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Clinical report

Atypical new-onset ascites due to a rare variant of cecal carcinoma in a patient with a ventriculoperitoneal shunt: A case report

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ABSTRACT

Introduction: Malignancy-associated ascites (MAA) is the second cause of new-onset ascites after cirrhosis with portal hypertension (PHT), and is usually related to peritoneal carcinomatosis. Ascitic fluid is an exudate, with low serum-ascites albumin gradient (SAAG), ≥500 lymphocytes/mm^3 and positive cytology. However, MAA may show atypical patterns. Signet ring cell carcinoma (SRCC) is a poor prognosis adenocarcinoma subtype with special clinical and endoscopic presentation.
Case summary: A 68-year-old female, without relevant medical history, with a ventriculoperitoneal shunt (VPS), presented a 1-week increase of abdominal perimeter, loose stools, hyporexia, and fever. In repeated paracentesis, ascites showed transudate properties, high SAAG, low cellularity, negative cultures, and cytologies. She didn't have neurological impairments nor VPS dysfunctions. Significant PHT and other ascites etiologies were excluded. Ascites persisted despite evacuation paracentesis and diuretics. Further diagnostic workup finally revealed peritoneal carcinomatosis probably originated in a cecal SRCC.
Conclusions: We report an atypical presentation of MAA (transudative ascites, SAAG suggesting PHT, low cellularity, and initially negative cytology) due to a rare adenocarcinoma subtype, representing a challenge regarding its unusual characteristics and difficulties to reach a final diagnosis.

Ascitis atípica de debut por una variedad rara de carcinoma de ciego en una paciente portadora de derivación ventrículo-peritoneal: reporte de un caso

Palabras clave:
Ascitis
Carcinomatosis Peritoneal
Hipertensión Portal
Cáncer Cecal
Adenocarcinoma de Colon
Carcinoma de Células en Anillo de Sello

RESUMEN

Introducción: La ascitis asociada a malignidad (AAM) es la segunda causa de ascitis de debut después de la cirrosis con hipertensión portal (HP) y suele relacionarse a carcinomatosis peritoneal. El líquido ascítico es un exudado, con gradiente de albúmina suero-ascitis (GASA) bajo, ≥500 linfocitos/mm3 y citología positiva. Sin embargo, la AAM puede presentar patrones atípicos. El carcinoma de células en anillo de sello (CCAS) es un subtipo de adenocarcinoma de mal pronóstico con una presentación clínica y endoscópica características.
Resumen del caso: Una mujer de 68 años, sin antecedentes de interés, portadora de una derivación ventrículo-peritoneal (DVP), consultó por aumento del perímetro abdominal, deposiciones diarreicas, hiporexia y fiebre de una semana de evolución. En paracentesis repetidas la ascitis presentaba características de trasudado, GASA alto, baja celularidad y resultado negativo para cultivos y citologías. Se excluyeron alteraciones neurológicas y malfuncionamiento de la DVP. La HP significativa y otras etiologías de ascitis fueron descartadas. La ascitis persistió pese a paracentesis evacuadoras y diuréticos. Tras realizar pruebas complementarias adicionales finalmente se objetivó la presencia de carcinomatosis peritoneal probablemente originada en un CCAS del ciego.
Conclusiones: Describimos una presentación atípica de AAM (trasudado, GASA sugestivo de HP, baja celularidad y citología inicialmente negativa) debido a un subtipo raro de adenocarcinoma, lo que representa un reto clínico considerando sus características inhabituales y las dificultades para conseguir un diagnóstico definitivo.

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Table 1
Blood test analysis on admission.

Laboratory parameter and normal range	Patient's value
C-reactive protein [<1 mg/dL]	**9.7**
Leukocytes [4.0–11.0 × 10^9/L]	**15.1**
Neutrophils [2.0–7.0 × 10^9/L]	**9.8**
Hemoglobin [120–150 g/L]	**88**
Platelets [130–400 × 10^9/L]	**407**
Aspartate aminotransferase (AST) [5–40 IU/L]	**62**
Alanine aminotransferase (ALT) [5–40 IU/L]	25
Gamma-glutamyl transferase (GGT) [5–40 IU/L]	**161**
Alkaline phosphatase (ALP) [46–116 IU/L]	**150**
Total bilirubin [0.2–1.2 mg/dL]	0.6
Albumin [34–48 g/L]	**28**
Total proteins [63–80 g/L]	**58**
Prothrombin time [80.0–100.0%]	**52**
Partial thromboplastin time [23.5–32.5 s]	**34.2**

