# Massive haematuria successfully managed by intravesical ankaferd in a haemodialysis patient complicated with disseminated intravascular coagulation

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**To cite:** Solak Y, Gaipov A, Ozbek O, *et al*. *BMJ Case Reports* Published online: 24 December 2012 doi:10.1136/bcr-2012-006699

## SUMMARY

Massive haematuria is a life-threatening condition, demanding immediate management of bleeding. The mortality is very high in the case of delayed management of bleeding, especially in elderly patients with concomitant comorbidity. The treatment options of haematuria are wide, and depend on underlying conditions. However, therapeutic choices are limited in the presence of massive and intractable haematuria caused by disseminated intravascular coagulation (DIC). Ankaferd blood stopper (ABS) is a novel, commercially available, haemostatic agent, which has been approved by the Ministry of Health for local use in Turkey. Here, for the first time in the literature, we report a case of diffuse intravesical bleeding stopped by intravesical use of ABS in a 72-year-old man, haemodialysis patient complicated with sepsis and DIC.

## BACKGROUND

Sepsis and disseminated intravascular coagulation (DIC) are inter-related conditions and can be seen in critically ill patients.[1] End-stage renal disease patients with inadequate dialysis and malnutrition have increased the risk of chronic inflammation and sepsis.[2] DIC usually presents with gastrointestinal tract, internal bleedings and external haemorrhages from intervention sites as well as derangements in coagulation parameters. To the best of our knowledge, isolated diffuse mucosal bleeding from the urinary bladder without apparent bleeding from other body parts in the case of DIC has never been reported to date.

Massive and intractable haematuria is a life-threatening condition, and is characterised by a severe blood loss and high mortality in delay of prompt treatment. Often, gross haematuria can accompany several diseases including urinary tract trauma and malignancy, leucaemia, haemangiomas, some renal parenchymal diseases and drug toxicities.[3] In general, gross bladder haemorrhage had been treated by intravesical irrigations of alum, formalin and prostaglandins, hydrodistention of the bladder and embolisation, depending on severity of haematuria and underlying conditions.[4] Unfortunately, nowadays many of these treatment modalities are obsolete because of their complications and/or unavailability.

Ankaferd Blood Stopper (ABS; Ankaferd Drug Cosmetic Co., Istanbul, Turkey) is a standardised mixture of five plant extracts, including 5 mg *Thymus Vulgaris*, 9 mg *Glycyrrhiza Glabra*, 8 mg *Vitis Vinifera*, 7 mg *Alpina Officinarum* and 6 mg *Urtica Dioica*, in a 100 ml of Ankaferd solution.[5] It is usually applied to stop superficial bleeding. The basic mechanism of action of ABS is the rapid induction of protein network in human blood that provides focal points for vital erythrocyte aggregation without affecting the coagulation factors.[6] Here, for the first time in the literature, we report a case of massive haematuria which was stopped by intravesical ABS irrigation.

## CASE PRESENTATION

A 72-year-old man who was undergoing maintenance haemodialysis for 5 months was admitted to our nephrology inpatient unit with complaints of weakness, anorexia, weight loss, nausea and vomiting. The patient had prostate hyperplasia for which he had undergone transurethral resection operation. The aetiology for end stage renal disease (ESRD) was unknown. His medical history was unremarkable. We investigated for an occult malignancy. At admission he had bilateral 1+ pretibial oedema and bilateral crackles at both lung bases. His blood pressure was 90/60 mm Hg. Heart auscultation revealed tachycardia (108/min) without any murmurs. Other aspects of physical examination were normal.

## INVESTIGATIONS

Laboratory data at presentation were as follows: urea 43 mg/dl, creatine 3.99 mg/dl, sodium 135 mEq/l, potassium 3.8 mEq/l, calcium 7.6 mg/dl, phosphorus 5.4 mg/dl, ESR 120 mm/h, C reactive protein (CRP) 41.4 mg/l, AST: 22 μ/l, ALT 12 μ/l, albumin 2.1 g/dl, total protein 6.6 g/dl, haemoglobin 8.4 g/dl, platelet count $410\times10^3/mm^3$, white blood cell (WBC) count $11.6\times10^3/mm^3$, ferritin 1032.5 ng/ml, i-PTH 12.3 pg/ml, CK-MB 1.7 ng/ml, troponin 0.04 ng/ml. Thoracal CT, abdomen and pelvic ultrasound examinations did not reveal any pathology. The patient continued his haemodialysis three times a week, schedule during the course of hospitalisation.

## DIFFERENTIAL DIAGNOSIS

Haematuria may be microscopic when urine is normal in colour, but there is an increased number of red blood cells (RBC) seen under a microscope, and macroscopic (gross haematuria), when we can see blood in the urine as pink, red or tea coloured. Several diseases can be presented with gross

haematuria and most common for elderly patients are neoplasma (bladder or renal cancer), benign prostatic hyperplasia and nephrolithiasis. Primary or secondary nephritis, urinary tract infection or trauma, polycystic kidney diseases and many haemotologic diseases can be one of the frequent causes of gross haematuria. In our case, massive intravesical bleeding was a single clinical symptom of DIC in elderly patients with ESRD.[3 7 8]

