

Pancreatic metastases from uterine cervix tumors – diagnostic challenge and therapeutic options

Nicolae Bacalbasa^{1,2}, Irina Balescu³, Valentin Varlas^{1,4}, Cristina Martac⁵, Ileana Pantea⁶, Mihaela Vilcu^{7,8}, Iulian Brezean^{7,8}, Alexandru Ciulcu⁹

¹Department of Obstetrics and Gynecology, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

²Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

³Department of Visceral Surgery, Ponderas Academic Hospital, Bucharest, Romania

⁴Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania

⁵Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

⁶Department of Diabetes and Nutrition, Transilvania University Brasov, Romania

⁷Department of Surgery, “Dr. I. Cantacuzino” Clinical Hospital, Bucharest, Romania

⁸Department of Surgery, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

⁹Department of Obstetrics and Gynecology, “Dr. I. Cantacuzino” Clinical Hospital, Bucharest, Romania

ABSTRACT

Pancreatic metastases represent rare eventualities, being more frequently encountered in colorectal, ovarian or breast cancer, other primaries being usually reported more often in autopsy studies. When it comes to cervical cancer, it usually is responsible for the development of local recurrences, lymphatic recurrences or hematogenous metastases in lungs. The aim of the current paper is to discuss about the possibility of developing pancreatic metastases from cervical cancer and to analyze the most efficient therapeutic strategies in such cases.

Keywords: uterine cervix cancer, metastases, pancreatic metastases, surgery, chemotherapy

INTRODUCTION

Despite efforts reported worldwide regarding screening programs for early detection of cervical cancer, a significant number of patients are still diagnosed in advanced stages of the disease, when relapse is the rule even if radical therapeutic strategies are initially applied [1]. In such cases, recurrent disease will occur via different patterns of spread such as lymphatic, hematogenous or peritoneal route [2,3]. When it comes to pancreas, malignant tumors developed at this level are most commonly represented by primary neoplasms, metastatic disease being rarely encountered. Even though, the most frequently cited malignancies leading to the apparition of pancreatic metastases are represented by colorectal, ovarian and kidney carcinoma [4]. When it comes to the incidence of pancreatic metastases from cervical cancer, it is a very scarce one, only isolated case reports being published so far [5,6]. As for the involvement routes of the pancreas

as site of metastatic disease, multiple mechanisms have been incriminated: lymphatic, hematogenous route or direct extension. As expected, in cervical cancer with pancreatic metastases, malignant cells usually reach the pancreatic parenchyma through the hematogenous route or via lymphatic route leading to the apparition of para-pancreatic metastatic adenopathies which will further invade the pancreatic parenchyma.

CLINICAL SIGNS AND SYMPTOMS IN PATIENTS WITH PANCREATIC METASTASES FROM UTERINE CERVIX CANCER

As expected, the signs and symptoms of patients with pancreatic metastases from uterine cervix cancer widely vary depending to the location of the lesions; therefore, while in cases in which the lesion is located at the level of the pancreatic head the main sign is represented by jaundice, in cases in which

lesions are located at the level of the pancreatic body and tail the main symptoms are represented by pain and vague abdominal discomfort; meanwhile, we should not omit the fact that in a significant number of cases these lesions remain asymptomatic for a long period of time, the patient being rather diagnosed at the time of performing scheduled follow up imagistic studies [7].

DIAGNOSTIC CHALLENGES IN PATIENTS WITH PANCREATIC LESIONS

In order to establish a right positive diagnostic in cases presenting pancreatic lesion, a pancreatic biopsy is mandatory. Although initially a pancreatic biopsy has been difficult to be retrieved and therefore a surgical procedure was needed, once the endoscopic ultrasound has been widely implemented, pancreatic biopsies became significantly more feasible to be obtained [8]. Another method through which the differential diagnostic could be orientated is by measuring the serum levels of tumoral markers such as CA 19-9, CEA and SCC. Therefore, while in cases in which a primary pancreatic lesion a significantly increased serum level of CA 19-9 is found, cases presenting metastatic lesions from uterine cervix neoplasms will report rather an increased level of SCC and normal or slightly increased serum values of CA19-9 levels [9-10].

