Radical surgical approach for synchronous ovarian and uterine cervix tumor with uterine cervix liver metastasis

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ABSTRACT

Synchronous ovarian and uterine cervix malignancies are extremely rare gynecologic neoplasia. In the meantime the presence of hepatic metastases originating from cervical cancer is another rare situation, the liver being more often a common site of metastases for ovarian malignancies. We present the case of a 63-year-old patient who was diagnosed with a moderately differentiated squamous cell cervical tumor with urinary bladder invasion associated with an ovarian tumor and liver metastases. An anterior exenteration and atypical liver resection were performed; the histopathological studies revealed the presence of a moderately differentiated squamous cell uterine cervix carcinoma and a well differentiated serous epithelial ovarian adenocarcinoma; the histopathological examination of the liver lesions confirmed the presence of a squamous cell type originating from the uterine cervix neoplasm.

Key words: ovarian cancer, cervical cancer, liver metastases, pelvic exenteration, synchronous tumors

INTRODUCTION

Synchronous gynecologic malignancies are rare situations, accounting for up to 0.63% of all gynecologic neoplasia, the most common eventuality consisting of the association of endometrial and ovarian cancer (1). However, most often when synchronous tumors are diagnosed preoperatively, the histopathological study comes to demonstrate that in fact there is a single primary, the second tumor being a metastatic lesion. Synchronous lesions involving both the ovary and uterine cervix are very rare situations, only few cases being reported so far (2,3). However, whenever the histopathological studies confirm the presence of two synchronous lesions with different histopathological origins in the uterine cervix and ovary respectively, the association of liver metastases is to be expected as distant metastases with ovarian origin moreover than uterine cervix origin. We present the case of a 63-year-old patient diagnosed with synchronous ovarian and uterine cervix lesions and liver metastases in which the histopathological studies revealed the uterine cervix origin of the liver lesion.
CASE REPORT

A 63-year-old patient presented for vaginal bleeding and hematuria; the local examination revealed the presence of a uterine cervix tumor invading the posterior wall of the bladder. The pelvic computed tomography confirmed the presence of a uterine cervix tumor invading the urinary bladder and the left uretero-vesical junction with secondary uretero-hydronephrosis while the abdominal sequences of the tomography revealed the presence of a liver lesion located in segment IVB. The patient was submitted to uterine cervix biopsy, the histopathological studies confirming the presence of a moderately differentiated squamous cell cervical tumor. The patient was submitted to neoadjuvant chemotherapy followed by surgery. Intraoperatively the association of a uterine and ovarian tumor was found. The patient was submitted to anterior pelvic exenteration, pelvic and para-aortic lymph node dissection. In the meantime the liver metastasis was resected by performing an atypical hepatectomy (figures 1-8). The histopathological studies confirmed the presence of a moderately differentiated squamous cell uterine cervix carcinoma and a well differentiated serous cell ovarian adenocarcinoma; in the meantime the studies of the specimen of atypical hepatectomy confirmed the uterine cervix origin of the liver lesion. Postoperatively the patient had an uneventful course, being discharged in the 11th postoperative day. One month after surgery she was re-addressed to the oncology clinic in order to be submitted to adjuvant oncologic treatment. At two year follow up the patient is free of any recurrent disease.

DISCUSSIONS

Synchronous gynecologic primary malignancies are rare situations, reported in 0.63% of patients diagnosed with gynecological neoplasia, the most common association consisting of endometroid carcinoma of the ovary and endometrium, in 40% of cases (1,2). This particular situation is associated with an improved prognosis due to the possibility of early diagnosis and low grade malignancy (2). However, in all cases with multiple gynecological tumors the final diagnosis of synchronous lesions is established after performing a histopathological examination in order to exclude the situation of a single primary tumor with synchronous metastases (3). The presence of synchronous lesions was explained by the theory of “field cancerization” which was exposed for the first time by Slaughter et al in 1953; the author referred to the possibility of developing synchronous tumors in organs with embryologically similar cells subjected to similar hormonal or carcinogens influences (4). Initially this process was described in malignant transformations of head and neck mucosa and was later extended to the genital organs system, defined as the “second mullerian system” (2,5). According to this hypothesis the second mullerian system consists of uterine cervix, fallopian tubes, ovarian and peritoneal surface cells which seem to share similar molecular receptors for carcinogenic stimuli leading in this way to the apparition of synchronous malignancies (6). However this mechanism can be incriminated in cases presenting similar histological subtypes (7).
Once the diagnosis of synchronous lesions was confirmed by histopathological and immunohistochemical studies, an adequate tumor staging for both primaries is mandatory in order to establish the most appropriate therapeutic protocol. When it comes to long term outcomes, the overall survival rates seem to considerably vary, being especially related to each tumor stage at diagnosis. However, it seems that patients diagnosed with multiple gynecologic neoplasms are not expected to have a poorer outcome in terms of survival compared to those with single site neoplasms (3).

