



## Pregnancy-associated large pelvic desmoid tumor: A case report of fetal-protective strategies and fertility preservation

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### 1. Introduction

Desmoid fibromatosis (DF) is a benign mesenchymal neoplasm representing less than 3% of all soft tissue tumors (Reitamo et al., 1982). While these tumors lack metastatic potential, they are locally aggressive with a high incidence of post-resection recurrence. DF growth has been linked to estrogen signaling through yet poorly understood mechanisms (Fiore, 2014). Consequently, they undergo accelerated growth during high estrogen states, often being diagnosed during or after pregnancy. Due to a significant spontaneous remission rate, stable DF tumors can be treated with observation and symptom management (Gounder, 2018). Progressive, morbid, or symptomatic pelvic DF are typically treated with surgical resection and/or systemic therapy (Kasper et al., 2011). Less commonly and usually in extra-abdominal tumors, radiation and cryoablation procedures have also been used successfully (Zhang et al., 2021). The optimal treatment strategy is still in debate due to DF's rarity and heterogeneous nature regarding anatomical location, clinical presentation, and disease progression (de Bree et al., 2009). In this case report, we describe the treatment strategies for a 28 year-old pregnant woman with a 27 cm retroperitoneal pelvic desmoid tumor, lasting 15 months with a focus on fetal and newborn health preservation.

### 2. Case report

The patient was a 28-year-old G2P1011 woman who presented to her primary care physician in July 2019 with complaints of sporadic abdominal cramping and back pain. Pelvic ultrasound identified a 13.3 cm (longest-axis) ovoid isoechoic mass (Figs. 1.A, 2.A). Magnetic resonance imaging identified the mass's origin as the right obturator internus while ultrasound guided biopsy and subsequent

immunohistochemistry (IHC) classified it as a B-catenin reactive, S100, HMB45, CD117, and DOG1 negative desmoid tumor. Four weeks after initial presentation, a normal 2-week intrauterine pregnancy was found via repeat serum beta human chorionic gonadotropin and early first trimester ultrasound. Given the high chance of presumably-estrogen-sensitive tumor growth during pregnancy, termination of the pregnancy, mass resection, and systemic therapy were recommended. After counseling, the patient desired to continue the pregnancy, declining mass resection and requested fetal health preserving treatment until delivery.

In October 2019, at 11 weeks fetal gestation, the patient experienced urinary retention, constipation, and right leg paresthesias. Pelvic ultrasound showed tumor growth to 17.7 cm with abutment of the right external iliac vein, potentially explaining her paresthesia. After discussing fetal-safety of treatment options, both with her local team and US-wide experts in DF, she chose and underwent conservative cryoablation using two freeze-thaw cycles with four probes. One month thereafter, magnetic resonance identified a mass with central necrosis but increased size to 22.6 cm (Figs. 1.B, 2.B). Fetal ultrasound showed continued healthy fetal development and growth.

Given the persistent large tumor with mass-effect after cryoablation and worsening urinary retention necessitating self-catheterization, the patient began doxorubicin therapy (75 mg/m<sup>2</sup>, 21-day cycles) in December 2019, at 19 weeks fetal gestation. After two cycles of chemotherapy, magnetic resonance showed a persistent 27.1 cm tumor with compression of the bladder, uterus, and iliac vessels. Further infusions were not performed due to continued tumor growth despite treatment and a nonfunctional PICC line. Interval fetal growth monitoring confirmed continued normal fetal development. Due to interval increase in tumor size (Figs. 1.C, 2.C) leading to urinary retention and

