Renal cell carcinoma presenting with malignant ascites

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Lesson
It is rare for renal cell carcinoma to involve the peritoneum and cause malignant ascites. Furthermore, it is uncommon for malignant ascites to be a presenting feature of this cancer. An unusual case of renal cell carcinoma presenting with malignant ascites is reported, and its response to sunitinib described.

Keywords
renal cell carcinoma, malignant ascites, sunitinib

A 67-year-old man presented with a three-week history of abdominal swelling and cough. Clinical examination revealed a distended abdomen, due to ascites, and no other abnormality. Investigations showed elevations of blood urea to 15.8 mmol/L and creatinine to 168 μmol/L. Other blood tests were unremarkable: haemoglobin 116 g/L, white cell count 5.6 × 10⁹/L, platelets 231 × 10⁹/L, albumin 35 g/L with normal liver biochemistry, CEA 1.2 ng/ml and CA19-9 122 U/ml. A computerised tomography (CT) scan of the chest, abdomen and pelvis revealed marked ascites with omental deposits and a large (8 cm × 9 cm) mass in the upper pole of the right kidney (Figure 1). A soft tissue mass in the right lung base and small bilateral pleural effusions were also noted.

Paracentesis was performed and 14 L of blood-stained ascitic fluid was drained from the abdomen. Cytological analysis of this fluid revealed cohesive clusters of cells with mildly enlarged nuclei and clear cytoplasm consistent with metastatic renal cell carcinoma (Figure 2(a)). Omental biopsies were obtained percutaneously, and histological analysis of these showed diffuse infiltration by a tumour composed of clear cells arranged in glands and nests. The tumour stained positive for cytokeratin MNF116, Vimentin, CD10 and renal cell carcinoma (RCC) immunomarkers, but negative for CK7, anti-placental alkaline phosphatase and alpha-fetoprotein. This staining pattern confirmed the tumour as a metastatic clear cell renal cell carcinoma (Figure 2(b)).

He was commenced on sunitinib (Sutent), a multiple receptor tyrosine kinase inhibitor. This was initially given in cycles but then continuously at a dose of 37.5–50 mg daily. The primary renal cancer was not resected. A few weeks after the initial ascitic fluid drainage, he required a second paracentesis because of ascites reaccumulation. However, he then made a good clinical response to sunitinib and required no further paracentesis. Repeat CT scan four months later showed no ascites, and a further scan at eight months additionally showed virtual resolution of peritoneal nodules and shrinkage/necrosis of the primary renal cancer. He remains well 18 months after diagnosis.

Discussion
RCC accounts for approximately 3% of all adult malignancies and is the third most common genitourinary tract tumour. RCC is often asymptomatic until the late stages of disease. Most RCCs are now detected incidentally due to the increasing use of sophisticated imaging techniques.¹ The classic triad of flank pain, haematuria and a palpable abdominal mass is now rare (6–10%) and indicates advanced disease.¹ Around 20% of patients present with paraneoplastic syndromes such as polycythaemia, hypercalcaemia, neuromyopathy, anaemia and amyloidosis.¹ More rarely patients present with symptoms of metastatic disease such as bone pain or a persistent cough.¹ Physical examination is often unremarkable, but findings of a palpable abdominal mass or cervical lymphadenopathy should prompt further investigations.

Almost one-third of patients with RCC have metastasis at diagnosis.² The most common metastatic sites include lung (50–60%), bone (30–40%), lymph nodes (6–32%), liver (8–40%) and brain (5%).² RCC also has a tendency to metastasise to rare sites, such as the pancreas, thyroid, parotid gland, skeletal muscle or soft tissue.² Peritoneal involvement is rare in RCC, and is found in less than 1% of patients with metastatic disease at post mortem.³
RCC metastasises by way of venous drainage, lymphatic routes and direct extension. In up to 23% of tumours the venous system has been invaded and in extreme cases the entire inferior vena cava is involved. Lymphatic spread of RCC is initially to regional lymph nodes, but may extend to lymph nodes above or below the level of the renal hilum. The mechanism for peritoneal involvement is not fully understood, but thought to be through haematogenous spread and direct extension.

Malignant ascites in patients with RCC is a rare phenomenon and can be difficult to diagnose cytologically. The cells from RCC are bland and therefore their cytological appearance can easily be confused with reactive mesothelial cells and macrophages. However, there are certain subtle features, both architectural and cellular, which favour a diagnosis of RCC.

The average survival of metastatic RCC patients is about four months, and only 10% of these patients survive for one year. Chemotherapy, hormonal therapy and radiotherapy have generally proved ineffective. Historically, immunotherapy with interleukin-2 and interferon-α has been the mainstay of treatment. However, novel molecular therapies, such as sunitinib, are now considered the standard-of-care treatment.

Conclusion

It is very rare for RCC to manifest itself with malignant ascites. In the absence of typical symptoms of RCC the diagnosis can be easily overlooked in patients with ascites. The relative lack of specific cytological features in aspirated ascitic fluid can also be misleading, although imaging is usually diagnostic. RCC should be considered as a rare cause of malignant ascites.
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