Another particular aspect of our case consists in the presence of liver metastases with uterine cervix cancer origin. It is well known that the incidence of hepatic
metastases from uterine cervix is very low when compared to other gynecologic malignancies such as ovary or breast. In the study conducted by Kim et al involving 1665 patients with uterine cervix carcinoma, only 20 of them (1.2%) developed liver metastases; in all but one case disseminated intrahepatic and extrahepatic tumors were present. The authors demonstrated that liver metastases in uterine cervix cancer usually develop in the context of systemic disease; in consequence, an improved survival couldn’t be expected (8).

Due to the rarity of uterine cervix liver metastases, there are only few studies regarding the benefits of liver resection in such cases, most often these patients being included in larger studies which focus on the benefits of liver resections for hepatic metastases with gynecologic origin.

In the study conducted by Sarah Kamel et al at John Hopkins Hospital, Baltimore, the authors introduced 87 patients diagnosed with liver metastases from gynecologic primaries including ovary, fallopian tube, uterine /endometrial or uterine cervix submitted to liver resection. Among the 87 patients, only 4% of them were diagnosed with uterine cervix malignancies. Following liver surgery 75% of patients developed recurrent disease; the main patterns of recurrence were intrahepatic only (in 15% of cases), extrahepatic only (in 33% of patients) and both intra and extrahepatic in 46% of cases. The reported median overall survival from the moment of diagnosis was 38 months for the entire cohort and was not influenced by location of the primary tumor, histological subtype, presentation, size, number or distribution of the liver lesions. Moreover, there was no significant difference between the median overall survival between patients submitted to liver surgery for ovarian cancer liver metastases when compared to those with non-ovarian primaries (221 versus 22 months, p=0.53) (9).

In a more recent study conducted by Jose Ramia, suggestively entitled: “Liver metastases from gynecological cancers: Time to resection?” the author included 20 relevant articles published on the topic of liver resection for hepatic metastases from gynecological origin. The division of the article into two main groups: liver metastases from ovarian and non-ovarian cancers come to suggest the preponderance of liver involvement due to ovarian malignancies when compared to all the other gynecologic malignancies (10). When it came to liver metastases from cervical cancer, the authors underlined the low incidence of this situation (ranging between 1.2 - 2.2%) and the poor prognosis (the overall survival of untreated patients being 10 months) (10,11). Due to the low number of reported patients with liver metastases from uterine cervix cancer prognostic factors or standardized criteria for liver resection are still a matter of debate. In Tangjitgamol’s study the most important prognostic factors for an improved outcome after surgery for liver metastases from cervical cancer seem to be the absence of extrahepatic disease, unilobar disease and the association of neoadjuvant chemotherapy; in cases with metachronous lesions a disease free interval of more than 2 years also seem to be a good prognostic factor; in the meantime survival did not seem to be influenced by the size or number of lesions. The same authors concluded that the presence of extrahepatic disease should not be transformed into an absolute contraindication for liver resection (11).

However, data regarding the benefits of liver resec-
tion for hepatic metastases from uterine cervix cancer remain scarce for the moment, larger prospective studies being necessary in order to determine which cases would be most likely to benefit from hepatic resections.

In our case the presence of an isolated liver metastasis enabled us to consider that the best therapeutic option should be association of hepatic resection.

**CONCLUSION**

Association of two synchronous gynaecologic malignancies is a rare situation. However the prognosis does not seem to be worsened by this association and the gynaecologic oncologist should submit the patient to surgery with curative intent whenever a complete removal of all tumor masses is possible; in these cases a benefit in terms of survival is expected. In our case the presence of hepatic metastasis was considered at the time of resection as a distant metastasis from ovarian cancer; however the histopathological studies revealed a surprising origin in the uterine cervix primary. However, performing an R0 resection provided a good control of the disease, the patient being free of recurrence at two year follow-up.

**REFERENCES**