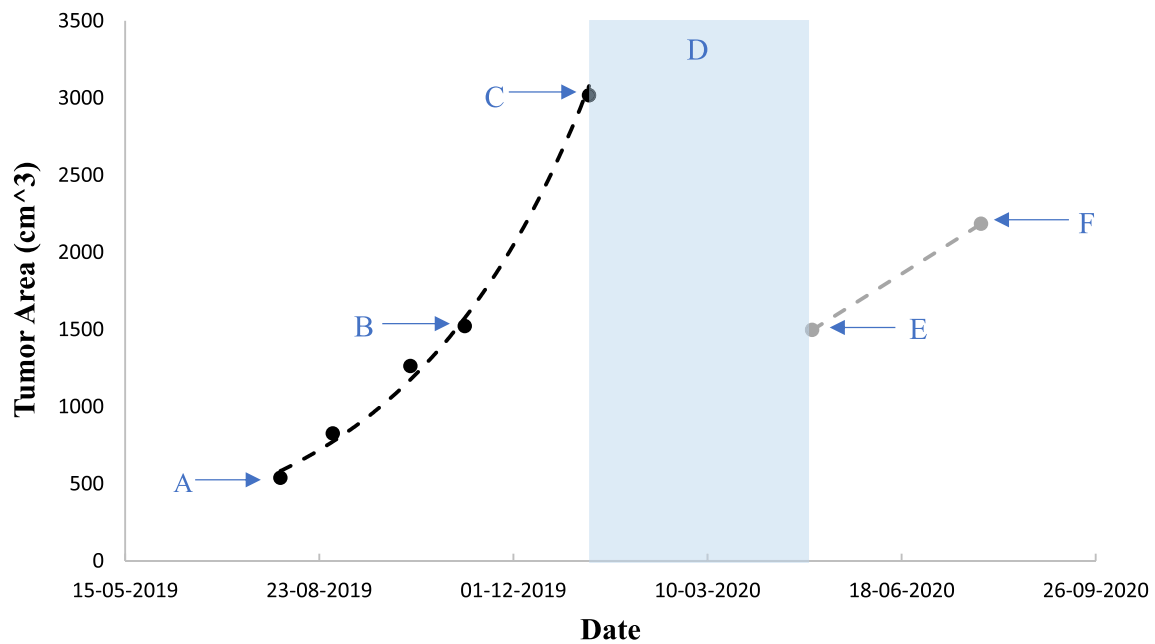
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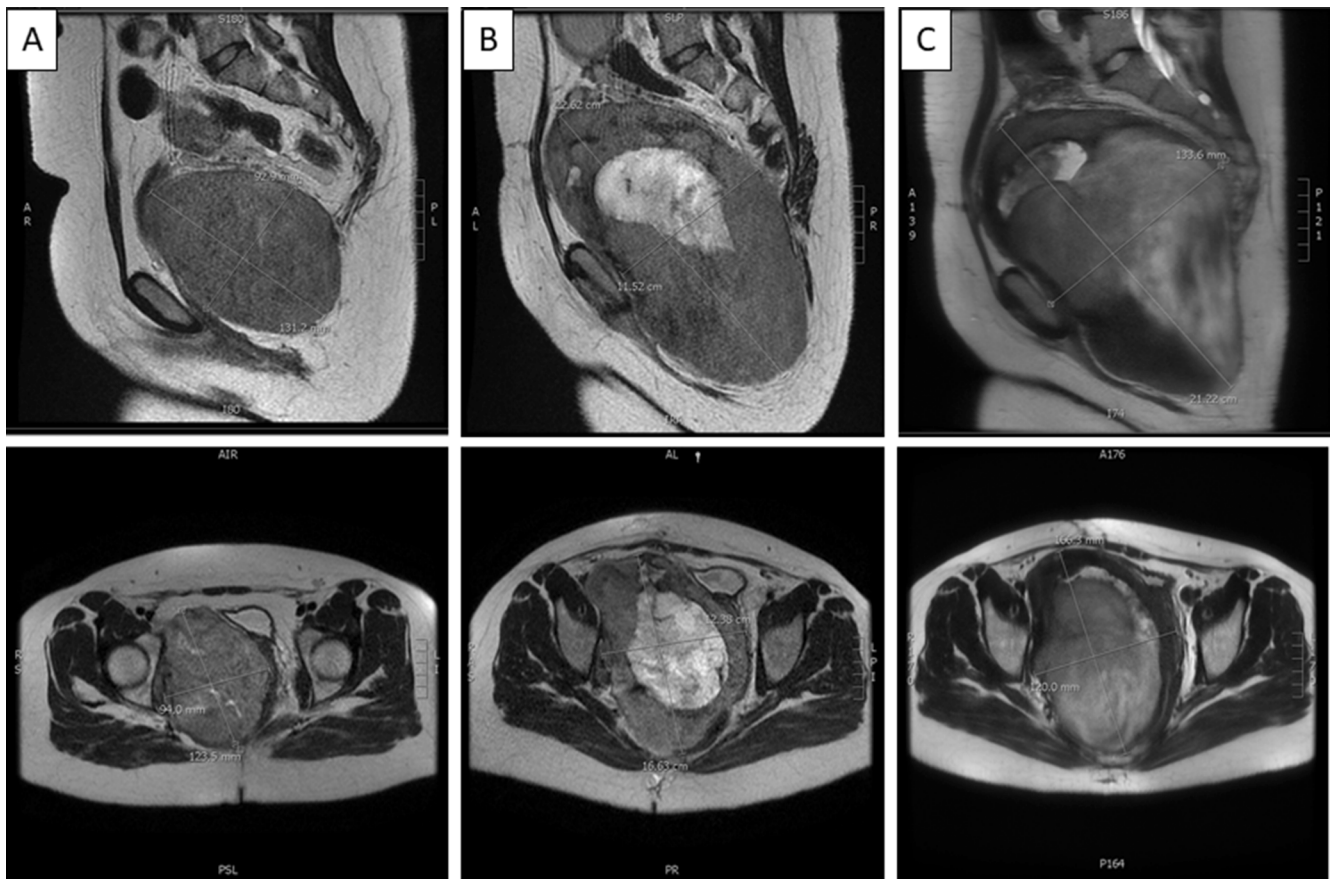
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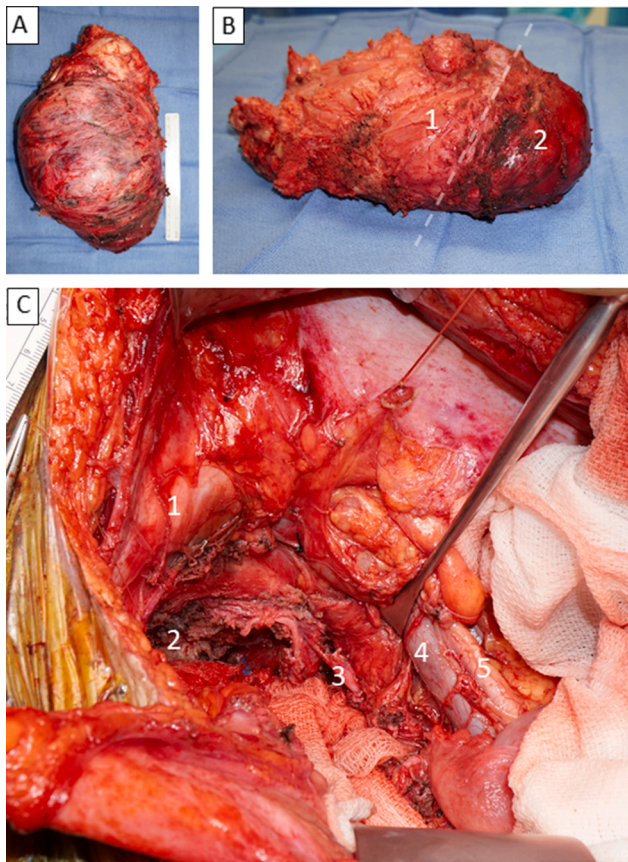
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**Fig. 1.** Tumor growth from time of diagnosis to time of removal. A) The patient’s desmoid tumor was first identified on imaging. B) The patient underwent cryoablation. C) The patient’s child was delivered via cesarian section. D) The patient was under a period of observation while caring for her newborn. E) The patient’s urinary symptoms returned. F) The patient’s tumor was surgically resected.



