Metástase de carcinoma epidermóide de esôfago em fígado cirrótico

Metastasis of Epidermoid Carcinoma of the Esophagus in Cirrhotic Liver

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RESUMO

O fígado, sendo órgão que serve de passagem para grande parte do sangue proveniente do sistema digestivo, é comumente sede de metástases de órgãos que drenam diretamente para esse sistema e de tumores primariamente localizados nos pulmões, mama, pâncreas, entre outros. Este relato apresenta o caso de um paciente apresentando metástases de carcinoma epidermóide de esôfago em fígado cirrótico. Esse achado é raro, com poucos relatos na literatura. A importância deste estudo se baseia no fato de que, segundo alguns estudos, o fígado cirrótico raramente é acometido por metástases de tumores localizados em outros órgãos. Por outro lado, há evidências sugerindo que esse evento possa ocorrer em freqüência não desprezível. Um importante mecanismo para explicar as razões para a raridade do caso aqui apresentado é que, de acordo com alterações hemodinâmicas inerentes à cirrose hepática, os êmbolos tumorais drenariam para os segmentos superiores do esôfago, não comprometendo o território portal. Baseado nesse relato, a importância de se identificar a presença de metástases hepáticas em fígados cirróticos é enfatizada, uma vez que esse achado pode alterar do modo significativo a conduta a ser ofertada.

UNITERMOS: Câncer de Esôfago, Cirrose Hepática, Metástases.

ABSTRACT

The liver, being an organ that through the portal system serves as a passage for most of the blood coming from the digestive system, is a common site of metastasis of organs that drain directly to this system, and tumors primarily located at the lung, breast and pancreas among others. This report presents the case of a patient with hepatic metastasis of epidermoid carcinoma of the esophagus in a cirrhotic liver. This condition is rare with few reports in the literature. The importance of this report is motivated by the fact that the cirrhotic liver, according to some authors, rarely hosts metastasis of primary tumors located in other organs. On the other hand, there is evidence to suggest that this event might occur with a frequency that is not despisable. An important mechanism that explains the extremely rare prevalence of hepatic metastasis of epidermoid carcinoma of the esophagus is that, according to the hemodynamic alterations found in cirrhosis, the tumoral embolus are forced to drain through the circulation by the medium and superior segments of the esophagus, not draining to the portal system. Based in this report, the importance of identifying the presence of metastasis in cirrhotic livers is emphasized, as its existence decisively changes the therapeutic approach that will be offered to the patient.

KEYWORDS: *Esophagela Cancer, Liver Cirrhosis, Metastasis.*

INTRODUCTION

The liver, being an organ that serves as a passage for most of the blood coming from the digestive system is a common site of metastasis of organs that drain directly to this system, and of other tumors primarily located at the lung, breast and muscular-skeletal system among others (1).

This report presents the finding of metastasis of epidermoid carcinoma of the esophagus in a cirrhotic liver and promotes a broad review of the literature. The importance of this discovery is motivated by the fact that the cirrhotic liver, according to some authors, rarely hosts metastasis of primary tumors located in other organs (2-5). Reasons that support this statement are plentiful and are discussed ahead. However, there is evidence to suggest that this event might occur without a worthless frequency (6, 7).

CASE REPORT

E.A.O., 60 years-old, Caucasian, referred to our Department of Surgery at Santa Casa Hospital of Porto Alegre presenting progressive dysphagia during one year and weight loss of 24Kg (30% of his weight) in this period.

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Smoker for 52 years, 24 cigarettes/day and ingestion, during 40 years, of an average of 400g/ethanol/day. Furthermore, presented chronic obstructive pulmonary disease and hepatic cirrhosis diagnosed at the age of 52.

During the hospitalization, a radiological study of thorax and esophagus was performed which revealed a straightening of the medium segment with an extension of 8 cm. Subsequently, he was submitted to upper digestive endoscopy, which demonstrated, at 30 cm of the superior dental arch, a vegetating lesion, infiltrative, obstructing the lumen of the organ, suggestive of neoplasia. The histopathologic study confirmed epidermiod carcinoma (Figure 1).

