

## BUDD-CHIARI SYNDROME AND UNSUSPECTED GASTRIC ADENOCARCINOMA\*

*SÍNDROME DE BUDD-CHIARI E ADENOCARCINOMA GÁSTRICO INSUSPEITO*

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**Abstract:** The Budd-Chiari syndrome has not been described in young patients with gastric cancer. A case of Budd-Chiari syndrome and carcinomatous lymphangitis is reported in a 28 years-old white man with unsuspected gastric cancer, presenting jaundice, hematemesis and dyspnea. Autopsy disclosed gastric adenocarcinoma invading vessels of the submucous and serous layers, with gastric and intestinal bleeding, liver and lung metastases. Multiple mixed (fibrin, platelets and tumor cells) microthrombi were observed in small pulmonary blood vessels, and both subpleural lymph vessels and lung interstitium contained metastatic tumor cells.

**Keywords:** Budd-Chiari Syndrome. Carcinomatous Lymphangitis. Gastric Adenocarcinoma. Stauffer's Syndrome. Hepatic Vein Thrombosis.

### 1- INTRODUCTION

Patients with advanced gastric cancer may develop haemostatic abnormalities, as hemorrhage, thrombosis, subdural hematoma, disseminated intravascular coagulation (DIC) and microangiopathic hemolytic anemia<sup>1,4</sup>. These changes have been related to paraneoplastic phenomena or bone marrow metastases, and may be the earliest manifestations, preceding the diagnosis of cancer<sup>2,4</sup>.

The Budd-Chiari's syndrome (BCS), characterized by abdominal pain, hepatomegaly, hepatic dysfunction and ascitis, has been associated with abdominal cancers producing mucin and followed by severe

centrilobular congestion and necrosis due to thrombosis or sluggish hepatic venous outflow<sup>5,6</sup>. BCS seems to be less uncommon than was once believed, and may represent a spectrum of disease, with varied presentation, depending on the balance between the rate of thrombosis and fibrinolysis<sup>6</sup>. Since BCS has been scarcely described in patients with gastric cancer<sup>7,8</sup>, the finding of ascitis, hepatomegaly and abnormalities in liver function tests usually indicate metastatic disease in these cases. The Stauffer's syndrome is another uncommon paraneoplastic condition, usually associated to renal carcinoma, lymphoma or leiomyosarcoma<sup>9,10</sup> that can also involve hepatomegaly, hepatic dysfunction with high liver enzymes, in

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addition to DIC and fibrinolysis, mimicking BCS clinical presentation. Nonetheless, the Stauffer's syndrome has not been described in patients with gastric adenocarcinoma.

The literature revision since 1966, through MEDLINE data base, showed that Budd-Chiari syndrome has not been described in young patients with gastric cancer. This condition has been associated with a high mortality rate.

In the present case, severe acute liver necrosis, due to hepatic sluggish blood flow, was the initial manifestation of a clinically unsuspected gastric adenocarcinoma in a 28-year-old male.

## 2- CASE REPORT

A 28-year-old white male unskilled laborer came to the hospital complaining of jaundice for a week, and abdominal pain one day before admission. He also referred asthenia, dyspnea, vomiting, and a recent episode of hematemesis. There was a previous history of episodes of lumbar pain and hematuria, in addition to obstipation with normal colonoscopy. On admission, he was severely ill, dyspneic, jaundiced and diaphoretic. Body mass index: 25.0kg/m<sup>2</sup> - Temperature: 37.5°C. The heart was rhythmic, 120bpm, and there were no murmurs. Blood pressure: 120/70mmHg. The lungs were clear. There was abdominal distension and tympanism, with painful decompression in epigastrium. The liver was painful and palpable 5cm below the right costal margin.

The patient's blood group was O, Rh-positive. The erythrocyte count 2.85x10<sup>6</sup>/mm<sup>3</sup>, with polychromasia and poikilocytosis, erythroblasts 2%, hemoglobin 7.9g/dl, hematocrit 26.6%, mean cell volume 93.4fl, leukocyte count 24,000/mm<sup>3</sup> (neutrophils: myelocytes 1%, bands 11%, segmented 71%, eosinophils and basophils 0%, lymphocytes 14%, monocytes 3%), platelets 67,000/mm<sup>3</sup>, glucose 108mg/dL, urea 70mg/dL, creatinine 0.7mg/dL, sodium 138mEq/L, potassium 3.9mEq/L, chloride 105mEq/L, calcium 7.9mg/dL, phosphorous 2.7mg/dL, magnesium 1.8mg/dL, direct bilirubin 7.25mg/dL, indirect bilirubin 1.86mg/dL, aspartate transaminase (AST) 194U/L, alanine transaminase (ALT) 273U/L, gama glutamil transpeptidase (gGT) 292U/L, alkaline phosphatase (AP) 190U/L, lactic dehydrogenase (LDH) 1,448U/L, and prothrombin activity 53%. Abdominal ultrasonography revealed hepatosplenomegaly and ascitis. Treatment included intravenous glucose, electrolyte solutions, red blood cells

