CASE REPORT
KAZUISTIKA

Musculoskeletal Tumors in Extremities Diagnosed During the Gestational Period: Case Series and Literature Review

Muskuloskeletální tumory končetin diagnostikované během gestační periody: případová studie a přehled literatury

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SUMMARY

Given the low incidence of musculoskeletal tumors during pregnancy, publications on the subject are scarce and treatment guidelines nonexistent.

We present five cases of musculoskeletal tumors in pregnant women, three with metastasizing malignant neoplasms and two with aggressive giant cell tumors. The three patients diagnosed during their gestational period were operated before the end of pregnancy, adapting surgical techniques to minimize risk to mother and fetus. Adjuvant therapies were postponed until the end of gestation. All newborns were delivered at term vaginally, except for one where a cesarean section was required. After a mean follow-up of 69.96 months (±56.38), all patients were free of disease, except for the one diagnosed with an extraskeletal myxoid chondrosarcoma who died at 4 years from diagnosis.

Surgery plays a key role in the treatment of musculoskeletal tumors diagnosed during pregnancy. These patients must be treated by multidisciplinary teams at sarcoma reference hospitals, involving the obstetrics team in the decision-making process, and adapting each step of the diagnosis and treatment to the gestational period.

Key words: pregnancy, musculoskeletal tumors, sarcoma, cancer, oncological surgery.

INTRODUCTION

The incidence of malignant neoplasms during gestation is 1 in 1,000 pregnancies, the most common being breast cancer (26%), cervical cancer (26%), leukemia (15%), lymphoma (10%), melanoma (8%), thyroid cancer (4%) and other neoplasms (11%) (14). The "other neoplasms" category includes musculoskeletal tumors, the occurrence of which has been found to be extremely rare. This means that there is currently a dearth of clear guidelines to go by when treating these patients (12). The handful of published studies includes Zarkavelis et al.'s review of the literature with 137 sarcomas diagnosed during pregnancy from 1963 to 2016, 53 of them osseous and 84 soft-tissue sarcomas (15), but the longest series included were published 30 years ago, which means that many of the techniques they describe have become obsolete due to the development of new therapeutic options that have changed the way sarcomas are managed. The longest series published in the last 10 years are Figheirom et al.'s 10-case series, which does not include limb diagnoses, and Postl et al.'s 8-case series (4, 11).

As far as giant cell tumors are concerned, apart from the recent study by Howard et al., all published series deal with isolated cases with presentation in extremities (5, 6, 9, 13).

The purpose of the present study was to present the experience gained by the authors in the diagnosis and treatment of bone and soft tissue tumors in pregnant women in extremities, and review the challenges associated with the management of these patients in a musculoskeletal tumor unit. The study was carried out in La Fe University Polyclinical Hospital.

CASE PRESENTATION

We present 5 pregnant women who were given a diagnosis of musculoskeletal tumor between 2006 and 2009. Patients' epidemiological data are given in tables 1 and 2.

Case 1

28-year-old woman diagnosed during the second trimester of pregnancy with myxoid liposarcoma in the posterior compartment of the thigh (Fig. 1). The patient underwent surgery during her third trimester of pregnancy. Surgery consisted in a wide resection with R0 margins. Adjuvant radiotherapy was administered after delivery. After six years of follow-up, the patient is disease-free.

Case 2

25-year-old woman in the second trimester of pregnancy presented a local recurrence of extraskeletal myxoid chondrosarcoma in the popliteal fossa (Fig. 2). During that trimester of pregnancy, a supracondylar amputation was performed, with a wound dehiscence as a complication that required a new surgery. The patient