## TREATMENT

At the sixth day of admission WBC count increased to $14.1\times10^3/mm^3$. CRP and procalcitonin were 73.8 mg/l and <0.05 ng/ml, respectively. We started piperacillin/tazobactam at 2.25 g three time a day. The general condition of the patient worsened at 11th day of hospitalisation; he gradually became unconscious and developed urinary retention for which we placed a urethral catheter. In total, 1500 ml of grossly bloody urine was evacuated via urethral catheter. At this time serum haemoglobin was 7.77 g/dl, WBC $22.7\times10^3/mm^3$, CRP 96.1 mg/l and procalcitonin 0.915 ng/ml. The patient was transfused with RBC suspensions and fresh frozen plasma (FFP). Transcatheter (retrograde) intravesical saline irrigation was performed to prevent obstruction of the urethra with blood clots. Antibacterial coverage was expanded with meropenem and teicoplanin. Cranial CT did not show any pathology. There was no neck stiffness and neurological examination did not demonstrate lateralising findings. With these measures, bleeding from the bladder did not stop and an urgent cystoscopy was undertaken to control the bleeding lesion. Cystoscopy revealed diffuse and extensive mucosal haemorrhage without any mass lesion. DIC diagnosis was confirmed with laboratory parameters including thrombocytopenia, hypofibrinogenemia and increased levels of d-dimer and fibrin degradation products. Despite intensive treatment of DIC and sepsis, massive haematuria was continued. During the treatment of DIC, 26 units of RBC suspension and 14 units of FFP were used. We used ABS for the treatment of diffuse intravesical haemorrhage. After initial saline irrigation, we administered intravesically 8 ml of ankaferd mixed with 400 cc saline and clamped transurethral catheter for 30 min. Gross haematuria was significantly reduced, but did not disappear. This procedure was repeated after 8 h, and finally haematuria was stopped.

## OUTCOME AND FOLLOW-UP

Intravesical bleeding did not recur thereafter. Haemoglobin levels increased to 11.9 g/dl. General condition of the patient worsened, and the patient died at the 60th day of hospitalisation because of refractory septic shock.

## DISCUSSION

Our case showed a typical clinical picture of an ESRD patient complicated with sepsis and DIC. Massive intravesical bleeding was an early and sole clinical symptom of DIC. Interestingly, to the best of our knowledge, there is no case report in which gross haematuria was the only clinical manifestation of DIC. Actually, because of this eccentric manifestation, we did not suspect underlying DIC, until we observe the diffuse mucosal bleeding from bladder walls and laboratory DIC diagnosis was evident. We thought that gross haematuria in an elderly male patient with haemodialysis was either due to bladder or prostate cancer. However, cystoscopy did not reveal such a finding. Surprisingly, the patient did not have other manifestations of DIC such as petechia/purpura, oral mucosal and gastrointestinal bleeding, oozing from venipuncture sites or internal haematoma. After excluding an underlying urinary tract malignancy, we were directed to the possibility of DIC in the context of severe sepsis. Laboratory parameters also confirmed the diagnosis of DIC.

Treatment actions in DIC based on treatment of underlying disorders if possible and correction of the deranged coagulation system mainly by FFP. Other agents such as fibrinogen, cryoprecipitate, platelet concentrates and antithrombotic drugs are adjunctive measures in the management of DIC.[1]

The algorithm of treatment actions in massive haematuria varies according to underlying diseases. Surgical treatments were well performed in the case of traumatic injury of the urinary tract and haemangiomas of bladder.[9] Some cases reported that gross haematuria caused by acute leucaemia was successfully treated with chemotherapy.[10] Topical management of bladder bleeding is one of the main treatment options. Treatment modalities such as irrigation of alum, formalin and fibrin-glue agents were reviewed by Choong *et al*.[4] However, most of these treatment actions are obsolete because of their low response and high complication rates. Besides, they require anaesthetic support.

ABS, as a novel haemostatic agent, has never been administered intravesically in a haematuric patient. We attempted to administer it after trying other conventional measures. There is a clinical experience in a few settings of mucosal bleeding with ABS. ABS was successfully used to manage the upper and lower gastrointestinal bleedings,[11 12] in the treatment of bleedings following total thyroidectomy, adenoidectomy and nephrectomy.[13–15] There is an animal model in which ABS was found to be effective in urinary bladder bleeding.[16] Study was conducted in 20 rats with surgically damaged mucosal wall of the bladder and compared efficacy of ABS versus 0.9% NaCl to stop the bleeding. Morphological examination was also performed to determine the histopathological changes of the bladder mucosa with ABS application. The results showed that ABS significantly decreased the bleeding duration and did not induce any fibrotic change in a rat bladder tissue.

In conclusion, massive haematuria is a life-threatening condition and can be a unique clinical symptom of DIC. This association should be kept in mind to make up prompt diagnosis and to choose correct algorithm of the treatment action. Our case illustrates the first example of successful application of ABS to stop massive haematuria. To consolidate this preliminary observation, further studies are needed to test efficacy of ABS in gross haematuria.

### Learning points

- Massive haematuria is a life-threatening condition and requires immediate management of bleeding.
- Massive intravesical bleeding may be an early and the sole clinical symptom of disseminated intravascular coagulation.
- Ankaferd blood stopper (ABS) is a novel haemostatic agent, and is a standardised mixture of five plant extracts, including 5 mg *Thymus Vulgaris*, 9 mg *Glycyrrhiza Glabra*, 8 mg *Vitis Vinifera*, 7 mg *Alpina Officinarum* and 6 mg *Urtica Dioica*, in a 100 ml of solution.
- ABS can be successfully used for the management of massive intravesical bleeding.

**Competing interests** None.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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