transfusion, and mechanical respiratory support. Notwithstanding, the clinical status worsened, with severe dyspnea, mental confusion, progressive jaundice (bilirubins: direct 13.99 and indirect 3.23mg/dL) and higher liver enzymes (AST 1,351, ALT 666 and LDH 4,560U/L). On the fourth day of admission, he died due to irreversible respiratory failure and circulatory shock.

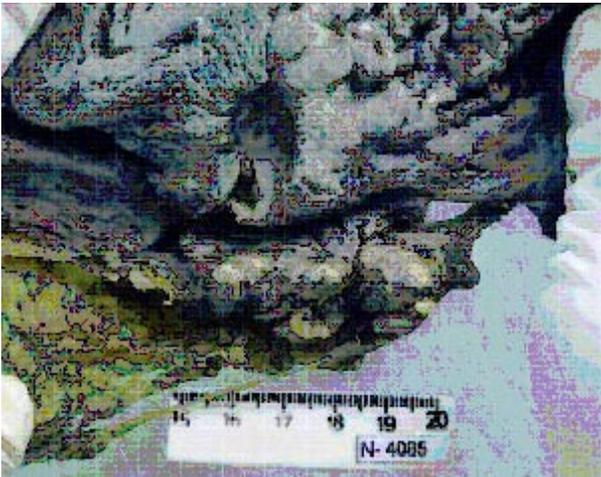
## Pathologic study

An ulcerated adenocarcinoma (diameter 2x4cm) with elevated borders and clear fundus (Fig. 1) was found in gastric body 7cm from pylorus. The tumor cells showed scanty cytoplasm and large polymorphic nuclei with rare mitoses, and were arranged like glands (Fig. 2). Similar neoplastic cells were also found in blood vessels from submucosa and serosa of the stomach. Hemorrhage through multiple punctiform lesions in the gastric mucosa, intense congestion and hemorrhagic foci in the intestinal mucosa, and hemorrhagic suffusions in the mesentery were noted. The liver weighed 2,650g, with several metastatic foci showing an aspect similar to the gastric tumor cells (Fig.3), in addition to severe diffuse congestion, necrosis and cholestatic aspect (Fig.4). The spleen weighed 365g, with very intense congestion and reduced number of lymphocytes. The lungs weighed 800g (right) and 605g (left), with moderate edema in the parenchyma and hemorrhagic focuses around the trachea and in pleural surface. Multiple diffuse emboli containing tumor cells and blood lamellar material were found in small and medium sized vessels. The gastric tumor cells were also observed in subpleural lymph vessels and in lung interstitium. The heart weighed 347g, and there was no evidence of arterial pulmonary hypertension. The encephalon weighed 1,470g, showing moderate diffuse edema and hyperemia. No neoplastic infiltration was found in the peritoneum and in the bone marrow samples.

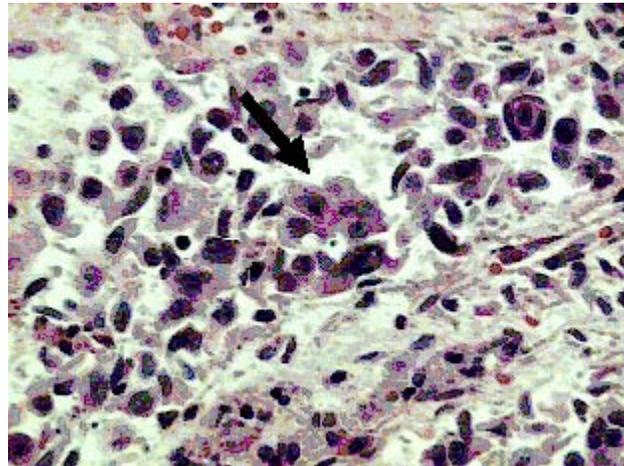
## 3- DISCUSSION

Gastric adenocarcinoma has been rarely described in white adults under 30 years<sup>1</sup>, and the clinical presentation may be very similar to many other clinical conditions. If patient's clinical situation worsens rapidly, in detriment of the differential diagnosis, the occult tumor stands to be found through autopsy studies<sup>4, 11, 12</sup>.