Table 1. Pregnant subjects diagnosed with a metastasizing malignant tumor

CASE	AGE	GESTATIONAL AGE AT DIAGNOSIS	LOCATION	AJCC STAGING	STAGING DIAGNOSTIC TESTS	HISTOLOGY	PRIMARY/ RECURRENT	TYPE OF SURGERY/ SPECIMEN MARGINS	GESTATIONAL AGE AT SURGERY	ADJUVANT THERAPIES AND TIME OF ADMINISTRATION	TIME AND DELIVERY ROUTE	CURRENT STATUS
1	28	SECOND TRIMESTER	POSTERIOR COMPARTMENT OF THIGH	IIIA	CHEST MR AND ABDOMINAL ULTRASOUND WITHOUT CONTRAST	MYXOID LIPOSARCOMA	PRIMARY	LIMB SPARING (R0)	THIRD TRIMESTER	ADJUVANT RT POSTPARTUM	AT TERM CESAREAN SECTION	DISEASE-FREE
2	25	SECOND TRIMESTER	POPLITEAL FOSSA	IIIB	THORACO-ABDOMINO PELVIC CT WITH CONTRAST	EXTRASKELETAL MYXOID CHONDROSARCOMA	RECURRENT	SUPRACONDYLAR AMPUTATION (RO)	SECOND TRIMESTER	NO	AT TERM VAGINAL ROUTE	DEATH (SYSTEMIC RELAPSE)
3	38	4 MONTHS POST-PARTUM, ONSET SYMPTOMS LAST TRIMESTER	ANTERIOR COMPARTMENT OF THIGH	IIIB	THORACO-ABDOMINO PELVIC CT WITH CONTRAST	RHABDOMYOSARCOMA	PRIMARY	LIMB SPARING (R0)	6 MONTHS POSTPARTUM	NEOADJUVANT CHEMOTHERAPY AND ADJUVANT RT POSTPARTUM	AT TERM VAGINAL ROUTE	DISEASE-FREE

Table 2. Pregnant subjects diagnosed with giant cell tumor

CASE	AGE	GESTATIONAL AGE AT DIAGNOSIS	LOCATION	CAMPANACCI	STAGING DIAGNOSTIC TEST PERFORMED	PRIMARY/ RECURRENT	TYPE OF SURGERY	GESTATIONAL AGE AT SURGERY	TIME AND DELIVERY ROUTE	CURRENT STATUS
4	35	1 MONTH POSTPARTUM	THIGH	UNCLASSIFIABLE NO METASTASIS	CHEST CT WITHOUT CONTRAST	RECURRENT	DISTAL FEMORAL REVISION AND RESECTION OF TUMOR	4 MONTHS POSTPARTUM	AT TERM VAGINAL	DISEASE-FREE
5	28	FIRST TRIMESTER	PROXIMAL TIBIA	II NO METASTASIS	CHEST CT WITHOUT CONTRAST	PRIMARY	CURETTAGE, BURRING, NITROGEN, HYDROHYAPATITE	SECOND TRIMESTER	AT TERM VAGINAL	DISEASE-FREE

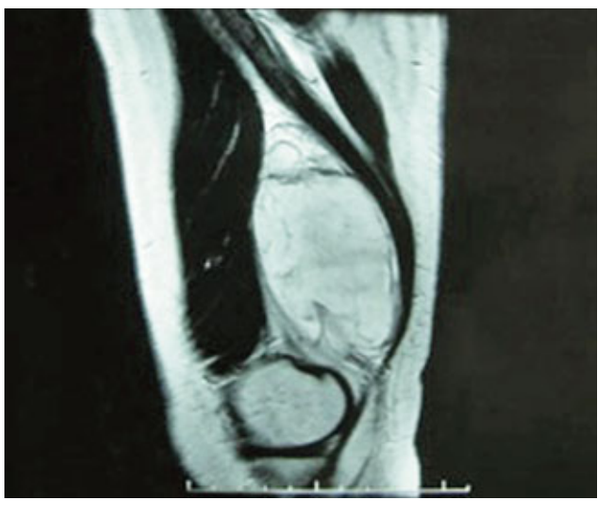

Fig. 1. Magnetic resonance imaging of myxoid liposarcoma located in the posterior compartment of the thigh.

suffered a systemic relapse at 6 months, which was accompanied by pulmonary metastases. Following aggravation of the metastasis, she was treated with chemotherapy and died 4 years following initial diagnosis.

