation in patients with AL amyloidosis: an 8-year study. *Ann Intern Med* 2004; 140: 85–93

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