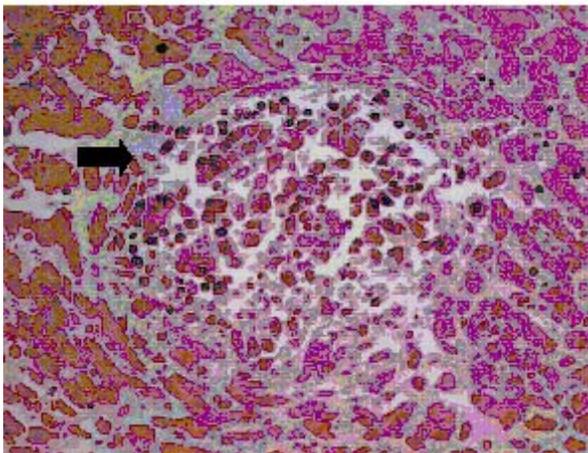
This 28-years-old white male with unsuspected gastric adenocarcinoma presented severe liver dys-



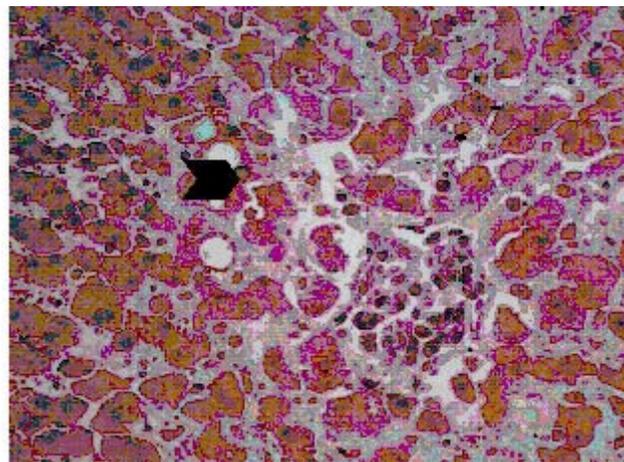
**Figure 1.** Ulcerated adenocarcinoma with elevated borders and clear fundus, located in gastric body.



**Figure 2.** Tumor cells showing scanty cytoplasm and large polymorphic nuclei with rare mitoses, arranged like glands (arrow) (Hematoxylin-eosin x250).