Introduction

MAA is the second leading cause of new-onset ascites, representing up to 10% of cases, after cirrhosis with PHT.[1] Peritoneal carcinomatosis (PC) is the underlying mechanism of MAA in more than 60% of patients, and lung cancer is the most frequently associated solid tumor to PC, with colon cancer accounting for around 13% of cases.[2] Amongst colon cancer patients, right-sided cancer and signet ring cell differentiation pose major risk factors for developing PC.[3,4] MAA with PC usually presents with ascitic fluid consistent of an exudate (proteins ≥2.5 g/dL), SAAG <1.1 g/dL, lymphocytes ≥500 cells/mm^3, and positive cytology. However, more than a quarter of patients with MAA show ascites consistent with PHT fluid (SAAG >1.1 g/dL and proteins <25 g/L) and others may present mixed patterns.[2]

Colon signet ring cell carcinoma (SRCC), a rare subtype of adenocarcinoma accounting for ~1% of colorectal cancers, is usually located in the right colon as a diffuse wall thickening instead of an intraluminal mass, leading to difficulties on recognition, and consequently an advanced stage diagnosis and poor overall survival.[4–6]

Case presentation

We present the case of a 68-year-old female, ex-smoker (cumulative tobacco consumption 45 packs/year), without alcohol use disorder nor current hepatic disease. One month previously to consulting a ventriculoperitoneal shunt (VPS) was placed as a treatment for normal pressure hydrocephalus, without any complications related to the procedure. She had a past medical history of solved hepatitis during childhood, depressive syndrome, lumbar spondylolisthesis, and osteoarthritis. She was under regular treatment with paroxetine, diazepam, pregabalin, omeprazole, and metamizole.

She attended the emergency department due to a 1-week history of increased abdominal perimeter, change in bowel habit consisting of loose stools without blood or mucus, hyporexia, and fever (37.5 °C). She associated gait instability and recurrent falls for the last month, without headache, visual disturbances, executive dysfunction, incontinence, or other neurological symptoms. At initial evaluation, she had no fever and vital signs were normal. Physical examination didn't reveal any new focal neurological deficit, surgical wound was not infected, breast and cervical nodes were palpable, abdomen was painless and distended suggesting new-onset ascites, together with peripheral edemas.

Blood tests results on admission are shown in Table 1, revealing elevated C-reactive protein, leukocytosis, neutrophilia, anemia, slightly elevated AST, GGT, and ALP with normal bilirubin, hypoalbuminemia, hypoproteinemia, and coagulation abnormalities. Urinalysis, cerebrospinal fluid studies, and blood cultures were normal.

An abdominal X-ray and cranial computed tomography (CT) were performed revealing that VPS was properly located and hydrocephalus remained stable, and discarded signs of bleeding. A chest X-ray only revealed mild bilateral pleural effusion (Fig. 1). Abdominal ultrasound and CT again showed a normopositioned shunt catheter, marked diffuse ascites, and normal liver morphology. Hepatotropic viruses testing was negative. An evaluation by the Neurosurgery department was requested which ensured normal functioning of VPS and patient was admitted to hospital for further diagnostic evaluation of new-onset ascites.

Repeated diagnostic paracentesis were performed on admission and at day 5, 12, and 19 after admission with results as shown in Table 2. Serum albumin levels on day 19 were 26 [34–48 g/L]. Serum tumor markers revealed CA-125 516 [<40 U/mL], CA-15.3 661 [<40 U/mL]. Neuroimaging was repeated with a normal cerebral magnetic resonance. An upper endoscopy didn't show any lesions nor endoscopic signs of PHT. Ultrasound tests were performed, revealing normality in uterus and breasts, showed no signs of ovarian masses and dismissed a gynecological origin of ascites. An echocardiogram was normal, excluding cardiac ascites.

Taking into account a high SAAG, >1.6 g/dL, and a low, 0.19, ascites-serum protein ratio (ASPR),[8] together with ascitic proteins <25 g/L compatible with a transudate, these findings suggested PHT but no signs of hepatic disease had been found in any of imaging tests performed.

