Ascites : not always the usual suspects

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Abstract

A case report of a 44-year-old woman with an infrequent cause of ascites, i.e. intraperitoneal urine leakage, is presented.

Urinary ascites due to spontaneous bladder rupture or fistula after radiation therapy for cervical cancer is not a rare complication and can develop several years after initial treatment.

Diagnosis of urinary ascites should be suspected in patients with ascites and a history of radiation therapy for a bladder or a gynaecological disease.

Measurement of urea and creatinine levels in urine, ascites and plasma is a simple and non-invasive diagnostic test. In physiological conditions, the ascites/plasma creatinine ratio approximates a ratio of one to one. This ratio is elevated to a value of ≥ 5/1 in case of urinary ascites.

Although cystoscopy and imaging techniques such as cystography and computed tomography (with or without cystography) are extremely helpful, definitive diagnosis is frequently based on intraoperative findings, because of the lack of pathognomonic symptoms or signs.

Surgery is the treatment of choice. (Acta gastroenterol. belg., **2012**, 75, **45-48**).

Key words : ascites, cirrhosis, bladder leakage, radiotherapy, radiation cystitis.

Abbreviations

SAAG : serum-to-ascites albumin gradient
Hb : hemoglobin
AST : aspartate aminotransferase
ALT : alanine transaminase
yGT : gamma glutamyl transpeptidase
CRP : C-reactive protein
LDH : lactate dehydrogenase
PMN : polymorphonuclear leukocytes

Introduction

Ascites is in almost 85% of all cases caused by cirrhosis. The other main causes are malignancy (10%), cardiac failure (3%), tuberculosis (2%) and pancreatitis (1%). Ascites due to urinary leakage is rare (1). In the diagnostic work-up, the two main issues that arise regarding ascites are the presence of ascitic fluid infection and portal hypertension. Abdominal paracentesis and appropriate ascitic fluid analysis with calculation of the serum-to-ascites albumin gradient (SAAG) can diagnose portal hypertension with approximately 97% accuracy when the SAAG is greater than or equal to 1.1 g/dL (2). However, as will be demonstrated in this case, when facing ascites, it is always necessary to use a broad diagnostic framework and also consider 'unusual suspects'.

Case report

A 44-year-old woman was admitted because of abdominal pain with signs of intestinal subobstruction, ascites and dyspnoea with bilateral pleural effusion. She had a history of a stage IB spinocellular cervical carcinoma treated with neoadjuvant chemoradiotherapy and radical hysterectomy in 2000. In 2005, she was admitted to another hospital with abdominal pain and ascites, with spontaneous recovery and no signs of tumour recurrence but no further diagnosis at that time. The patient lived in a social housing facility, was unemployed, had a 25 pack-year smoking history and reported a regular alcohol use of 6 units a day. On examination, her blood pressure was 92/60 mm Hg, heart rate 102 beats per minute, and temperature 36.2°C. She had a cachectic appearance and weighed 38 kg (for a height of 158 cm) on admission. The cardiac examination was normal. On pulmonary examination, there were diminished breath sounds in the basal areas on both sides. There was abdominal distension and slight diffuse but no rebound tenderness on palpation. There was a normal appearance of the lower extremities with absence of oedema.

Laboratory blood results showed elevated inflammatory parameters and elevated liver enzymes (Table 1).

Because of evolution towards respiratory insufficiency, the patient was transferred to the intensive care unit. Thoracocentesis showed a transudative effusion (Table 2). A pleural pigtail catheter was inserted for continuous drainage with good clinical response. Cytological analysis of the pleural fluid was negative. A tuberculin skin test was negative, as was the Ziehl-Neelsen stain on the pleural fluid.

A thoracoabdominal CT-scan with intravenous contrast enhancement showed the presence of diffuse ascites, bilateral pleural effusion and absence of pulmonary or intra-abdominal lesions.