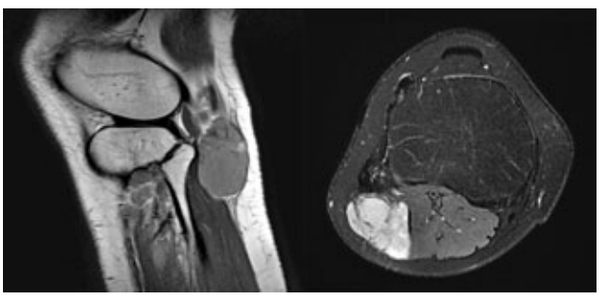

Fig. 2. Magnetic resonance imaging of local recurrence of extraskeletal myxoid chondrosarcoma in the popliteal fossa.

Case 3

38-year-old woman was diagnosed 4 months after delivery with pleomorphic rhabdomyosarcoma in the anterior compartment of the thigh, but onset symptoms appeared in the last trimester of pregnancy (Fig. 3). The patient was operated 6 months following delivery with a limb sparing technique. The patient was given neoadjuvant chemotherapy and adjuvant radiotherapy. After five years, the patient remain free of disease.

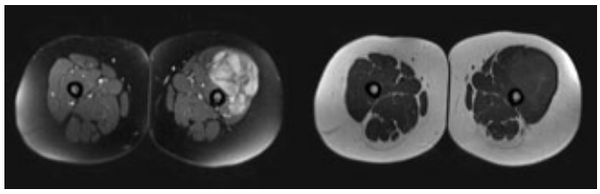

Fig. 3. Magnetic resonance imaging of pleomorphic rhabdomyosarcoma in the anterior compartment of the thigh.

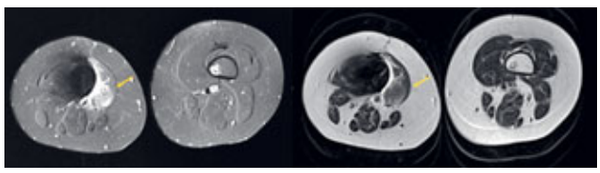

Fig. 4. Magnetic resonance imaging of a soft tissue relapse in the thigh of a osseous giant cell tumor. Artifacted images are caused by the tumoral knee prosthesis placed as initial treatment of the pathology.

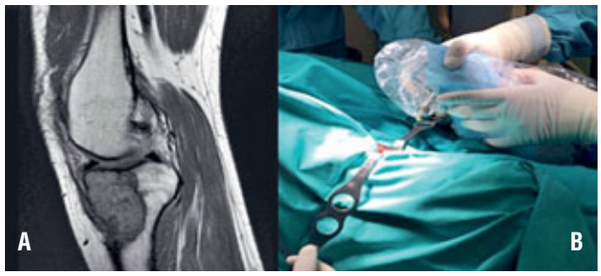

Fig. 5A. Magnetic resonance imaging of a lytic lesion in the proximal tibia corresponding to a giant cell tumor. The relationship between the tumor and the knee joint can be observed. Fig. 5B. Intraoperative administration of adjuvant nitrogen in treating a giant cell tumor to avoid the use of phenol in a pregnant patient

Case 4

35-year-old woman who during the first month postpartum was diagnosed with a relapse in the soft tissue of the thigh of a previously-treated osseous giant cell tumor (Fig. 4). The patient did not present with distant metastasis. Surgery treatment consisted in a resection of the neoplasm and a revision of the primary femoral component, which had become loose. An intraoperative histologic analysis confirmed the diagnosis. After two years' follow-up the patient was free of disease.

Case 5

28-year-old woman diagnosed with an osseous giant cell tumor in the proximal tibia during the first trimester of pregnancy. The neoplasm was classified as Campanacci grade II (Fig. 5A) and did not present with distant metastasis. The procedure was performed during the second trimester of pregnancy and consisted of curettage and high-speed burring of the lesion, followed by the application of liquid nitrogen as local adjuvant, and cavity filling with hydroxyapatite (Fig. 5B). Four years later, no signs of the disease were observed.