**Figure 3.** Neoplastic embolism (arrow) in central vein branches (Hematoxylin-eosin x250).

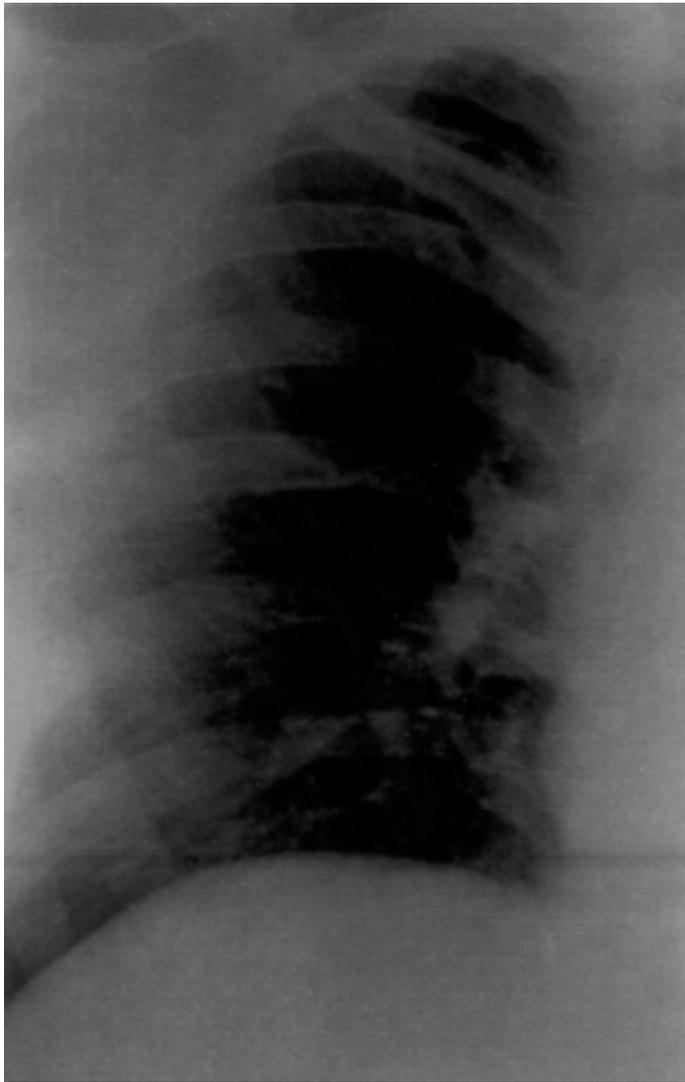


**Figure 4.** Detail of post-sinusoidal congestion and cholestasis (Hematoxylin-eosin x200).

function and gastrointestinal bleeding, in addition to breathlessness, pulmonary neoplastic thromboembolism and carcinomatous lymphangitis, without evidence of bone marrow metastases.

The diagnosis of gastric cancer was established exclusively through autopsy in this case. Noteworthy, retrospective analysis of the thorax roentgenogram allowed us an indirect evidence of the malignancy, based on normal heart silhouette associated to very subtle opacities in medium lung fields, appearing as short parallel horizontal lines extending to the pleural surfaces, resembling the Kerley B lines, as described in typical cases of lung carcinomatous lymphangitis<sup>11/14</sup> (Fig. 5).

Data from autopsy studies of thromboplastin-like producing tumors, indicate that the frequency of thromboses is mostly age-related and associated to disseminated bone metastases. Moreover, thromboembolism and/or carcinomatous lymphangitis have been seldom described in younger patients with gastric cancer<sup>1</sup>. In the present case, the lack of bone marrow invasion suggests some role of paraneoplastic phenomena in the development of severe venous congestion and acute liver necrosis. Noteworthy, gastroesophageal varices and peritoneal carcinomatosis were not found in this patient, which is consistent with the diagnoses of hepatic vein thrombosis and Budd-Chiari's syndrome.



**Figure 5.** Radiography of the thorax showing discrete opacities in lung fields, appearing as short parallel horizontal lines extending to the pleural surfaces, resembling the Kerley B lines.

The widespread arterial tumor embolism of the lungs could explain the patient's respiratory distress. However, the absence of right ventricular hypertrophy-dilation, pulmonary hypertension or hemorrhagic infarcts, seems to emphasize the influence of lymphangitis as the cause of the pulmonary changes<sup>14</sup>

Lumbar pain and hematuria, in addition to increased prothrombin time and high serum levels of AP, AST, ALT, LDH and gGT<sup>9</sup> could raise the clinical suspicion of Stauffer's syndrome; however, autopsy findings of BCS and secondary hepatic disruption may allow the exclusion of that hypothesis.

Despite of respiratory support, intravenous fluids and red blood cells transfusion, the patient developed refractory respiratory failure and irreversible circulatory shock and died in a short time. The intense thrombocytopenia and prolonged prothrombin time due to acute liver failure may have contributed to the gastrointestinal bleeding and hypovolemia. Since fibrin microthrombi were not found in more than three different organs<sup>4</sup>, the diagnosis of DIC was not established in this case in spite of thrombocytopenia and prolonged prothrombin time.

Abdominal pain and hematemesis could indicate the presence of gastric cancer; however, the rapid deterioration of clinical status hindered the gastroduodenal studies. Like in the vast majority of cases, since diagnosis of BCS could not be established concomitant with early stage malignancy, safe procedures would not be effective for clinical management of the present hepato-renal dysfunction<sup>7</sup>.

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**RESUMO:** A síndrome de Budd-Chiari não tem sido descrita em pacientes jovens portadores de câncer gástrico. Relata-se caso de síndrome de Budd-Chiari e linfangite carcinomatosa em homem branco de 28 anos, portador de câncer gástrico insuspeito, apresentando icterícia, hematêmese e dispnéia. O estudo de autópsia revelou adenocarcinoma gástrico infiltrando vasos das camadas submucosa e serosa, com sangramento do estômago e intestino, além de metástases hepáticas e pulmonares. Múltiplos microtrombos mistos (fibrina, plaquetas e células tumorais) foram observados em pequenos vasos sanguíneos pulmonares e tanto os vasos linfáticos subpleurais quanto o interstício pulmonar continham células tumorais metastáticas.

**DESCRITORES:** Adenocarcinoma. Gástrico. Linfangite Carcinomatosa. Síndrome de Budd-Chiari. Síndrome de Stauffer. Trombose de Veia Hepática.

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