

**Title:**

**Trousseau syndrome preceding the diagnosis of colon cancer**

**Authors:**

Daniel Alvarenga Fernandes, Fernando Brandão Alcântara Santos, Fernanda Veloso Pereira, Carlos Eduardo Garcez Teixeira, Zoraida Sachetto, Ilka de Fátima Ferreira Santana Boin, José Barreto Campello Carvalheira, Fabiano Reis

DOI: 10.17235/reed.2024.10728/2024

Link: [PubMed \(Epub ahead of print\)](#)

**Please cite this article as:**

Fernandes Daniel Alvarenga , Santos Fernando Brandão Alcântara, Pereira Fernanda Veloso , Teixeira Carlos Eduardo Garcez , Sachetto Zoraida, Boin Ilka de Fátima Ferreira Santana , Carvalheira José Barreto Campello, Reis Fabiano.

Trousseau syndrome preceding the diagnosis of colon cancer. Rev Esp Enferm Dig 2024. doi:

10.17235/reed.2024.10728/2024.

*This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.*

## Trousseau syndrome preceding the diagnosis of colon cancer

Daniel Alvarenga Fernandes<sup>1</sup>, Fernando Brandão Alcântara Santos<sup>1</sup>, Fernanda Veloso Pereira<sup>1</sup>, Carlos Eduardo Garcez Teixeira<sup>2</sup>, Zoraida Sachetto<sup>2</sup>, Ilka de Fátima Ferreira Santana Boin<sup>3</sup>, José Barreto Campello Carvalheira<sup>1</sup>, Fabiano Reis<sup>1</sup>

- 1- Department of Anesthesiology, Oncology and Radiology. School of Medical Sciences, University of Campinas, Campinas, São Paulo, Brazil.
- 2- Department of Internal Medicine, Rheumatology, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo, Brazil.
- 3- Department of Surgery, School of Medical Sciences, University of Campinas (UNICAMP). Campinas, São Paulo. Brazil.

### **Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### **Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## ABSTRACT

Trousseau Syndrome (TS) is defined as the occurrence of thromboembolic events prior to or simultaneously with the diagnosis of visceral neoplasia. In cases of multiple thromboembolisms, considering the possibility of TS, a screening for neoplasms may be warranted. We present a case study of a 61-year-old female who presented a neurological deficit. Brain magnetic resonance imaging (MRI) showed multiple hyperintense bihemispheric foci in subcortical and cortical regions involving three different vascular territories in the FLAIR sequence, associated with restricted diffusion inferring cytotoxic edema and indicating that they were all recent ischemic lesions, raising the hypothesis of TS. The patient underwent neoplastic screening with a subsequent diagnosis of colon cancer. TS should be considered when the patient presents thromboembolic events without an established cause. The three-territories-sign (TTS) is an essential radiographic biomarker related to cancer-associated ischemic stroke (CAIS). We propose that our findings be considered for the inclusion of guidelines that determine the investigation of an occult tumor (particularly gastric, pancreatic, lung, and colorectal) in patients who present thrombotic events, especially TTS.

**KEYWORDS:** Trousseau syndrome. Thrombosis. Occult neoplasm. Magnetic resonance imaging. Colon cancer. Abdominal imaging.

Dear Editor,

We present a case study of a 61-year-old female who presented a neurological deficit characterized by sudden left arm weakness and impairment of finger flexion, with the diagnosis of evolving stroke. Brain magnetic resonance imaging (MRI) raises the hypothesis of Trousseau Syndrome- TS (Figure 1A, 1B). The patient underwent abdominal computed tomography (Figure 1C, 1D) and colonoscopy with biopsy. The anatomopathological study showed moderately differentiated, partially ulcerated adenocarcinoma originating from a tubulovillous adenomatous lesion with high-grade dysplasia. We could not demonstrate KRAS mutations in colonic tumors in our patient.

Three weeks after the initial symptoms, the patient presented with a new ischemic cerebrovascular event evidenced by a new brain CT, with extensive damage to the left hemisphere, undergoing full anticoagulation. In the context of having an advanced neoplastic, we did not indicate craniectomy and indicated treatment with comfort measures. The patient died on the same day.

## DISCUSSION

In acute ischemic stroke (AIS) in more than one vascular territory, the propensity to attribute them to cardioembolic events such as atrial fibrillation (AF) is greater (1). However, other diagnostic hypotheses arise in the absence of cardioembolic events such as atrial fibrillation (AF). Thromboembolisms in at least three distinct cerebral vascular territories - a three-territory sign (TTS)- are more associated with the concomitant presence of neoplasms (2). The occurrence of TTS is six times more prevalent in patients with neoplasms than in those with AF, highlighting its importance as a particular radiographic marker for AIS resulting from neoplasms, with a higher frequency of restriction on diffusion pattern (MRI) when compared to patients with ischemia of cardioembolic origin (3).

Although considerable studies published in the last decade have shown that KRAS mutations are an influential risk factor for developing thromboembolic phenomena in digestive tract neoplasms, we could not demonstrate KRAS mutations in colonic tumors in our patient (4). Regarding the neoplasm primary site, lung, gastric, pancreatic, and

colorectal cancer are the most commonly related to cancer-associated ischemic stroke- CAIS (5). The association between scoring systems, laboratory, and radiological features may be useful in distinguishing CAIS from other causes of stroke.

Due to the pathophysiology of TS, in which the hypercoagulable state arises from the tumor and its pro-coagulatory molecular mechanisms, the gold-standard therapy is eradicating tumor cells.

The TTS emerges as an essential radiographic biomarker of a CAIS. We propose that our findings be considered for the inclusion of guidelines that determine the investigation of an occult tumor (particularly gastric, pancreatic, lung, and colorectal) in patients who present thrombotic events, especially TTS. This could potentially lead to a significant improvement in patient care and outcomes.

#### REFERENCES:

- 1- de Amorim JC, Torricelli AK, Frittoli RB, et al. Mimickers of neuropsychiatric manifestations in systemic lupus erythematosus. *Best Pract Res Clin Rheumatol.* 2018;32(5):623-639.
- 2- Finelli PF, Nouh A. Three-Territory DWI Acute Infarcts: Diagnostic Value in Cancer-Associated Hypercoagulation Stroke (Trousseau Syndrome). *AJNR Am J Neuroradiol.* 2016 ;37(11):2033-2036.
- 3- Khorana AA, Francis CW, Culakova E, et al. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. *J Thromb Haemost* 2007;5:632–4.
- 4- Pérez CG, Abad CB, Bautista GH, et al. KRAS mutations in pancreatic cancer: could we talk about a risk factor for the development of thromboembolic phenomena? *Rev Esp Enferm Dig.* 2024;116(4):236-237.
- 5- Navi BB, Reiner AS, Kamel H, et al. Association between incident cancer and subsequent stroke: stroke risk in cancer patients. *Ann Neurol.* 2015; 77(2): 291-300.



**Figure 1.** Brain magnetic resonance imaging (MRI) showed multiple hyperintense foci in subcortical and cortical regions involving three different vascular territories in the FLAIR sequence (**Figure 1 A**), associated with restricted diffusion (**Figure 1 B**) inferring cytotoxic edema and indicating that they were all recent ischemic lesions, raising the hypothesis of TS. **Abdominal Computed Tomography (Figure 1 C, D)** showed thickening of the ascending colon compatible with an expansive tumor.