The abdominal ultrasonography demonstrated an enlarged liver with regular contours, portal vein measuring 1.3 cm and the presence of ascites. The analysis of the ascites suggested the presence of portal hypertension and malignant cells were not identified. The computed tomography of the thorax identified the neoplasm, apparently limited to the organ.

The patient was classified as a cirrhotic Child-Pugh-Turcotte score C with an epidermoid carcinoma of the esophagus, located in the medium segment, clinically staged as IIA (T3NOMO).

After effective clinical treatment of the ascites the patient was submitted to palliative surgery of esophageal tunnelization with prosthesis number 19. During the procedure, a focal lesion on the liver near the diaphragm was identified and the histopathologic examination of the lesion confirmed the diagnosis of cirrhosis (Figure 2) and metastasis of epidermoid carcinoma. The patient was therefore submitted to gastrostomy and esophageal tunnelization with an innocuous PVC prosthesis, nº 19, from Ethicon, Johnson & Johnson®. So, the anatomopathological stage was IV (T3NOM1).

On the third day of post-operatory, spontaneous bacterial peritonitis was diagnosed as well as loss of renal function. Treatment for the infection was established and the patient was discharged from the hospital 28 days after surgery.

DISCUSSION

The presence of hepatic metastasis is relatively frequent if normal livers are considered. However, when analyzing this finding in cirrhotics it is considered as a rare occurrence. Many physiopathogenic mechanisms are discussed in literature (8-11).

The first case report of metastasis in a cirrhotic liver was described by Hanot and Gilbert in 1888, being initially attributed to a primary neoplasm of the liver (8). On the following year, Poulain identified that in reality it was

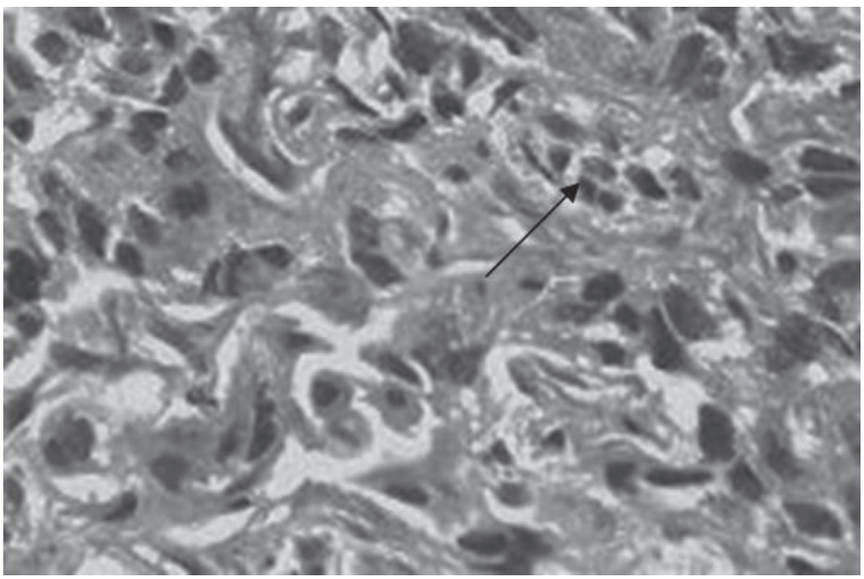


Figura 1 – Epidermoid carcinoma of the esophagus (HE 400X).

