Severe hyponatremia secondary to rectal adenocarcinoma: Mckittrick–Wheelock syndrome

Hiponatremia severa por adenocarcinoma de recto: síndrome de Mckittrick-Wheelock

McKittrick–Wheelock syndrome is a rare condition described in the context of distal colorectal tumours (in particular villous adenomas, although there have been cases in tubulovillous adenomas and adenocarcinomas), consisting of extreme acute depletion of electrolytes related to secretory diarrhoea. It is difficult to estimate the prevalence of this syndrome, as it is believed to be underdiagnosed, with only the most severe cases being identified.[1]

We present the case of an 80-year-old female patient with locally advanced adenocarcinoma of the rectum, for which she underwent a first intervention with a colostomy performed. She subsequently started adjuvant radiotherapy prior to definitive surgery. The patient was referred to Accident and Emergency after suffering a syncope. Blood tests (Table 1) showed no blood gas abnormalities. The family reported abundant rectal discharge of transparent watery secretions in the previous days. Suspecting McKittrick–Wheelock syndrome, fluid and electrolytic replacement was started with 0.9% saline, but there was no response regarding blood analysis values. She was switched to a 3% hypertonic saline infusion, and sodium levels went up in subsequent tests. After stabilising the patient's blood sodium, we transitioned to oral replacement (500 mg of NaCl every eight hours) with good tolerance, and she had sodium levels at the discharge of 134 mEq/l. She made a good recovery as an outpatient, maintaining adequate electrolyte levels and undergoing surgery one month later without complications in the immediate postoperative period.

McKittrick–Wheelock syndrome was first described in 1954 in the context of extensive villous adenomas (>3–4 cm in diameter) in the rectosigmoid region. This type of adenoma has the particular characteristic of producing enormous amounts of mucin, which has a high concentration of electrolytes (mainly sodium, potassium and chlorine). This leads to significant secretory diarrhoea, as the secretions volume exceeds the rectal mucosa's reabsorption capacity. The symptoms consist of profuse diarrhoea, initially without repercussions at the analytical and haemodynamic level, thanks to renal adaptation. However, although the time frame can vary, they will develop dehydration, acute kidney injury of prerenal aetiology and electrolyte imbalances such as hyponatraemia, which can become severe.[2] Most patients are asymptomatic, in what is called the ''latent phase'' and may remain so for several years until they reach the ''decompensation phase''.[1] This can make diagnosis complex, especially in cases where there are no haemodynamic repercussions. In the case reported here, the patient already had deterioration in her general condition and analytical repercussions, with acute impairment of kidney function and severe hyponatraemia.

Table 1 Laboratory test results in Accident and Emergency.

Plasma	
Na (corrected)	119 mEq/l
K	5.5 mEq/l
Osmolality, calculated	275 mOsm/kg
Creatinine	3.81 mg/dl
Urine	
Na	13 mmol/l (54–190)
K	94 mmol/l (20–80)

When making a differential diagnosis of hyponatraemia, first of all, it is essential to confirm that it is true hyponatraemia, with decreased plasma osmolality. Extracellular volume then needs to be assessed, which, in our case, was decreased due to dehydration. Lastly, when making the differential diagnosis of the origin of the losses, it is important to quantify ions in urine.[3] Our patient had a low urinary sodium concentration, suggesting that the losses were secondary to diarrhoea and supporting the suspicion of McKittrick–Wheelock syndrome.

The pathophysiology of this syndrome is not fully understood, but immunohistochemical studies have shown an overexpression of COX-2 and an increase in prostaglandin E2 in the secretions.[4] The treatment of choice is intensive fluid therapy prior to surgical excision of the tumour, which brings about a complete cure. However, alternatives have been proposed, such as the use of indomethacin or octreotide for patients who are either not eligible for or are awaiting surgery.[1]

In conclusion, McKittrick–Wheelock syndrome should be suspected in a patient with a previous medical history of colorectal carcinoma and secretory diarrhoea with repercussions on fluid/electrolytic balance. Clinical suspicion in these cases is particularly important, as early diagnosis and early surgical treatment determine the patient's future survival.

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Julia Costas Eimil*, Paula Sánchez-Sobrino, Olaia Díaz Trastoy

Servicio de Endocrinología y Nutrición, Complejo Hospitalario Universitario de Pontevedra, Pontevedra, Spain

*Corresponding author.
E-mail address: julia.costas.eimil@sergas.es (J. Costas Eimil).

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Hepatic undifferentiated embryonal sarcoma in a young adult

Sarcoma embrionario indiferenciado hepático en adulto joven

Undifferentiated embryonal sarcoma of the liver (UESL) is an aggressive cancer with a very low incidence (0.1%–2% of liver tumours).[1] Although it also occurs in adults, it is more common in childhood.[2] Accurate preoperative diagnosis is a challenge. Survival has improved with the current treatment of complete surgical resection and chemotherapy.[3] We present a new case of UESL and discuss the central aspects of this type of cancer.

