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Leser-Trèlat sign and gastric adenocarcinoma: case report and literature review

Sinal de Leser-Trélat e adenocarcinoma gástrico: relato de caso e revisão de literatura

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PALAVRAS-CHAVE: Ceratose seborreica. Síndromes paraneoplásicas. Adenocarcinoma. Câncer gástrico.

INTRODUCTION

Leser-Trélat sign (TLS) is a rare condition characterized by the sudden eruption of multiple seborrheic keratoses associated with internal neoplasia, occurring before, during, or after its detection.[1-3] It has been described in adenocarcinomas (gastrointestinal, breast, ovary, uterus, prostate, kidney, and lung), lymphoproliferative diseases, and in metastatic situations.[1] Keratotic lesions are rounded, hyperpigmented (brown to black in color) due to the accumulation of keratin in their composition, with a warty appearance, varying in size, located in the chest and back, extremities, face, abdomen, neck, and armpits.[4] It may course with pruritus and acanthosis nigricans.[1] The sudden appearance, with a rapid increase in number and size of these lesions, is probably related to the release of tumor growth factor alpha.[5] This report, approved by the institutional ethics committee, added to the literature review warns that the presence of the Leser-Trélat sign points to the need for investigation of malignancy, especially of the digestive tract.

CASE REPORT

A 58-year-old woman, anicteric, presented with excessive itching and pigmented papular lesions on the chest and face, eruptive, with progressive enlargement for about 1 year. She underwent previous treatments for scabies and allergy in primary care, with no response. In the consultation with a dermatologist, multiple seborrheic keratoses and suspicion of TLS were detected. In the investigation, laboratory tests revealed: AST 193, TGP 373, Gamma-GT 1768, BD 2.[6] BI 0.[9] BT 3.[5] and alkaline phosphatase 1001. Ten months later, she was diagnosed with duodenal papilla neoplasia based on a suggestive clinical picture, weight loss, abdominal pain, together with tomography showing ill-defined thickening of the pancreatic head and the second duodenal portion (Figure 1). The anatomopathological analysis revealed moderately differentiated tubular adenocarcinoma with signs of metastasis to regional lymph nodes (Figure 2).

The case was classified as T2N1M0 (stage IIA), submitted to Whipple operation (pancreaticoduodenectomy) and neoadjuvant chemotherapy with gemcitabine with good tolerance. Then she underwent chemotherapy with 5-fluorouracil and leucovorin. With tumor removal, there was total improvement of pruritus and progressive reduction of keratotic lesions, and 1 month after the surgical procedure, the liver profile and bilirubin were normal. After 1 year, CT scans showed no recurrence or metastases (Figure 3). The patient remained under periodic follow-up with satisfactory evolution.

FIGURE 1 — Computed axial tomography scan of the abdomen showing ill-defined thickening of the head of the pancreas and the second portion of the duodenum

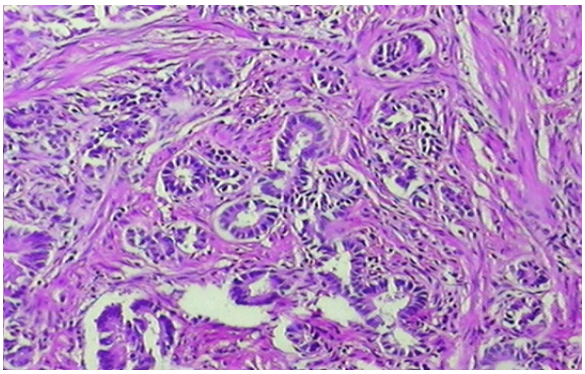

FIGURE 2 — Moderately differentiated and invasive duodenal papillar tubular adenocarcinoma (H&E)