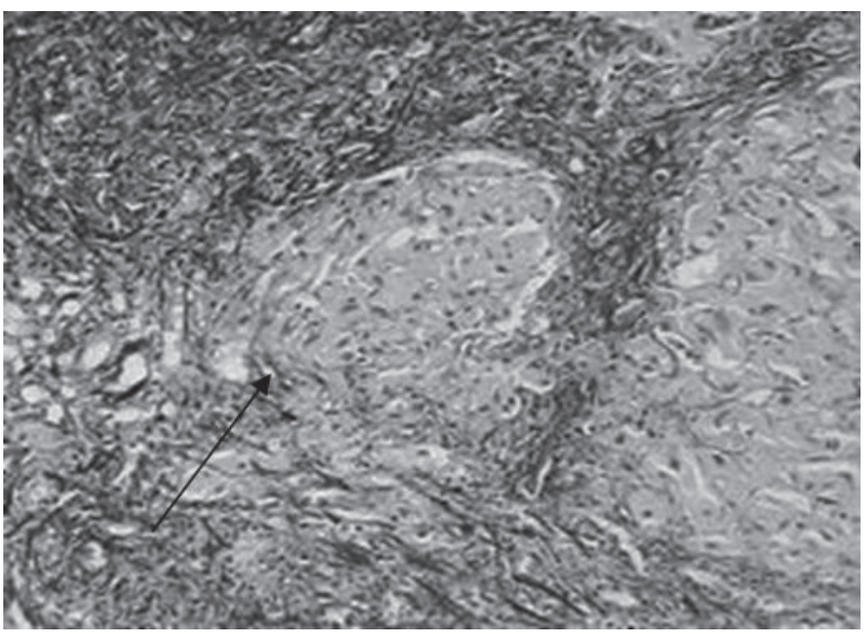


Figura 2 – Complete septal fibrosis with microscopic nodules (Picrosirius 200X).

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a metastasis of gastric carcinoma, being him the first to differentiate a primary tumor from the metastases that involve the liver (9). It is important to point out that when nodules are identified in a cirrhotic liver, consideration must be given to the possibility of the presence of hepatocellular carcinoma, bearing in mind that the annual incidence of this neoplasm varies between 1 and 4% amongst cirrhotic patients, and that the image examinations may provide valuable support for the diagnosis, dispensing, in many occasions, the histopathologic examination and the level of tumor markers (10).

Metastasis of esophageal neoplasms in cirrhotic livers were considered at the first time by Lisa *et al* in 1942 (11). Posteriorly, in 1953, Wallach *et al* demonstrated the presence of hepatic metastasis in a cirrhotic patient and an esophageal lesion of 4 cm, ulcerated, located 5 cm above the diaphragmatic hiatus (2). After these two reports, there was no other similar report according to the search made in Medline on November, 2006.

Many authors refers that metastasis in cirrhotic livers are a rare finding (2, 5, 11). However, others disagree with this statement, suggesting that the cirrhotic liver has a meaningful susceptibility to present metastasis (6, 7).

Many observational works, based on necropsies, verified a smaller prevalence of extra-hepatic carcinoma metastasis in cirrhotic livers. The first one was performed by Colwell *et al*, in 1905 in which 2634 necropsies of patients which presented extra-hepatic carcinoma were analyzed, of which 27 cirrhotic. Of these, the liver hosted metastasis in 2 cases (12). From a total of 10156 necropsies made between 1935 and 1952, Wallach *et al* reported in 1953, 3 cases of metastasis in a total of 67 cirrhotic patients and extra-hepatic tumors (2). In 1957, Lieber *et al*, in a sample of 26895 necropsies over 20 years, verified, of 50 patients with cirrhotic livers, the presence of 5 metastasis, which primarily did not involve the liver (13). In 1961, Ruebner *et al* documented two cases of metastasis in cirrhotic livers in a total of 54 patients with extra-hepatic neoplasms (14). One year later, in Boston, Norkin *et al* analyzed 15713 necropsies between 1945 and 1960 at the Mallory Institute of Pathology, finding 121 cases with both cirrhosis and extra-hepatic neoplasm, of which 37 presented metastasis (4). Analyzing these studies, it is possible to observe that the prevalence of hepatic metastasis of neoplasms that primarily did not involve the liver and the presence of cirrhosis varies between 3.7 and 10%.