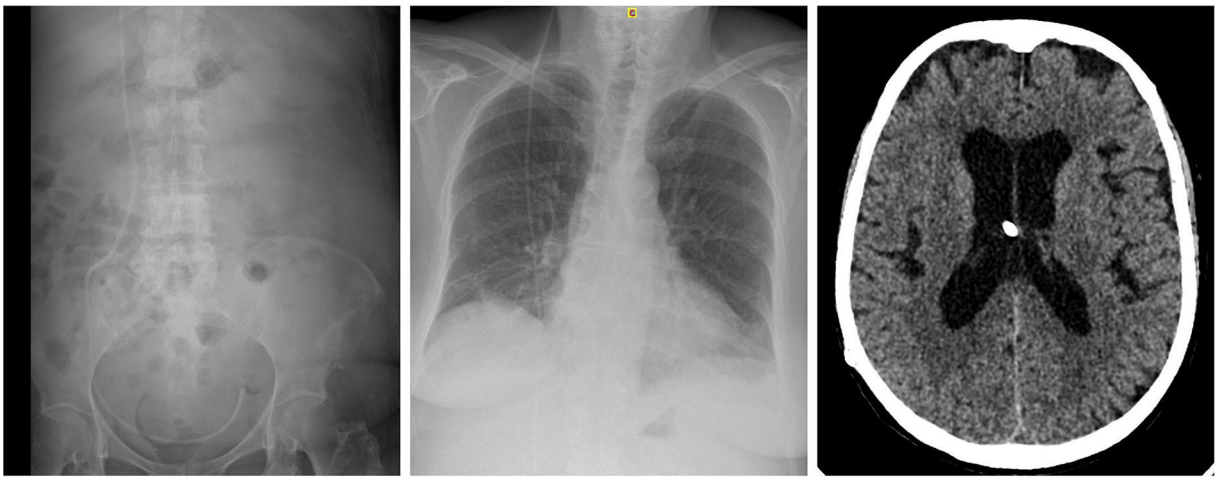

Fig. 1. Initial abdominal X-ray, chest X-ray, cranial CT.

Table 2
Repeated diagnostic paracentesis. Ascitic fluid analysis.

Parameter and normal range	Admission	Day 5	Day 12	Day 19
Macroscopic features [clear, straw-colored]	Clear, straw-colored	Clear, straw-colored	Clear, straw-colored	Clear, straw-colored
Proteins [<30 g/L]	**11**	**11**	**12**	<**10**
Albumin [<30 g/L]				<**10**
Erythrocytes [<1000 cells/mm^3]	20	90	430	
Nucleated cells [<500 cells/mm^3]	240	240	260	
Neutrophils [3–33%]			40	
Lymphocytes [<50%]			37	
Glucose [65–110 mg/dL]	86	113	118	156
Lactate dehydrogenase [<400 IU/L]			66	56
Adenosine deaminase [8.6–20.5 IU/L]			13	
Microbiological culture [negative]	Negative	Negative	Negative	
Acid-fast bacilli stain [negative]		Negative	Negative	
Cytology [non-malignant]	Non-malignant	**Initially: non-malignant (Reassessment: atypical cells positive for carcinoembryonic antigen)**	Non-malignant	

New radiological tests were performed to identify the origin of ascites and a thoracoabdominal CT scan revealed a cecum wall thickening and multiple sclerotic bone lesions on vertebral lumbar bodies, sacrum and ilium. Positron emission tomography-CT revealed hypermetabolic activity in cecal wall, peritoneum, thoracic lymph nodes, pleura, and bones, with normal activity in stomach and ovaries. A colonoscopy was performed reporting difficulties for luminal distension during insufflation in cecum and thickening of intestinal folds in ileocecal valve region without visible lesions, from which biopsies were taken (Fig. 2). Pathological studies of colon samples revealed cecal mucosa was infiltrated by signet ring cells.

On evolution, the patient presented non-responsive ascites despite repeated evacuative paracentesis and diuretic therapy (furosemide plus spironolactone), functional decline, development of nausea, and worsening of hyporexia. Meanwhile, analytical impairments showed no improvement since consulting, except for resolution of leukocytosis, with persistent elevated C-reactive protein, and no variations in hepatic function tests, coagulation parameters, and blood count. Renal function remained in range for the whole hospitalization.

A delayed complementary test on cytology from diagnostic paracentesis at day 5 (Table 2) revealed atypical cells positive for carcinoembryonic antigen, suggesting a malignant adenocarcinoma origin.

The final diagnosis was a new-onset MAA, of atypical characteristics, due to peritoneal carcinomatosis in a patient with a disseminated signet ring cell carcinoma probably originated from a cecum adenocarcinoma. Patient associated tumor extension to mesentery, thorax, and bones, and a recent history of uncomplicated VPS placement.

Oncospecific treatment was dismissed and palliative care support was started in accordance with the patient, who unfortunately died some weeks after admission.

Discussion

Macroscopic characteristics, SAAG, protein quantification, and cell count are considered initial ascitic fluid tests in new-onset ascites in order to elucidate its etiology.

Amongst potential causes of high SAAG ascites, cirrhosis with PHT, hepatic vein obstruction, congestive heart failure, nephrotic syndrome, and other etiologies were excluded. Considering that the patient had a recent placement of a VPS, sterile cerebrospinal fluid ascites, a rare complication that may present with SAAG >1.1 g/dl and low ascitic proteins,[7] was also dismissed. ASPR, a novel approach in evaluating ascites proteins, with greater diagnostic accuracy than SAAG,[8] was 0.19, with results <0.5 also suggesting ascites due to PHT.

