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MINIREVIEW

DETERMINATION OF PERITONEAL LAVAGE TUMOR MARKER CONCENTRATIONS IN GASTRIC CANCER

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Summary

Gastric cancer remains one of the most lethal malignancies worldwide, with a high capacity of developing peritoneal recurrences. The apparition of peritoneal seeding in the setting of a case diagnosed with gastric cancer represents the most common cause of death. Due to this aspect, researchers' attention was focused on determining which are the most efficient methods in order to provide an early diagnosis of a possible peritoneal recurrence. This is a literature review regarding the role of determination of peritoneal lavage tumor marker concentrations in patients previously diagnosed with gastric cancer.
Key words: gastric cancer, tumor markers, peritoneal lavage

Résumé

Détermination des concentrations des marqueurs tumoraux dans le liquide péritonéal chez les patients avec du cancer gastrique

Le cancer gastrique reste l'une des tumeurs malignes les plus meurtrières dans le monde entier, avec une forte capacité de développer des récurrences péritonéales. L'apparition de métastases péritonéales dans les cas diagnostiquées avec un cancer gastrique représente la cause la plus fréquente de décès. En raison de cet aspect, l'attention des chercheurs s'est concentrée déterminer laquelle est le plus efficace méthode de diagnostic précoce de la récidive péritonéale. Ceci est une revue de la littérature concernant le but de la détermination de la concentration des marqueurs tumoraux dans le liquide de lavage péritonéal chez les patients déjà diagnostiqués avec du cancer gastrique.
Mots-clés: cancer gastrique, marqueurs tumoraux, lavage péritonéal

Introduction

The measurement of tumor marker concentrations in the peritoneal lavage fluid can be used in order to detect the risk of peritoneal recurrence and to give the possibility of establishing the adjuvant treatment and of improving the postoperative follow-up (1,2). Peritoneal recurrence is the most common cause of death in patients with stomach cancer (2).

Tumor markers in peritoneal liquid of patients with gastric cancer

A study realized by L. L Fernandes et al included 32 patients diagnosed with gastric carcinoma and treated by gastrectomy. The authors measured the concentrations of CA 72-4 in the venous blood and in the peritoneal washing, using cut-off values of 7 U/ml for serum and 0.61 U/ml for the peritoneal washing. The results showed a good correlation between the serum CA 72-4 concentrations (which had a mean of 6.55 U/mL ± 15.30) and the peritoneal washing CA 72-4 concentrations (which had a mean of 8.50 U/mL ± 26.72). Both concentrations were well correlated with the lymph nodes involvement. Only the peritoneal washing concentrations of CA 72-4 correlated well with the invasion into the serosa and with the presence of more advanced stages of stomach cancer (1).

A study realized by D. Hoskovec et al included 52 patients, 32 of them diagnosed with gastric cancer and 20 of them diagnosed with pancreatic cancer. The authors measured the concentrations of CEA and CA 19-9 in the

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serum and peritoneal cavity. The results showed a good correlation between the tumor marker values and the stage of the disease. Patients diagnosed with the first two stages of disease have higher CEA and CA 19-9 levels in the serum than in the peritoneal cavity (but most of them had normal concentrations). Patients diagnosed with stages III or IV of the disease had higher levels in the peritoneal cavity than in serum. The study concluded that the concentrations of tumor markers in the peritoneum and serum can suggest the route of dissemination (hematogenous and intraperitoneal) and that they can detect the risk of an early peritoneal recurrence of the disease, in which case a R1 resection would be made (2).

A study realized by M. Yamamoto et al investigated the prognostic significance of tumor markers in peritoneal lavage in patients diagnosed with advanced gastric cancer. The study included 229 patients. Their intraoperative concentrations of CEA, CA 125 and CA 19-9 in peritoneal lavage were measured by means of a chemiluminescent enzyme immunoassay. The sensitivity of CEA for the detection of peritoneal dissemination was higher than that of CA 125 and CA 19-9 (75.8% at a specificity of 90.8%). The factors that could predict the peritoneal dissemination were positive cytology, CEA level in peritoneal lavage ($\geq$ 0.5 ng/ml), serosal invasion and CA 125 concentration in peritoneal lavage (3).

A study realized by S Mandorwski et al in 2002 included 40 patients diagnosed with gastric adenocarcinoma, all stages, and 24 patients with benign diseases. The authors measured the concentrations of CEA and CA 72-4 in blood and in peritoneal washed. 25% of the cases had increased concentrations of CEA, 47.5% of the cases had increased concentrations of CA 72-4. The patients diagnosed with stages III and IV of the disease had higher levels of CEA and CA 72-4. The authors concluded that the highest sensitivity in the detection of gastric cancer was achieved by CA 72-4 from all the serum markers and by CEA from all the markers measured in the peritoneal fluid (4).

A study realized in 2014 by Yamamoto M et al evaluated the role of CEA (cut-off value of 0.5 ng/ml) and CA 72-4 (cut-off value of 1.3 U/ml) peritoneal wash concentrations (measured by a chemiluminescent enzyme immunoassay) in the estimation of prognosis in patients with gastric carcinoma. The study included 193 patients. The results showed that the peritoneal wash levels of CEA, CA 72-4 and the invasion of the serosa can be considered as independent factors for the prediction of the peritoneal dissemination. The patients could be divided in four categories, each of them being characterized by a certain 5-year survival. A first group was characterized by normal CEA and CA 72-4 peritoneal wash levels and had a 87% percentage of 5-year survival. A second group was characterized by normal CEA concentrations and high CA 72-4 values and had a 68% percentage of survival. A third group was characterized by increased CEA levels and normal CA 72-4 concentrations and had a 38% percentage of survival. The fourth group had increased concentrations of both tumor markers in the peritoneal wash and had the lowest survival rate (20%). The conclusion of the study was that the association of the tumor markers is a more accurate way of determining the sites of recurrence (5).

A study realized in 2013 by S. Tamura MD et al included 141 patients diagnosed with advanced gastric cancer. The authors determined the mRNA of CEA and CK-20 in the peritoneal lavage of these patients using the RT-PCR.The results showed the factors that could predict the overall survival in multivariate analysis: CEA and CK-20 measured by RT-PCR, CK-20 alone measured by RT-PCR in association with the pathological N-stage. They also showed that the factors that could predict recurrences after surgery in multivariate analysis were CEA and CK-20 measured by RT-PCR, CEA in association with the pathological T-stage, pN-stage and histological grade (6).

A study realized by Chang-Ho Jeon, MD, et al included 117 patients with gastric carcinoma. They were investigated for CEA and MAGE A1-A6 RT-PCR in the peritoneal washes after curative surgery. 9.4% of the peritoneal fluids were positive for MAGE expression and 32.5% of the peritoneal fluids were positive for CEA expression. 32.5% of the RT-PCR-positive patients had recurrences and 5.2% of the RT-PCR-negative patients had recurrences. In univariate analysis, MAGE and CEA expressions were considered to be independent prognostic factors for recurrence. In multivariate analysis, MAGE expression proved to be the best predictor of recurrence (7).

Conclusions

As a conclusion, the survival of these patients can be improved by the association of various tumor markers, by the use of newer detection techniques and by the performing of these measurements from different sites and fluids. For this purpose, more research is still needed.

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