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CASE REPORT

Massive Weight Loss Due to Carcinoid Tumor

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Summary
Neuroendocrine tumors are more common than previously thought and represent a group of malignancies that need special consideration regarding diagnostic and therapeutic approach. High level of suspicion is required to diagnose these tumors, thus delayed recognition and metastases are common. Vast options for surgical and nonsurgical treatment exist, including liver transplantation in special cases.
Key words: carcinoid, neuroendocrine tumor, liver metastases, weight loss, surgical treatment

AIM OF THE DEMONSTRATION

To emphasize the difference in approach to patients with liver metastases (LM) caused by neuroendocrine tumors (NET) and to discuss various causes of weight loss for patients with oncologic disorders.

CASE REPORT

A 43-year-old male patient was complaining of persistent diarrhea, massive weight loss of 70 kilograms in the previous year and reduced appetite. In addition, the patient had primary arterial hypertension, gouty arthritis and type two diabetes mellitus. He first visited his family physician, who noticed hepatomegaly and weight loss. Physician considered the possibility of an oncologic disease involving the liver. Blood and urine tests revealed normochromic normocytic anemia, elevated liver transaminases and cholestatic enzymes, hypoproteinemia and highly elevated ferritin. Abdominal computed tomography (CT) disclosed multiple hepatic lesions, but no other focus of disease. CT scan was followed by colonoscopy and upper endoscopy with biopsy. These investigations failed to demonstrate any tumor. So the patient was referred to a clinical university hospital and biopsy of the hepatic lesions was performed under ultrasonographic guidance. Biopsy results revealed that hepatic lesions are actually metastases of low-grade NET (Fig.1). Further evaluation is necessary to determine the location of primary tumor. Appropriate modalities for this purpose include capsule endoscopy, somatostatin receptor scintigraphy or positron emission tomography. The most probable primary tumor location is the small bowel as location in large bowel, lungs, stomach and pancreas has been excluded. Regarding the histology of NET, the patient is considered a candidate for surgery.

DISCUSSION

The importance of recognition of NETs and awareness about the therapeutic options could not be overemphasized, since the incidence and prevalence of NETs has persistently increased in the past thirty years to reach 5.25/100,000 and 35/100,000, respectively (7). Another problematic feature is that the clinical manifestations of NETs are variable and often non-specific, which leads to an average gap between first signs and diagnosis of NET of approximately 5-7 years, hence the LM are present in 50-75% of patients with small bowel NETs at presentation (2). Although diarrhea is the second most common symptom for patients with carcinoid syndrome (present in 50% of cases), the syndrome itself is present in approximately 20% of cases of midgut NET, with increasing incidence if LM are present (4). Cachexia is a well-known feature of oncologic disorders and is present in 50% of cancer patients. A myriad of inflammatory cytokines, such as TNF-α, INF-γ, IL-1 and IL-6, are responsible for development of cachexia. The main mechanisms involved are ubiquitin proteasome system that causes muscle breakdown, and impaired leptin and ghrelin signal pathways which generates inefficient metabolism and anorexia (6). While the aforementioned factors are common for all cancer patients, weight loss probably is secondary to chronic diarrhea in this particular case. Both hypermotility and hypersecretion contribute to development of diarrhea in patients with carcinoid syndrome with serotonin being the causative factor (5). Elevated blood serotonin levels are especially characteristic for midgut NETs with LM which is the most likely diagnosis for this patient (5). Unlike cancer cachexia, serotonin induced chronic diarrhea can be effectively managed with somatostatin analogues which illustrates that not all oncologic patients and not all weight losses should be perceived as similar. Another difference in the management of NET patients with LM is the possibility to use a wide spectrum of surgical and non-surgical treatment methods. Surgery, whenever possible, should be pursued despite the fact that curative surgery is possible in only 10% of patients with LM (4). Regardless of the presence or absence of liver metastases resection for the primary tumor and associated mesenteric lymph nodes is recommended (4). It is important to separate three distinct groups regarding the distribution of LM, which will affect both survival and surgical approach. Solitary unilobar LM can be managed by one-stage resection of primary tumor and LM with 5-year survival of nearly 100% (1). If bilobar involvement with one larger mass and accompanying smaller lesions is present, surgical resection in two stages can still be performed, with 5 year survival of 84% (1). High recurrence of 90% in 5 years must be noted (1).

When diffuse LM are present and surgery is not possible, other options like somatostatin analogs, peptide receptor radionuclide therapy, transcatheter arterial embolization or chemoembolization and molecular targeted therapy still remain (3). It is fascinating that for highly selected patients liver transplantation is considered a possibility, which is almost unique in case of malignant tumour. Transplantation is an option for patients with diffuse LM or hormonal disturbances if other treatment modalities fail. Minimal criteria for consideration are well differentiated (G1, G2) NETs with primary tumor resected prior to transplantation, no extrahepatic tumors and expected mortality below 10%. Age < 50 years is favorable (3).