An abdominal paracentesis with ascitic fluid analysis was performed (Table 3). This showed a SAAG of 2.8 g/dL which was compatible with portal hypertension. The ascitic neutrophil count was 1021/μL, diagnostic of

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Table 1. — **Laboratory blood results**

		Normal value
Hb	11.2 g/dL	11.7-15.7
White blood cell count	31500/μL	4-10000
Blood Platelets	166000/μL	149-409000
Prothrombine time	48%	70-120
Total bilirubin	1.9 mg/dL	0.3-1.2
AST	36 U/L	0-31
ALT	105 U/L	7-31
yGT	348 U/L	9-36
Alkaline phosphatase	182 U/L	30-120
CRP	16.1 mg/dL	0-0.5

Table 2. — **Analysis of pleural fluid**

		Normal value
White blood cells	280/μL	0-1000
Total protein	2.2 g/dL	
Glucose	1.12 g/L	
LDH	120 U/L	

Table 3. — **Ascitic fluid analysis**

White blood cells	1380/μl
PMN	74%
Red blood cells	< 30000/μl
Albumin	0.6 g/dl
Glucose	1.12 g/L
LDH	774 U/L

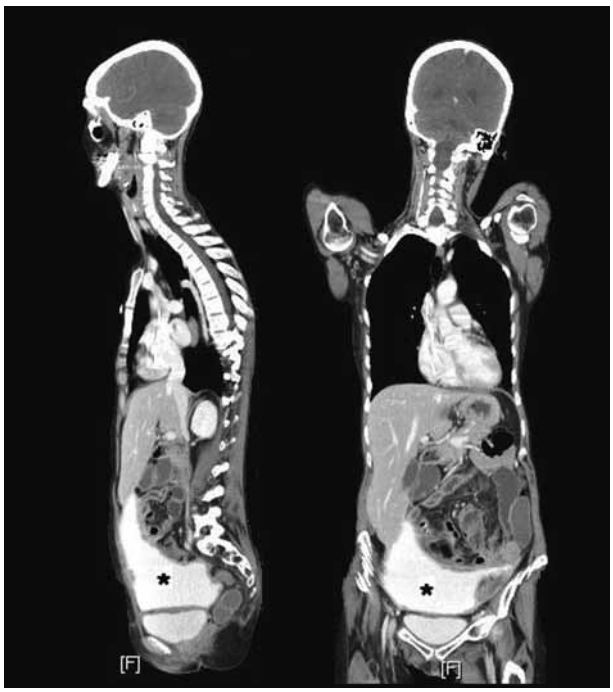

Fig. 1. — Computerized tomography scan showing a large contrast-filled intraperitoneal collection (asterisk) indicating intraperitoneal urine leakage.

spontaneous bacterial peritonitis. Gram's stain, Ziehl-Neelsen stain and culture were negative, and the patient was treated with intravenous amoxicillin-clavulanic acid. Ascitic cytology analysis showed no arguments for malignancy.

Given the history of alcohol abuse and the suspicion of portal hypertension, alcoholic liver cirrhosis was suspected. An ultrasonography of the liver with duplex sonography of the hepatic veins and the portal vein was normal, which could rule out Budd-Chiari syndrome, veno-occlusive disease or portal vein thrombosis. Viral and auto-immune serology were negative and there was no cirrhosis configuration on CT. A liver biopsy was performed which demonstrated grade 1 steatosis and scarce cholestasis without fibrosis. Transjugular measurements showed a wedged hepatic vein pressure of 7 mm Hg, a free hepatic vein pressure of 3 mm Hg and a hepatic vein pressure gradient of 2 mm Hg, excluding portal hypertension.

Echocardiography showed no arguments for systolic or diastolic heart failure and absence of signs of pericarditis constrictiva or restrictive cardiomyopathy. Gynaecological examination showed no signs of malignant tumour recurrence. A 24 h-urine collection showed no arguments for a nephrotic syndrome.