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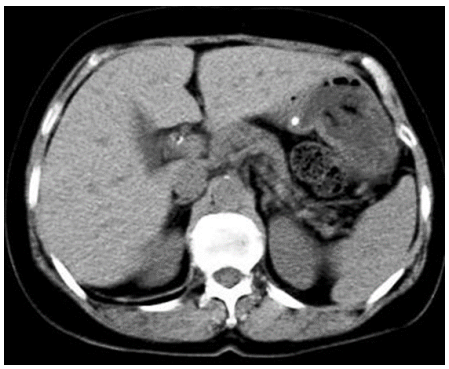

FIGURE 3 — Computerized axial tomography 1 year after surgical resection showing no recurrence or metastases

DISCUSSION

Adenocarcinomas are malignant tumors originating from glandular histology and, in the case of this report, involve the duodenal papilla. When there is a neoplastic process in it, it is common to have a clinical association with cholestatic jaundice at the expense of direct bilirubin, excessive pruritus, abdominal pain, choluria, and fecal acholia.[6] Initially, they may be asymptomatic.

The most prevalent adenocarcinomas of the digestive system affect the stomach and liver. Gastric tumors have a high incidence in developing countries, with adenocarcinoma in 95% of cases. The prevalence is accentuated in men, in the age group between 60 and 70 years.[7] Liver tumors are more present in a secondary way as a result of metastases. Among the primary carcinomas, hepatocellular carcinoma is the most frequent (80% of cases), with more aggressive predicates, but it is usually diagnosed late because it is asymptomatic until there is a strong deficit in liver architecture and functionality.[8,9]

The therapeutic planning of gastric adenocarcinoma depends on the staging, age and general health of the patient, type of tumor, chances of cure and specificities of each case. The main resources are surgery, chemotherapy, targeted therapy, immunotherapy, radiotherapy and palliative care, and most of the time a combination of these resources is used, associated with the support of a multidisciplinary team.[10]

Anamnesis, physical examination, and cutaneous signs helped in the initial suspicion, and laboratory tests, imaging, and biopsies were later requested for confirmation and staging in an oncology service. In the present case, there was a correlation between the clinic and the laboratory findings, such as elevated liver enzymes and bilirubin, imaging tests (Figure 2), and anatomopathological analysis of material obtained by upper gastrointestinal endoscopy, confirming the diagnosis. Staging guided treatment and prognosis.

The processes for the development of TLS are still unknown; however, it is believed to be induced by factors that lead to neoplasia. Changes in serum levels of human growth factors, including TGF-α, TGF-α, and epidermal growth factor (EGF), have been implicated in the pathogenesis of the signal.[5,11] Its reappearance after treatment may indicate recurrence of the neoplasm. With the removal of the neoplastic lesion, there is regression of seborrheic keratoses, although they can be treated with chemical cauterization, liquid nitrogen, laser, among other resources.[2] In this patient, the pruritus may have resulted from the skin lesions and/or cholestasis and, as well, the TLS also regressed.

The abrupt eruption of seborrheic keratoses in SLT is notorious and should not be confused with generalized seborrheic keratosis of gradual onset or other dermatoses. It should be noted that seborrheic keratoses may present variations in their surface, symmetry, coloration, and subtypes, and may be confused with viral wart, pigmented nevus, melanoma cancer, and non-melanoma on clinical examination. The efficacy of its diagnosis can be improved with dermoscopy and, eventually, with excisional biopsy for histopathological study and confocal microscopy.[26,27] Pruritus occurs in almost half of the patients, but also in seborrheic keratoses not associated with malignancy and in other diseases, which should be excluded.