All diagnostic and therapeutic decisions were based on the recommendations of the musculoskeletal tumor committee.

None of the patients suffered a miscarriage; all of them were delivered through the vaginal route, except for the patient with myxoid liposarcoma, where a cesarian section was required. None of the patients exhibited any problems regarding the development of the fetus.

DISCUSSION

The development of musculoskeletal tumors is rare, but their diagnosis during pregnancy is even rarer (12). Although the few papers published on the occurrence of this condition in pregnant women show a wide histological variation, it would seem that osteosarcoma is the most common histological type (4, 12, 15). In spite of this, our series did not include any malignant osseous tumors. We only found two giant cell tumors, a rarely metastasizing entity, and three high-grade soft tissue sarcomas.

Performance of imaging tests is essential to study the tumors present in these patients. However, they must be carried out with extreme care to minimize the risk of damaging the fetus. According to the American College of Obstetrics and Gynecology, radiation must be kept below 50 mGy during the first trimester as this is the period when the embryo is at its most vulnerable (7). This means that performing at all as the radiation doses involved are usually under 0.001 mGy. Chest CT would not entail any problem either as the radiation emitted stands at around 0.2 mGy, but the use of abdominal or pelvic CT must be thoroughly justified as radiation levels in those cases could reach up to 50 mGy (7). The kinds of MRI commonly performed for a localized analysis of neoplasms do not entail any risk whatsoever for the embryo (8). Nonetheless, the use of contrast media, which are often indicated in these studies, is not exempt from controversy as there is no agreement in the literature regarding their innocuousness in these patients. The current recommendation is that their use should be limited to cases where they can represent a significant benefit in terms of the information provided (7). In our series, the patient diagnosed with a giant cell tumor during her first trimester was subjected to a chest CT as a diagnostic study; the two patients diagnosed during their second trimester were given a chest MR and an abdominal ultrasound in one case, and a thoraco-abdominopelvic CT in the other. Only one patient was administered a contrast medium, on a decision made by the multidisciplinary team. In patients diagnosed after childbirth, the standard procedure was applied. The decision of what tests to carry out in each patient therefore depends on several factors such as the type of neoplasm and the trimester of pregnancy the patient is in. Options should be specifically discussed as part of the work of multidisciplinary care teams.

Surgery is the mainstay of bone and soft tissue tumors treatment. Following the recommendations of the American College of Obstetricians and Gynecologists, "medically necessary surgery should never be delayed regardless of trimester" (1). Moreover, no study has as yet shown that anesthetic agents administered at conventional doses can be teratogenic (1). In spite of this, it is vital to adapt OR procedures to minimize the risk of fetal damage. For example, during the operation of the patient with a giant cell tumor in the proximal tibia, we were forced to change our standard technical technique taking into account that the subject was in her second trimester of pregnancy. In the first place, we had to minimize the use of the C-arm and of bone cement on account of the, albeit low, risks they posed (2). Furthermore, phenol had to be replaced by liquid nitrogen as an adjuvant agent (3). Surgery in these patients should always be performed under strict fetal monitoring by the obstetrics team.

As regard adjuvant treatment, if chemotherapy is indicated based on the tumor's histologic type, it may be administered from the second trimester. Application during the first trimester could result in malformations, delayed intrauterine growth or even fetal death. Use of radiotherapy should be restricted during the gestational period as it has been associated with impaired fetal development and fetal death, and with the appearance of neoplasms during childhood. For those reasons, its administration should be deferred until after delivery (10).

Some reports have related the appearance of these neoplasms and their treatment in pregnant women with an increased incidence of pre-term deliveries and cesarian sections (4). All patients in our series were delivered at term, with only one case requiring a cesarian section.

