Calcification within the lesion of liver metastases is a well-known phenomenon. It occurs in 12-27% of hepatic colorectal metastases, but its clinical significance and its influence on prognosis are controversial. The calcification is either produced by the tumor itself or represents dystrophic calcification secondary to necrosis and/or haemorrhage within the tumor before or during chemotherapy. We here present the image findings of a case of colon cancer with liver metastases which calcified following 5-fluorouracil chemotherapy.

Key words: calcification, colorectal cancer, 5-fluorouracil, liver metastases

Colorectal carcinoma is one of the most common cause of cancer-related death in Taiwan. In recent years, cytotoxic chemotherapy using 5-fluorouracil has been the treatment of choice for metastatic colorectal cancer and the objective response is achieved in 25% of the patients [1]. Liver metastases occur in up to 40% of patients with colorectal cancer [2]. These metastases are usually hypovascular and vary in size from large coalescent lesions occupying a major part of an hepatic lobe to small lesions less than 1 cm in diameter. Survival period with liver metastases is 6-15 months. Length of survival is known to correlate with the degree of differentiation of the primary tumor as well as the volume of tumor presented within the liver [3-5].

Calcification is known to occur in 12-27% of liver metastases and is easily identified on both CT (computerized tomography) scan and ultrasound [6-8]. The significance of calcification in hepatic colorectal metastases is not known, although calcification is thought to be associated with the mucinous variant of colorectal cancer [3]. The prognosis of calcified liver metastases is still controversial [9].

CASE REPORT

A 41-year-old female patient was a victim of chronic hepatitis B virus infection. She had multiple liver and gastric metastases from sigmoid colon cancer diagnosed in March 1999. Abdominal CT showed multiple metastases with fine calcification in both hepatic lobes (Fig. 1a,b). She was treated with high dose 5-fluorouracil (5-FU) 2600 mg/m² chemotherapy weekly. After 26 courses of chemotherapy, the liver metastases became heavily calcified on unenhanced CT images (Fig. 2a,b). There is no tumor found in sigmoidoscopy.
Complete response was impressed and the chemotherapy was stopped in September 1999. However, a follow-up CT scan in December 1999 showed two new lesions, one about 10 mm at S7 and another about 18 mm at S5/6 of right lobe of liver (Fig. 3a,b). Metastatic lesions in progression were considered.

She was then treated with irinotecan (CPT-11) 125 mg/m² in repeated 4-week cycle that consisted of 3 consecutive weeks followed by 1-week break. At first, stable disease with regressive change of the calcified masses was noted (Fig. 4a,b). However, after 4 cycles of treatment, CT scan revealed further progression of the disease in May 2000 (Fig. 5a,b) and no further treatment was arranged. The patient took herbal medicine and was then loss of follow-up. Unfortunately, progressively deteriorated liver function, jaundice and ascites developed since August 2000. The patient died of hepatic failure in November 2000.

DISCUSSION

Colorectal cancer is the third most common cause of cancer-related deaths in both men and women in Taiwan. Despite the introduction of multiagent chemotherapy and improvements in surgical techniques, the overall survival rate has not increased significantly over recent decades and the 5 years survival rate remains less than 50% [1].

Hepatic metastases are common, occurring at the time of presentation in 11-25% of patients and in a further 20-30% of patients after resection of the primary tumor [1,2].

Calcification within liver metastases is a well-known phenomenon, but little attention has been given to this feature with regards to its significance, if any, in terms of evaluating therapeutic response. Calcification of liver metastases is seen most frequently in primary mucinous adenocarcinomas, common in...
Calcification of liver metastases in colon cancer following chemotherapy

Colorectal cancer, and can be demonstrated in ovarian cancer, breast cancer, renal cancer, thyroid cancer and neuroblastoma [9-10]. Calcification in the liver may also be seen in primary benign and malignant tumors [11]. The calcification is either produced by the tumor itself or represents dystrophic calcification secondary to necrosis and/or hemorrhage within the tumor before or during chemotherapy [12].

Figure 3. a one new lesion about 10 mm at S7 of right lobe of liver. b another new lesion about 18 mm at S5/6 of right lobe of liver

Figure 4. a and b One year later, regression of the metastatic lesion in S7 and S4/5 were noted in the initial period of chemotherapy with CPT-11

Figure 5. a and b several variable sized calcified masses with recurrent tumor were noted
Hale et al. [9] studied a group of 265 patients with locally advanced or metastatic cancer. Twenty-nine (11%) patients had calcified liver metastases at presentation and 10 (4%) developed calcification during chemotherapy. Analysis of the lesions showed that the most frequent (22 of the 29 patient with calcified liver metastases) characteristic was fine calcification (< 1 mm in size or linear) with a variable distribution. The most frequent change on treatment was alteration in the extent of calcification. Calcification developed during treatment was usually central within the lesion (8 of the 10 patient with calcification developed during chemotherapy). Liver metastatic calcification may not carry any prognostic significance in colorectal cancer.

In another study, Easson et al. [13] looked at a group of 112 patients with hepatic colorectal metastases. In their study, nine patients had calcification of hepatic metastases at presentation, and 22 developed calcification during chemotherapy, giving an overall incidence of 28%. They found that the presence of calcification was independent of degree of tumor differentiation, the presence of mucinous adenocarcinoma, or hepatic tumor burden. They also found that the presence of calcification was a highly significant prognostic factor indicating improvement in survival, which is in contrast to the result of the previous report which showed that the presence of calcification had no relationship to patients’ survival.

In summary, we have presented the imaging finding of a colon cancer with calcified liver metastasis following 5-FU chemotherapy which is rarely encountered in clinical practice. Calcification in liver metastases from colorectal cancer develops in over 12-27% of patients and has a varied appearance and variable course on therapy. The prognosis of calcified liver metastases is still under debating.

REFERENCE

大腸癌肝轉移在接受5-Fluorouracil化學治療後鈣化：一病例報告

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12-27%的大腸直腸癌併肝轉移會有鈣化的現象，但它的臨床表現及對預後的影響仍有爭議。鈣化是由於腫瘤本身產生或次發於接受化學治療前或後腫瘤內的壞死或出血。在此，我們報告一例大腸癌併肝轉移，在接受化學治療後出現完全鈣化的現象。

關鍵詞：鈣化；大腸癌；5-Fluorouracil；肝轉移