In conclusion, this case illustrates the extent of difficulties, our ever growing knowledge and recent advantages in management of NET patients.

Conflict of interest: None

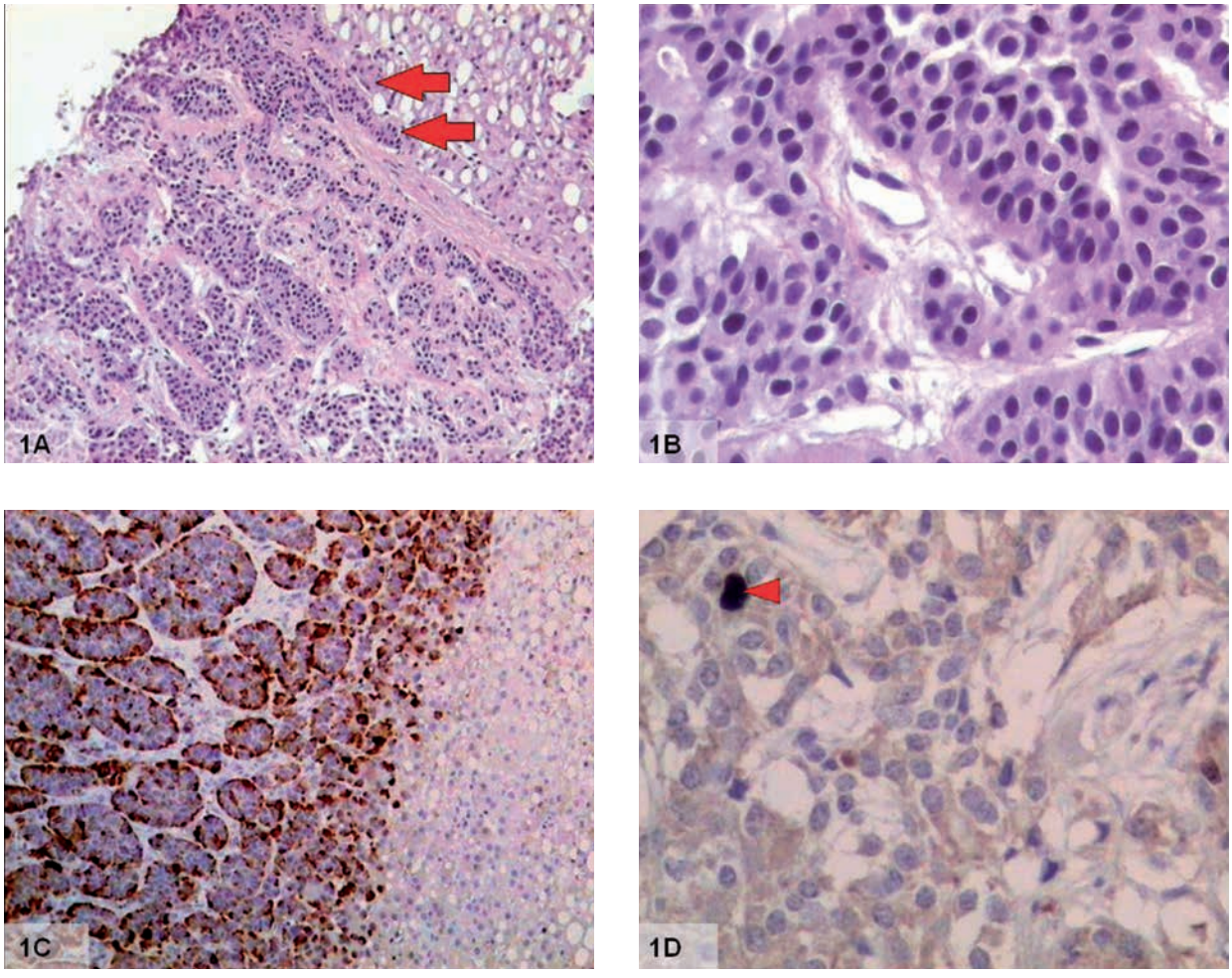

Fig. 1. Liver metastasis of low-grade neuroendocrine tumor (NET). 1A, Tumor architecture in core biopsy. Note the invasive growth (arrows) and trabecular architecture of the tumor as well as steatosis in the surrounding liver. Hematoxylin-eosin (HE), original magnification (OM) 100x. 1B, Morphology of NET cells. Note the nuclear uniformity and low amount of well-vascularised stroma. HE, OM 400x. 1C, Intense cytoplasmic expression of chromogranin A in NET cells. Immunoperoxidase (IP), OM 100x. 1D, Low proliferation fraction (0.8%) by Ki-67. A single proliferating cell is highlighted by an arrowhead. IP, OM 400x.

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