Second line testing, including repeated microbiological cultures, cytology, levels of glucose, lactate dehydrogenase, adenosine deaminase,

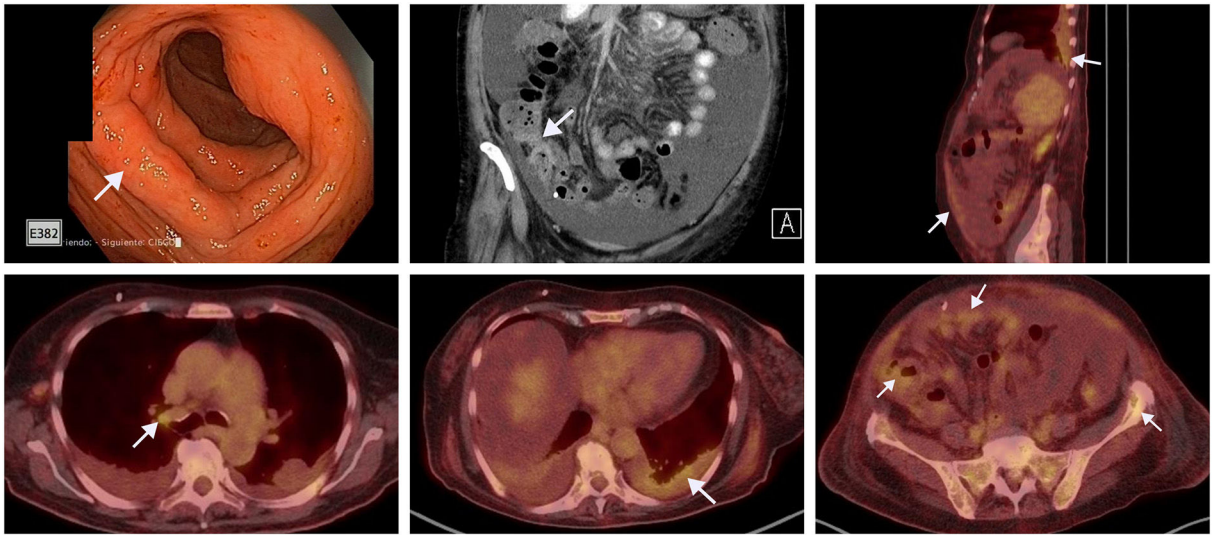

Fig. 2. Endoscopic image revealing intestinal folds thickening in ileocecal valve region. Abdominal CT and positron emission tomography-CT showing cecum wall thickening and hypermetabolic activity in several areas.

and acid-fast bacilli stain were all initially inconclusive. Only after several days a cytology complementary test provided a positive result that led to a final diagnosis. As a consequence, this clinical case represented a diagnostic challenge considering the atypical characteristics of MAA, initially negative cytology, recent VPS placement and difficulties to find an origin for MAA.

This work emphasizes that a neoplastic origin should be considered in patients with ascitic fluid with PHT features, once PHT has been ruled out and with a congruent clinical presentation (change in bowel habit, fever, hyporexia, weight loss). In fact, up to 20% of patients with MAA may present with a transudate, and in rare cases like ours will not meet common characteristics as high lymphocyte count, low SAAG, and positive cytology.[9]

Some limitations were faced for the management and reaching of an unequivocal final diagnosis in this case report since macroscopic mucosal lesions suggestive of adenocarcinoma were not described by optical diagnosis during colonoscopy, and atypical cells compatible with adenocarcinoma were only identified in ascites fluid cytology. However, colon SRCC is a rare subtype of adenocarcinoma with special characteristics on its clinical and endoscopic presentation which may also require an in-depth study to be recognized and identify its origin. Most tumors are infiltrative with exophytic type being unusual, which make it difficult to recognize lesions during colonoscopy, and leading to be diagnosed by histopathology. As a consequence, and in combination with an unspecific clinical presentation, most patients are diagnosed at advanced stages with multiple-site spread and peritoneal dissemination in up to 50% of them. This explains why SRCC has a poorer prognosis compared to non-SRCC adenocarcinomas.[5,6]

The case we report fulfills the clinical and endoscopic presentation previously described in the literature, supporting our final diagnosis. One highly improbable alternative is that these cells had been metastasis from an unknown primary origin considering that stomach, ovaries, and breast studies were all normal.[10] Finally, in this case, endoscopic procedures were not repeated attending patient's preferences and end-stage oncologic disease.

Conclusions

New-onset MAA may present with atypical characteristics including transudative ascites, high SAAG suggesting PHT, low cell count, and repeatedly negative cytology despite peritoneal carcinomatosis. When facing such a diagnostic challenge, a thorough differential diagnosis and keeping a high level of suspicion may be necessary to reach a final diagnosis.

Ethical considerations

Research ethics committee was consulted on how to obtain consent for case report writing after patient's death. A close relative was contacted to ask for permission as a representative.

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Declaration of Competing Interest

None.

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