

Osseous metastases associated with gastrointestinal neoplasia during pregnancy

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Abstract

The article represents an analysis of a confirmed case of digestive neoplasia noted during the last trimester of pregnancy, in which we tried to assess osseous metastases, in correlation with their clinical development and histopathological features. The International Agency for Research on Cancer reported that during the year of 2018, in Romania, a total of 11.076 new cases of colorectal cancer were documented, ranking this type of neoplasia as the 2nd among the most common types of cancer in our country.

Keywords: pregnancy, osseous, metastases, digestive, neoplasia

Introduction

Cancer during pregnancy implies medical, ethical, psychological, and religious issues; it involves two people, the mother and the foetus, and the medical team should aim for optimal maternal treatment and safeguard the foetal well-being. The main reason for the high incidence of neoplasia during pregnancy is due to the trend of having a child late into the reproductive years, and as such, we

expect to find more and more cases of cancer complicating pregnancy due to maternal age.

Pregnancy-associated gastric and colorectal cancer is very rare. The diagnosis is suggested at an advanced stage of neoplasia because the symptoms (bloating, frequent headaches, or rectal bleeding) during pregnancy are not uncommon during pregnancy, and are not considered suspicious. Standard interventions in diagnosing, staging, and treatment of cancer may be harmful for the unborn baby, but there

are also interventions that are safe to use during pregnancy.

X-ray imaging and CT scans are considered relatively safe during pregnancy, as long as they do not extend to the abdomen or the pelvis. As such, investigations of this type involving the head or chest are usually safe during pregnancy, as they do not directly expose the fetus to radiation. Radiographies and CT scans of the abdomen or pelvis should only be performed if absolutely necessary - if the calculated potential benefits outweigh the risks to the fetus. MRIs, ultrasound, and biopsies are safe in pregnancy. Gadolinium-free abdominal MRI may be used in cases in which a high risk of metastasis is suspected in previous examinations. Gadolinium can cross the placenta and stimulate malformations, so the use of gadolinium during pregnancy is contraindicated, especially in the first trimester of pregnancy. Tumor markers are unreliable; they can be modified by pregnancy and therefore do not often show accuracy during this period [2,3].

The process of metastasizing involves loss of intercellular cohesion, cell migration, angiogenesis, access to systemic circulation, survival in circulation, evasion of local immune responses, and growth at distant organs [4].

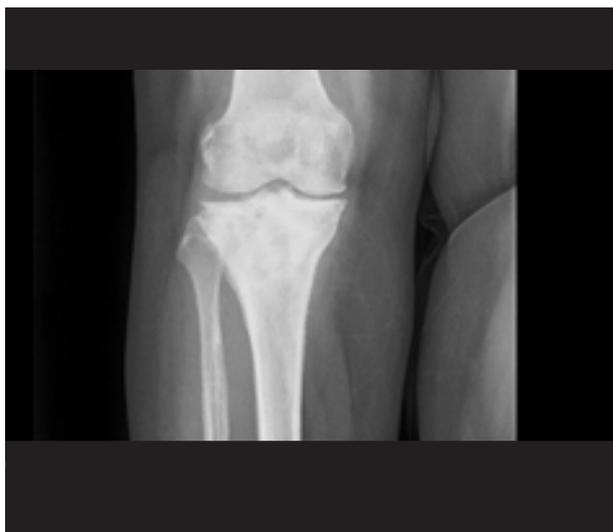


Fig. 1 Bone Metastases (collection University Emergency Hospital Bucharest)

Bone metastases are one of the first signs of disseminated disease in cancer patients [2], and typically indicate a short-term prognosis in cancer patients. However, osseous metastasis from ovarian cancer is rare, but the increasing pathological stage of ovarian cancer may contribute to the risk of bone metastasis (especially in the cases with lung or lymphatic dissemination) [3].

The bone is a common metastatic site and bone metastases most commonly affect the axial skeleton, thus, bone metastases represent a major cause of morbidity in patients diagnosed with advanced-stage malignant diseases. Morbidities, like pathological fractures and spinal cord compression/ paralysis, cause impairment in activities of daily life and affect the prognosis due to the deterioration of the patient's general condition and discontinuation of treatment for the primary disease. Approximately 70% of all malignant bone tumors are metastatic in origin.

Case report

We reported a case of colon cancer discovered during the last trimester of pregnancy in a 36-year-old primiparous pregnant woman - 33 weeks of gestation - with previous complaints of abdominal pain, who was admitted to the Department of Obstetrics

and Gynecology of the University Emergency Hospital, Bucharest, for uterine contractions and minor rectal bleedings.

The patient had no family history of cancer and denied any use of alcohol, cigarettes, or intravenous drugs.

She also described that in the past she suffered episodes of low abdominal pain and constipation and had multiple hospitalizations for subocclusive episodes. Also, during these admissions, she was diagnosed with enlarged liver and hepatic hemangiomas, which were detected during the physical exam of the patient - a liver that was palpable at about 20 cm inferior to the 10th rib. No other palpable masses have been identified, except for a viable singleton pregnancy estimated to be about 33 weeks' gestation. Vaginal examination revealed a short cervix and a fetus in breech presentation.

