Pregnancy in Women with Metastatic Sarcomas

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Disclosures of potential conflicts of interest may be found at the end of this article.

ABSTRACT

Successful pregnancy in women with metastatic cancer is rare in the published literature. We report here on four women with sarcoma who started and conducted their first pregnancies while in metastatic disease. All four pregnancies were first pregnancies, and all four women are long-term survivors from 20 to 248 months after pregnancy. One patient had three pregnancies. All four women stopped systemic cancer treatment during their pregnancies, and two had RECIST progression during treatment interruption. Three patients still have unresectable metastatic disease, whereas one is in complete remission. In selected metastatic sarcomas with indolent courses, successful pregnancies are possible with no or minor impact on cancer progression and with prolonged life duration after pregnancy. As metastatic cancer becomes more often a chronic disease, this possibility opens important practical and ethical questions on how to best to advise women of childbearing age with metastatic cancers who are long-term survivors. The Oncologist 2020;25:e2010–e2012

INTRODUCTION

Women with metastatic cancers almost never consider pregnancy and motherhood because of uncertain life expectancy, fear of cancer progression, and/or incompatible treatments. Metastatic sarcomas are heterogeneous diseases with a median survival now close to 18 months [1]. However, survival beyond 5 years has been observed in 5% to 8% of patients with advanced sarcomas, even without complete remission [1–3]. Several histotypes of sarcoma—for example, low-grade fibromyxoid sarcoma (LGFiMS), epithelioid hemangiendothelioma (EHE), and gastrointestinal stromal tumor (GIST)—may have indolent natural history, prolonged spontaneous stabilization, or slow growth [4–7]. Sarcomas affect all ages and genders, including young women of childbearing age [1, 7]. The possibility of initiating and conducting a successful pregnancy in metastatic cancer is almost not reported in the literature [8, 9]. We report here on four women with sarcoma who started and conducted their first pregnancies while in metastatic disease.

METHODS

The electronic patient records of the Centre Léon Bérard from the year 2000 were screened using the UNICANCER natural language processing tool ConSoRe (https://www.sword-group.com/en/news/projet-consore) for “pregnancy” in “metastatic sarcoma.” Among 63 files retrieved, three were of patients who initiated and conducted pregnancies with a metastatic sarcoma. An additional case was retrieved from the patient advocacy group Info Sarcomes (infosarcome.org).

Clinical Cases

The first patient, aged 25 years, presented in 2015 with multiple lung, skin, and liver metastases of an EHE with WWTR1 rearrangement [4]. After 4 years without treatment and stable disease (SD), new liver and skin sites were slowly growing. Doxorubicin was considered, but the patient started a first pregnancy in 2019, delivering a healthy child, aged 11 months as of July 2020. Although the patient had SD during pregnancy, slow progression is now observed on skin nodules 5 years after diagnosis.

In 1998, the second patient, aged 19 years, was resected of an LGFiMS. In 2004, lung, liver, and soft part metastases were diagnosed and treated with intermittent cytotoxics. She was enrolled in the pazopanib pivotal trial [6], achieving SD as best response. After 14 months (in 2011), she decided to go off study to start a pregnancy. Thirteen months after stopping treatment she became pregnant after an in vitro fertilization (IVF) procedure performed in another country. After the successful delivery, the disease was progressing and was treated again with pazopanib. As of 2020, she has a performance status of 1 and SD under pembrolizumab with a healthy 8-year-old child, 16 years after unresectable metastatic relapse.

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The third patient, aged 29 years, was diagnosed in 2004 of \textit{KIT} exon 11–mutated GIST, metastatic to the liver. She received imatinib from 2004 to 2008 with a partial response and underwent complete resection of liver metastases in 2006. Since then, she has been in complete remission (CR) with no treatment. Three attempts of IVF since 2015 enabled a first successful pregnancy in 2018, with delivery in April 2019 at the age of 44. As of July 2020, she is now in CR with a healthy 1-year-old child, 16 years after a diagnosis of metastatic GIST.

The fourth patient, aged 25 years in 1997, presented with an advanced thoracic LGFMS. Doxorubicin and ifosfamide induced disease stabilization. While the disease was in slow progression in 2000, interferon-alpha was given, providing SD as best response. The patient decided to attempt pregnancy after 1 year of SD. The treatment was interrupted thrice, allowing three successful pregnancies without sarcoma progression. The patient stopped all cancer treatments in 2017. As of 2020, she is working and has 19-, 16- and 13-year-old children, 23 years after diagnosis of advanced LGFMS (Fig. 1).

**DISCUSSION**

Starting a pregnancy with a metastatic cancer is not usually considered because of the uncertainties of life expectancy, of the effects of cancer treatments on the fetus, and of the possibility that treatment interruption could lead to disease progression and death. To our knowledge, this is the first report of successful pregnancies started in women with histologically documented metastatic sarcomas followed by prolonged survival.

All four pregnancies were first pregnancies, and all started more than 4 years after a diagnosis of metastatic or unresectable disease, with a history of slow disease progression and performance status of 0. All women are long-term survivors after pregnancy (20 to 248 months). All four stopped systemic cancer treatment during their pregnancies. Treatment interruption resulted in documented progression of the disease in three of the four patients, but treatment reintroduction after pregnancy enabled tumor control in all three patients. Three of the four patients still have metastatic disease; one is in long-term complete remission.

In most reports, pregnancies in patients with metastatic cancer were discovered while the patient was on treatment. Starting and conducting a pregnancy with a proven diagnosis of metastatic cancer, as presented here, is seldom reported [9]. This raises important ethical questions [10].

The ethical principles in such complex situations include avoiding as much as possible the potential harm of a...
pregnancy to the mother, avoiding the risk of the treatment (and of the cancer) to the fetus, and preserving the autonomy of choice for the informed patient. The physician must share with the patient all information on the risk and uncertainties of the pregnancy and treatment interruption on cancer progression as well as its impact on survival [8–10]. In all four cases, it was expressed that no or too few data were available on these questions but that cancer treatments, cytotoxics and antiangiogenics, were often contraindicated during all or part of the pregnancy. In all four cases, to start and conduct the pregnancy was the final decision of the patient, informed by the physician and the team. In two patients, an IVF was required and performed in other countries to comply with national legislation. Whether natural conception and IVF, including egg donation, is appropriate in patients with metastatic disease also requires a careful ethical analysis.

These four exceptional clinical cases open an important question for women who are long-term survivors with metastatic sarcomas. In carefully advised patients with slowly growing metastatic sarcomas, successful pregnancies were here possible with no detectable impact on cancer growth and with a prolonged life duration for the mother. This is an important option for women of childbearing age as metastatic cancer becomes more often a chronic disease.

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DISCLOSURES
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