Since the analysis of the ascites pleaded for portal hypertension, unlike the fact that a transjugular liver catheterisation with measurement of the hepatic venous pressure gradient could exclude portal hypertension, all the performed examinations and results were re-evaluated.

Because of the history of cervical cancer, malignant recurrence was strongly suspected, despite the normal cytological analysis of ascites and pleural fluid and the normal gynaecological work-up. An additional PET-CT was ordered. The CT-images showed a large contrast-filled intraperitoneal collection, indicating intraperitoneal urine leakage (Fig. 1). This had not been seen on the first CT-scan because there was no delayed excretory phase obtained. The supplementary analysis of the original ascites samples on admission showed a creatinine concentration of 14.42 mg/dL and a urea concentration of 2.09 g/L, which resulted in an ascites/plasma creatinine ratio of 20/1. This indeed suggested a urinary origin of the ascites. Post hoc analysis of the pleural fluid was not possible. A supplementary cystoscopy was performed, confirming an organised fistula at the posterior wall of the bladder with urinoma formation.

The patient underwent an exploratory laparotomy with cystotomy and excision of the fistula tract. Anatomopathological examination of the surgical specimen showed presence of granulation tissue and was negative for malignant cells. The patient recovered well

during the postoperative phase with no recurrence of intra-abdominal fluid accumulation.

Discussion

Ascites caused by urine leakage out of the urinary tract is a relatively rare entity. It can be the result of trauma or spontaneous bladder perforation due to an outlet problem of the bladder or due to bladder wall lesions (3,4).

Urinary ascites as a result of an outlet problem of the bladder is frequently observed in newborns with vesicoureteral reflux or obstruction. Outlet obstruction of the bladder is also seen in neurological diseases (tabes dorsalis, multiple sclerosis, myelomeningocele, tumours with nerve involvement) and in case of detrusor-sphincter dyssynergia. Radiation therapy can as well induce degeneration or fibrosis of the pelvic nerve, which can result in neurogenic bladder dysfunction (3,4,5). Organic bladder or urethral lesions (bladder neck papilloma, stricture, calculus, periurethral inflammation and tumours) may also cause obstruction. Uterine prolapse or enlargement, adnexal disease or tumour, impacted gravid uterus or obstructed labour are other possible causes (5).

Spontaneous bladder perforation due to pathological bladder wall changes has already been described in patients who received radiotherapy for cancer of the bladder, uterus or cervix (3). Late complications of radiation therapy for cervical cancer occur in about 5 to 15% of patients (3). Frequent complications are fibrosis, hematuria due to radiation cystitis, and development of a urinary fistula or a ureteral/urethral stricture. The incidence of these complications is related to the radiation dose, fractionation and the volume irradiated (3). A spontaneous rupture of the bladder is less common and is often caused by radiation cystitis. In a group of 143 retrospectively followed patients with cervical carcinoma who underwent high-dose intracavitary brachytherapy, three (2.1%) developed intraperitoneal rupture of the urinary bladder (3). The incidence of this complication appeared to be not infrequent compared with those of other complications, such as irradiated bladder, ureteral/urethral stricture, and fistula.

In our patient, several predisposing factors for spontaneous bladder rupture were identified : radiation cystitis (caused by radiation-induced obliterative endarteritis, which diminishes the blood supply in the vesical arteries), prior surgery, radiotherapy of the bladder dome, and possibility of hysterectomy-induced neurogenic bladder.

Spontaneous bladder perforation has also been described in other types of bladder wall lesions like tuberculous and non-tuberculous cystitis, carcinomatous infiltration of the bladder wall, prolonged use of cyclophosphamide, bladder diverticula, and in case of atherosclerotic plaque emboli.

Spontaneous perforation is mostly seen intraperitoneal (extraperitoneal perforation is generally associated with traumatic events) at the level of the superoposterior bladder wall which is the thinnest portion of the bladder and offers the least resistance to a sudden change in intravesical and intra-abdominal pressure (5).