The patient was anemic at the time of presentation, with hemoglobin (Hb) level of 9.2 g/ dL and hematocrit (Ht) measure of 28.3%. Other laboratory data, including liver function tests, cancer markers and a basic chemistry panel, were pathologically modified. Tumor markers were also severely elevated: α -fetoprotein 56.46 IU, cancer antigen (CA) 19-9 1652.5 IU, CA 125 220.9 IU. Ultrasound examination detected large volume liver tumors with intense vascular signal at Doppler examination. A malignant process was suspected, but the primary tumor was not determined.

MRI examination also highlighted global hepatomegaly with small amount of ascites surrounding the liver and right pleural effusions.

The pregnancy was terminated by Caesarean section at 33 weeks of gestation. An interdisciplinary surgical team composed of obstetricians and surgeons performed the intervention under general anesthesia. A single live preterm male baby, with a

weight of 1750 g and an Apgar score of 8 was delivered. Intraoperative frozen section examination confirmed the presence of a moderately differentiated colonic-type adenocarcinomatous proliferation. A stenotic tumor was detected at the level of the descending colon, 10 cm inferior to the left colic flexure. The surgical team performed a left hemicolectomy and colo-colonic anastomosis - HP examination of the hemicolectomy specimen revealed a moderately differentiated (G2) adenocarcinomatous proliferation.

The patient was discharged after 14 days with good general condition, afebrile, supple abdomen, mobile with breathing, gastrointestinal transit recovered, supple postoperative wound.

Discussions

Digestive cancers are mildly osteophilic tumors. Bone metastases tend to occur late in these types of neoplasias. Although, in some cases, metastatic osseous diffusion is revealed, in the vast majority of cases, bone involvement accompanies multivisceral metastatic disorders (liver, lung, lymph node or peritoneal). Correct evaluation of the frequency of bone metastases in digestive cancers is difficult because the literature data are scarce. The frequency reported depends on the detection methods used: imaging guided by clinical symptoms, detecting asymptomatic lesions by radionuclide or MRI bone scan or during the autopsy series. Although all bones can be the site of a metastasis, the preferential distribution of these lesions is the spine and long bones [9].

The number of women with colorectal cancer exceeds the number of men by 1.5 times, with the average age of 60 years and 3.6% being in the fertile period. 300 cases of pregnancies associated with colorectal cancer

are presented in literature, the average age of the pregnant women being 32 years old [5]. Most authors consider that ending the pregnancy is the best decision. In colorectal cancer cases complicated with peritonitis, the authors recommend surgical intervention

and ending the pregnancy without needing the informed consent of the patient. Other authors argue that when pregnant women do not accept the termination of the pregnancy, it must continue until 32-34 weeks and then cesarean section is recommended [6].

Table 1. Management of digestive neoplasia during pregnancy [8]

Gastric Cancer	First trimester - 12 wks	We propose termination of pregnancy, in case of negative informed consent, the pregnancy will be extended to 32-34 weeks, then the pregnancy will be resolved by Caesarean section followed by specialized oncological treatment.
	Second trimester - 22 wks	Extension of pregnancy to 32-34 weeks, ending the pregnancy by Caesarean section + specialized oncological treatment.
	Third trimester - 34 wks	Extension of pregnancy to 32-34 weeks, ending the pregnancy by Caesarean section + specialized oncological treatment.
Bowel and colon cancer	First trimester - 12 wks	We propose termination of pregnancy, in case of negative informed consent, the pregnancy will be extended to 32-34 weeks, then the pregnancy will be resolved by Caesarean section followed by specialized oncological treatment
	Second trimester - 22 wks	"Watch-and-wait" until delivery in week 32-34, ending the pregnancy by Caesarean section + specialized oncological treatment.
	Third trimester - 34 wks	Extension of pregnancy to 32-34 weeks, ending the pregnancy by Caesarean section + specialized oncological treatment.
Rectal cancer	First trimester - 12 wks	We propose termination of pregnancy, in case of negative informed consent, the pregnancy will be extended to 32-34 weeks, then the pregnancy will be resolved by Caesarean section followed by specialized oncological treatment.
	Second trimester - 22 wks	"Watch-and-wait" until delivery in week 32-34, ending the pregnancy by Caesarean section + specialized oncological treatment.
	Third trimester - 34 wks	Extension of pregnancy to 32-34 weeks, ending the pregnancy by Caesarean section + specialized oncological treatment.

Conclusion

The association of colorectal cancer with pregnancy is insignificant. 33 cases were described in literature until 1962, increasing to 131 cases in 2006 [7,8]. In these cases, the

authors recommend ending the pregnancy, and if the colorectal cancer was diagnosed in second or third trimester, management is determined individually, associating the cesarean section with the surgical treatment of the neoplasia.

Conflict of Interest statements

Authors state no conflict of interest.

Informed Consent and Human and Animal Rights statements

Informed consent has been obtained from all individuals included in this study.

Authorization for the use of human subjects

Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies, is in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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