TABLE — Characteristics of patients with Leser-Trélat sign associated with gastrointestinal tract neoplasia, according to the literature

Cases	Gender and Age	Location of CSs	Site of neoplasia	Initial manifestations of neoplasms	Diagnostic method of neoplasia	Neoplasm Treatment	Ref
1	H, 70	Back	Stomach and duodenum	Malaise and heartburn	EDA	Gastrectomy	12
2	M, 39	Thorax	Sigmoid colon	NU	NU	Rectosigmoidectomy	13
3	M, 49	Scalp, face, forearm, back, right shoulder and chest	Stomach with body metastasis	Weight loss, anorexia, abdominal pain, dyspepsia, dysphagia, and ascites	UGI and biopsy	Palliative chemotherapy	14
4	H, 62	Face, neck, chest, back and limbs	Liver	Fatigue, upper abdominal discomfort, and weight loss	Abdominal USG, MRI, and biopsy	Surgery	15
5	H, 57	Back	Straight	Change of bowel habit, thin stools, and rectal bleeding	Colonoscopy and biopsy	NU	16
6	H, 65	Neck and back	Esophagus	Progressive dysphagia and weight loss	UDE, colonoscopy, biopsy, CT scan of the chest, abdomen, and pelvis	Gastrostomy, radiotherapy and chemotherapy	17
7	H, 67	Chest and abdomen	Stomach with liver metastasis	Dyspepsia, aerophagia, reflux symptoms, and weight loss	EDA, biopsy and PET-CT	Esophagogastrectomy, cholecystectomy, splenectomy, and chemotherapy	18
8	M, 70	Trunk	Bile ducts	Weight loss, jaundice, clear stools, and abdominal pain	TC and CA 19-9 elevated	ERCP, palliative care	19
9	H, 68	Face, left arm and waist	Liver	Asymptomatic	CT and biopsy	Liver resection	20
10	H, 80	Torso and back	Gastrointestinal tract with body metastasis	Weight loss, right hypochondrium pain, nausea, and vomiting	USG, elevated CEA, CT, and biopsy	NU	21
11	H, 61	Face, neck, chest, back and head	Stomach with pancreatic metastasis	Hyperpigmentation of trunk and face, upper abdominal pain	Elevated CEA and biopsy	Chemotherapy and gastrectomy	22
12	NI, 92	Thorax and back	Pancreas with peritoneal metastasis	Asthenia, hyporexia and weight loss	NU	Palliative care	23
13	M, 41	Armpit, groin, navel, neck, shoulders and anus	Stomach with body metastasis	Asymptomatic	Elevated CA 19-9 and CA125, gastroscopy and CT	Palliative chemotherapy	24
14	M, 49	Upper and lower extremities	Metastatic liver to lymph nodes, lung, and bones	Arthralgia, weight loss, abdominal fullness, and loose stools	CA 19-9 and alpha-fede protein elevated and TC	Chemotherapy	25

CSs = seborrheic keratoses; Tto = treatment; Ref = references; H = man; M = woman; NI = not informed; UDE = upper gastrointestinal endoscopy); US = ultrasound; MRI = magnetic resonance imaging; CT = computed tomography; ERCP = endoscopic retrograde cholangiopancreatography

In order to deepen the correlation between gastric neoplasms and TLS, case reports were searched with the keyword: "Leser Trelat sign" and those associated with neoplasms of the digestive system were manually chosen. A total of 14 reports published in the last 10 years in the Scielo, Pubmed and VHL indexes were selected (Table).

A review of the literature 12-25 denotes the scarcity of these publications (Table 1) and reveals that TLS affects the thorax and back of males (57% of cases), adults and the elderly, with an earlier manifestation at 39 years of age. The most common neoplastic sites are the stomach and liver, respectively, with gastric tumors in primary primacy, and hepatic tumors in a secondary and metastatic manner.

As a final message and considering the limitations of this study, the possible potential of the Leser-Trélat sign as a paraneoplastic sign becomes evident, especially in gastric and hepatic sites. Therefore, when semiological signs suggestive of it are perceived, dermoscopy analysis, laboratory markers, and imaging tests are necessary to look for neoplastic complications, with the use of a specific biopsy if there is suspicion of a suitable site.

Authors' contributions

Conceptualization: Giulia Tonon
Methodology: Pedro Henrique Pereira Corradini
Writing (original draft): Katia Sheylla Mallta Purim
Writing (proofreading and editing): All authors

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