An interesting case in which a positive diagnostic was established intraoperatively was reported by Ogata et al. therefore, the authors presented the case of a 78 year old previously healthy patient investigated for jaundice and diagnosed with a pancreatic head lesion causing compression of the common bile duct and of the main pancreatic duct in association with increased cholestasis markers and normal values of CA19-9. The patient was proposed for a pancreatoduodenectomy with a preoperative diagnostic of primary tumor of the pancreatic head; intraoperatively a peritoneal nodule at the level of the Douglas pouch was observed and was biopsied, the frozen section raising the suspicion of a squamous cell carcinoma. The patient was further submitted to a pelvic examination which demonstrated the presence of a cervical tumor; in this context a double malignancy (with pancreatic and uterine cervix origin) was suspected and therefore, a pancreatoduodenectomy was performed as planned, the cervical tumor being considered to be suitable for oncological treatment. Surprisingly, the histopathological studies of the specimen of pancreatoduodenectomy demonstrated the presence of squamous cell carcinoma islets, therefore conducting to the diagnostic of a pancreatic metastasis from cervical cancer. Although the patient was submitted to oncological treatment for stage IV cervical cancer, she died of disease 10 months later [6].

THERAPEUTIC STRATEGIES IN PANCREATIC METASTASES FROM UTERINE CERVIX CANCER

As mentioned before, pancreatic metastases from cervical cancer usually present a systemic contamination with circulating malignant cells; therefore, in a significant number of cases the pancreas represents only a site in which hematogenous cells seed and conduct to the apparition of metastatic disease. Therefore, when we have to deal with a patient with multiple metastatic lesions, as expected the most appropriate therapeutic strategy will remain systemic chemotherapy. Meanwhile, if the pancreatic lesion causes serious complications which might significantly impact on the overall survival and on the quality of life – such as jaundice – an invasive maneuver should be performed in order to diminish the cholestatic syndrome and to prepare the patient for the administration of systemic therapy. In cases in which multiple metastatic lesions are present and resection of the pancreatic lesion is senseless, minimally invasive procedures such as stent placement in the common biliary duct in order to alleviate jaundice and offer the chance for the patient to be submitted to systemic chemotherapy might be the option of choice [11].

In isolated cases in which pancreatic lesions are in fact the expression of oligometastatic disease, surgery with potential curative intent might be taken in consideration. However, we should not omit the fact that pancreatic surgery is by definition a difficult procedure, associated with increased rates of postoperative complications; therefore such procedures should be reserved for patients with a good general status and should be performed in specialized, tertiary centers [7].

CONCLUSIONS

Pancreatic metastases from uterine cervix malignancies represent a relatively rare event which is usually associated with a poor prognostic due to the fact that is the sign of disseminated neoplastic impregnation. In rare cases in which oligometastatic disease is encountered, resection might be taken in consideration. Meanwhile, in cases in which disseminated lesions are present and jaundice affects the quality of life, other interventional procedures such as stent placement might be needed in order to alleviate the symptoms and to offer the patient a better condition in order to be submitted to palliative treatment. However, due to the extremely low number of cases, a standard therapeutic strategy is not well defined, the main experience originating from isolated case reports.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(1):7–34.
2. Li H, Wu X, Cheng X. Advances in diagnosis and treatment of metastatic cervical cancer. *J Gynecol Oncol.* 2016;27:e43.
3. Deng K, Yang C, Tan Q et al. Sites of distant metastases and overall survival in ovarian cancer: a study of 1481 patients. *Gynecol Oncol.* 2018;150:460–465.
4. Adsay NV, Andea A, Basturk O et al. Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature. *Virchows Arch.* 2014;444(6): 527-535.
5. Wastell C. A solitary secondary deposit in the pancreas from a carcinoma of the cervix. *Postgrad Med J.* 1966;42(483):59-61.
6. Ogawa H, Tsujie M, Miyamoto A et al. Isolated pancreatic metastasis from uterine cervical cancer: a case report. *Pancreas.* 2011;40(5):797-798.
7. Ogata S, Kimura A, Kameda K et al. Pancreatic metastasis of uterine cervix cancer mimicking a primary cancer. *Dig Sys.* 2018;2(1):1-2.
8. Kuwatani M, Kawakami H, Asaka M et al. Pancreatic metastasis from small cell carcinoma of the uterine cervix demonstrated by endoscopic ultrasonography-guided fine needle aspiration. *Diagn Cytopathol.* 2008;36(11):840-842.
9. Nishimura C, Naoe H, Hashigo S et al. Pancreatic metastasis from mixed adenoneuroendocrine carcinoma of the uterine cervix: a case report. *Case Rep Oncol.* 2013;6(2):256-262.
10. Manuel V, Rocha E, Fortini G et al. Uterine cancer presenting as obstructive jaundice. *Int J Womens Health.* 2016;7(8):261-263.
11. Levey JM. Endoscopic biliary drainage for metastatic squamous cell carcinoma of the cervix. *Gastro Endoscopy.* 2000;51(1):97–99.