Musculoskeletal tumors in pregnant women are a rare condition, whose diagnosis and treatment requires a multidisciplinary approach to safeguard the safety of both the mother and the fetus. For that reason, it is of the essence to involve the obstetrics team in every decision affecting these patients.

References

1. ACOG Committee on Obstetric Practice. ACOG Committee Opinion No. 474: nonobstetric surgery during pregnancy. Obstet Gynecol. 2011;117(2 Pt 1):420–421.
2. Downes J, Rauk PN, Vanheest AE. Occupational hazards for pregnant or lactating women in the orthopaedic operating room. J Am Acad Orthop Surg. 2014;22:326–332.
3. Ferguson KK, Meeker JD, Cantonwine DE, Mukherjee B, Pace GG, Weller D, McElrath TF. Environmental phenol associations with ultrasound and delivery measures of fetal growth. Environ Int. 2018;112:243–250.
4. Figueiro-Filho EA, Al-Sum H, Parrish J, Wunder JS, Maxwell C. Maternal and fetal outcomes in pregnancies affected by bone and soft tissue tumors. AJP Rep. 2018;8:e343–e348.
5. Fujibuchi T, Matsumoto S, Shimoji T, Ae K, Tanizawa T, Gokita T, Hayakawa K, Motoi N. Two-stage surgery on pregnant woman with a giant cell tumor of bone who refused blood transfusion: A case report. J Orthop Sci. 2017;22:169–172.
6. Howard EL, Gregory J, Tsoi K, Evans S, Flanagan A, Cool P. Comorbidities and pregnancy do not affect local recurrence in patients with giant cell tumour of bone. Cureus. 2020;12:e9164.
7. Jain C. ACOG Committee Opinion No. 723: Guidelines for Diagnostic Imaging during Pregnancy and Lactation. Obstet Gynecol. 2019;133:186.
8. Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley WG Jr, Froelich JW, Gimbel JR, Gosbee JW, Kuhni-Kaminski E, Larson PA, Lester JW Jr, Nyenhuis J, Schaefer DJ, Sebek EA, Weinreb J, Wilkoff BL, Woods TO, Lucey L, Hernandez D. ACR guidance document on MR safe practices: 2013. J Magn Reson Imaging. 2013;37:501–530.
9. Kim JA, Park JS, Park SY, Jin W, Park YK, Han CS, Ryu KN. Aggressive behavior of a giant cell tumor involving the metacarpal bone during pregnancy: case report. J Korean Soc Radiol. 2011;64:509–513.
10. Peccatori FA, Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G; ESMO Guidelines Working Group. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(Suppl 6):vi160–170.
11. Postl LK, Gradl G, Von Eisenhart-Rothe R, Toepfer A, Pohlig F, Burgkart R, Rechl H, Kirchhoff C. Management of musculoskeletal tumors during pregnancy: a retrospective study. BMC Womens Health. 2015;15:48.
12. Puvanesarajah V, Spiker AM, Shannon BA, Grundy M, Levin AS, Morris CD. Evaluation and management of the pregnant patient with suspected primary musculoskeletal tumor or metastatic carcinoma to bone. Surg Oncol. 2016;25:212–222.
13. Sharma JB, Chanana C, Rastogi, Gupta SD, Kumar S, Roy K, Malhotra N. Successful pregnancy outcome with elective caesarean section following two attempts of surgical excision of large giant cell tumor of the lower limb during pregnancy. Arch Gynecol Obstet. 2006;274:313–315.
14. Van Calsteren K, Heyns L, De Smet F, Van Eycken L, Gziri MM, Van Gemert W, Halaska M, Vergote I, Ottevanger N, Amant F. Cancer during pregnancy: An analysis of 215 patients emphasizing the obstetrical and the Neonatal outcomes. J Clin Oncol. 2010;28:683–689.
15. Zarkavelis G, Petrakis D, Fotopoulos G, Mitrou S, Pavlidis N. Bone and soft tissue sarcomas during pregnancy: a narrative review of the literature. J Adv Res. 2016;7:581–587.

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