However, there are works that suggest that the presence of metastasis in cirrhotic livers does not differ from those with healthy livers. In 1966, Frable *et al*, undertook a study with 4166 necropsies in a period of 11 years, of patients that had been hospitalized at the Memorial Hospital and had died of extra-hepatic carcinoma. He found that in 31 of these cases the association between cirrhosis and cancer existed, and affirmed that this prevalence did not differ in cases where the liver was normal (7). Another study that supports this argument was performed experimentally with rats, in which cancer and cirrhosis was induced, verifying that cirrhotic livers are a fertile field for the development of neoplasic extra-hepatic metastasis (6). However, the existent difference between the histopathological characteristics of mice and human livers should be considered. When revising 250 necropsies of Japanese patients that died of colo-rectal cancer, Uetsuji *et al* did not find any cases of hepatic metastasis amongst 46 cirrhotic livers. On the other hand, 20% of the patients with no previous hepatic diseases presented hepatic metastasis (15).

Before this diversity of findings, a meta-analysis was performed considering the main studies undertaken with this objective. Seventeen studies were selected, of which 11 contemplated on the established requisites to be included. A prevalence of 37.3% of hepatic metastasis in necropsies of patients without cirrhosis was observed, over 23.7% of patients with cirrhosis ($p<0.001$). However, the authors drew attention to the existence of a meaningful proportion of cases of metastasis in cirrhotic livers, although less relevantly (5).

In order to justify the hypothesis that a cirrhotic liver presents less susceptibility to host metastasis, some theories are considered as those preconized by Lisa *et al* that suggest that the cirrhotic liver possesses a smaller capacity to aggregate tumorous embolisms due to the alteration in the blood flow, lymph system and ducts inherent in the physiopathologic process of this disease (11). It is important to consider the delayed blood flow in portal hypertension mainly in cases of portal embolus, forcing the flow to collaterals, such the porto-cava circulation. Vanbockricj *et al*, verified that when evaluating the hematogenic dissemination of extra-hepatic neoplasms, the prevalence was of 71% in patients with cirrhosis and 76% in patients who did not present concomitant hepatic diseases (16). This finding provides the possibility of the hematogenic dissemination to cirrhotic livers being low, contributing in this way to the rarity of hepatic metastasis in this situation. In relation to the morphology, attention must be drawn to the care needed when analyzing the cellular characteristics of livers with intense fibrosis and inflammation, which may lead to diagnostic mistakes, as well as the caution needed when performing various histological cuts in order to verify the presence of micro-metastasis.

It must be considered that the cirrhotic patients have a smaller survival due to the natural history of the disease, when compared to the rest of the population, possibly leading to a smaller time period for the metastasis to occur in these situations (2, 4, 13, 14, 16). The alterations related to deficit of hepatic function and its influence in tumor growth must be considered and is still an area that needs a better comprehension (2).

Another possibility that must be contemplated is that an increase in inhibitors of metalloproteinases and spe-

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cially, alterations of the lecithinase or of its locations of junction to cirrhotic livers might contribute in the explanation of this rare phenomenon (17). Some hepatic diseases are accompanied by the increase in levels of serum asialoglycoproteins, which increase in the presence of structural alterations in the plasma membrane of hepatocytes whose surface recognizes the lecithinases and eliminates the asialoglycoproteins, which in its turn might carry groups of carbohydrates characteristic of tumorous cells or serve as building-blocks for neoplasic embolisms. As there is a decrease in the levels of lecithinases, the adhesiveness to these embolisms in cirrhotic livers should be lower. These livers present high concentrations of metaproteinase inhibitors and lower enzymatic quantity (16). In this way, the lecithinases and their points of junction might respond to the physiopathogenic processes involved in the appearance of hepatic metastasis in the presence of cirrhosis, making this organ less susceptible to extra-hepatic neoplasic metastasis in this situation (12).

An important mechanism that explains the extremely rare prevalence of hepatic metastasis of epidermoid carcinoma of the esophagus is that, according to the hemodynamic alterations found in cirrhosis, the tumoral emboli sms are forced to drain through the circulation by the medium and superior segments of the esophagus, not draining to the portal system (4).

Based on this report, the importance of identifying the presence of metastasis in cirrhotic livers is emphasized, as its existence decisively changes the therapeutic approach that will be offered to the patient.

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