A simple and non-invasive test in establishing the diagnosis is measurement of urea and creatinine levels in urine, ascites and plasma. Normally, urinary creatinine levels are much higher than those in plasma. In case of intraperitoneal urine leakage, the ascitic creatinine levels fluctuate somewhere between those in plasma and urine. This can be explained by the high resorption rate of creatinine from the peritoneal cavity towards the plasma (down the concentration gradient) and the hyperosmolarity of urine which leads to a progressive increase in the volume of the ascitic fluid. The net effect is an ascitic creatinine level in between that of plasma and urine. In physiological conditions, the ascites/plasma creatinine ratio approximates a ratio of one. This ratio is elevated to a value of ≥ 5/1 in case of urinary ascites (5). The ascitic creatinine level in this patient (measured by retrospective analysis on an earlier sample) showed a creatinine level of 14.42 mg/dL leading to an ascites/plasma creatinine ratio of > 20/1. Further specific diagnostic work-up consists of computed tomography (with or without cystography), retrograde cystography and cystoscopy, which is also used to exclude other bladder pathology.

The primary treatment is surgery, with identification and confirmation of the bladder wall defect, lavage of the peritoneal cavity, wide excision of the bladder wall defect, reconstitution of the intact bladder and prolonged suprapubic or urethral drainage of the bladder to assure adequate healing. Explorative surgery is also used to exclude primary or recurrent malignant disease (3,4).

In conclusion, we can state that spontaneous intraperitoneal rupture of the urinary bladder after radiation therapy for cervical cancer is not a rare complication and can develop several years after the initial treatment. Diagnosis of this condition is very difficult because of the lack of pathognomonic symptoms or signs. Mortality of bladder rupture is not low and mortality rates of more than 25% have been described (6). Therefore, the possibility of a spontaneous bladder rupture has to be considered when a patient presents with lower abdominal pain after radiation therapy. When facing a patient with ascites and a history of radiation therapy for a bladder or a gynaecological disease, intraperitoneal urine leakage has to be excluded. In this case, the a priori probability for ascites due to alcoholic cirrhosis seemed high. The serum-to-ascites albumin gradient (SAAG) was high (2.8 g/dL), which pointed in the direction of portal hypertension. However, the SAAG was falsely elevated because, in fact, it was a serum-to-urine gradient. Other elements that put us on the wrong track were the elevated liver enzymes (mainly ALT and yGT), the (initial) abnormal clotting tests and the fact that the patient came from a socially deprived area, was a heavy smoker, had a cachectic appearance and reported a regular alcohol use of 6 units a day. As this case illustrates, in determin-

ing the underlying aetiology of ascites, particularly in patients with a history of alcohol abuse or those with a history of malignancy it remains important to use a broad diagnostic framework and also acknowledge 'unusual suspects'.

References

1. RUNYON B.A. Management of adult patients with ascites due to cirrhosis : an update. *Hepatology*, 2009, **49** : 2087-2107.
2. RUNYON B.A. *et al*. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. *Ann. Intern. Med*., 1992, **117** : 215-220.
3. FUJIKAWA K., YAMAMICHI F., NONOMURA M., SOEDA A., TAKEUCHI H. Spontaneous rupture of the urinary bladder is not a rare complication of radiotherapy for cervical cancer : report of six cases. *Gynecol. Oncol*., 1999, **73** : 439-42.
4. ADDAR M.H., STUART G.C., NATION J.G., SHUMSKY A.G. Spontaneous rupture of the urinary bladder : a late complication of radiotherapy. Case report and review of the literature. *Gynecol. Oncol*., 1996, **62** : 314-6.
5. PEETERS P., COLLE I., SENNESAEL J., VERBEELEN D. Relapsing ascites and uremia due to urinary bladder leakage. *Eur. J. Intern. Med*., 2001, **12** : 60-63.
6. PISER J.A., KAMER M., ROWLAND R.G. Spontaneous bladder rupture owing to atherosclerotic emboli : a case report. *J. Urol*., 1986, **136** : 1068-70.