This was a 20-year-old woman with no relevant previous medical history who presented with vomiting and a palpable mass in the right hypochondrium. Abdominal ultrasound (Fig. 1A) and magnetic resonance imaging (Fig. 1B) showed a 12.5 × 12 × 10 cm multilocular cystic lesion in the right lobe of her liver. There were no abnormalities in her complete blood count, liver function tests or tumour markers. The preoperative radiological diagnosis was biliary cystic neoplasm. Bisegmentectomy V–VI was performed (Fig. 1C). She was discharged 24 h later with no postoperative complications. The pathology study revealed a high-grade undifferentiated embryonal sarcoma with free surgical margins. Microscopically, large spindle-shaped sarcomatous epithelial cysts were identified with high mitotic activity and hyaline globules. Immunohistochemically we found expression for desmin with activity for MYOD1 and negativity for beta-catenin, P53, P16 and myogenin. The patient was started on chemotherapy with vincristine, actinomycin-D and cyclophosphamide. Over the follow-up carried out to date (six months) there have been no signs of recurrence.

UESL was first described by Stocker and Ishak in 1978.[2] It is the third most common primary hepatic malignancy in childhood after hepatoblastoma and hepatocellular carcinoma. In adults, it is usually seen in women in their thirties or forties.[1] No obvious aetiological factors have yet been found, suggesting that it derives from the malignant transformation of a mesenchymal hamartoma.[1] The most common location is the right lobe of the liver; as in our case, it is usually more than 10 cm in size.[4]

Clinical presentation is variable, ranging from asymptomatic to non-specific symptoms (fever, weight loss and gastrointestinal symptoms) to severe symptoms caused by tumour rupture or liver failure.[1,2] An abdominal mass may be palpable on physical examination, with or without associated abdominal pain. There are no typical laboratory data of UESL,[3] with liver function tests and tumour markers usually normal, but elevation of transaminases, sedimentation rate and leucocytosis may be found.[3]

The radiological findings of UESL are not specific. Ultrasound usually shows a large, benign-appearing cystic-solid mass.[3] Computed tomography shows a large multi-septated hypodense mass with central necrosis. Magnetic resonance imaging is particularly useful for detecting small multifocal nodules and assessing vascular-biliary structures and hilar lymphadenopathy. The presence of a hypointense border caused by the peri-tumour fibrous pseudocapsule, intratumour bleeding, and heterogeneous enhancement both in the periphery and in the solid tumour components on late T1-weighted images are suggestive of UESL.[2,5]

The differential diagnosis of UESL is complex. The age of the patient can be indicative. The main differential diagnoses in the paediatric population are mesenchymal hamartoma, hepatoblastoma and biliary embryonal rhabdomyosarcoma.[3] In adults, it includes hepatocellular carcinoma, biliary cystic neoplasms, gastrointestinal stromal tumour, angiomyolipoma, epithelioid haemangioendothelioma and malignant melanoma.[3] An accurate, early diagnosis is key to increasing the chances of long-term survival.

The definitive diagnosis of UESL is based on histopathological examination and immunohistochemical evaluation. Macroscopically, it usually involves a single, heterogeneous lesion with a cystic-solid appearance, greyish in colour, with areas of necrosis delimited by a fibrous pseudocapsule.[3] Microscopically, the pseudocapsule separates the lesion from the surrounding liver parenchyma.

The variable expression of histiocytic, muscular and epithelial markers suggests that it originates from primitive stem cells. Most are positive for vimentin, desmin, CD68, B2-cell lymphoma, α1-antitrypsin and CD10. The lack of expression for the hepatocyte paraffin-1 antibody differentiates it from hepatoblastoma and hepatocellular carcinoma.[1]

Complete surgical resection and chemotherapy are the mainstays of UESL treatment. The combination of surgery and chemotherapy has improved outcomes, increasing five-year survival from 40% in the 1980s to the current 70%.[1–5] If R0 resection does not seem possible at diagnosis, neoadjuvant chemotherapy can be started.[5] Negative resection margin, tumour size less than 15 cm, and combination therapy (surgery and chemotherapy) are independent prognostic factors.[3–5] The presence of extrahepatic disease does not seem to significantly impact the prognosis and should not be considered a contraindication for surgery.[4] Liver transplantation may be an alternative for the technically unresectable disease after neoadjuvant chemotherapy or recurrence.[3,5] Recurrences usually occur within two years after surgery, with a higher rate if the resection margins are positive.[3]