**Fig. 2.** Sagittal (top) and axial (bottom) magnetic resonance images of patient’s desmoid fibromatosis at time of diagnosis (A 13.3 cm), 1-month post-cryoablation (B, 22.6 cm), and post-cesarean section (D, 27.1 cm).



**Fig. 3.** The removed desmoid tumor measuring 27 × 15 cm (A-B, ruler is 15 cm), with distinguishable retroperitoneal (B.1) and peritoneal (B.2) regions. Extensive resection of the mass from the right pelvic side wall revealed the pubic bone (C.1), tumor origin site (C.2), disrupted obturator nerve (C.3), right external iliac vein (C.4), and right external iliac artery (C.5).

difficulty with defecation, the decision was made to deliver the fetus at 35 weeks gestation via planned cesarean section. The newborn weighed 7 lb 9 oz with a 5-minute Apgar of 8.

Postpartum prolactin mediated estrogen-suppression is likely responsible for a slight reduction of the tumor's size to 26 cm with consequent improvement in urinary and bowel symptoms. Desiring to breastfeed her infant, the patient declined further systemic therapy and opted for a period of observation (Fig. 1.D). After 6 months, while still breastfeeding, the patient began experiencing urinary retention, requiring intermittent self-catheterization several times per month (Fig. 1.E). In October 2020, due to the recurrence of obstructive symptoms, the patient underwent exploratory laparotomy with findings consistent with a 26 cm retroperitoneal pelvic tumor found to have marked adherence to the sacrum, right pelvis, right ureter, bladder, vagina, and rectum (Figs. 1.F, 3). After 9 h of radical tumor resection, patient also underwent right obturator nerve repair, vaginal repair, umbilical hernia repair and right ovarian transposition. Ultimately, a 27 cm × 15 cm × 8 cm tumor originating from the right obturator internus and pelvic floor was removed. Notably, gynecologic organs were spared to preserve fertility and right ovary was transposed in anticipation of post-operative radiation to surgical bed. Subsequent pathological analysis found a soft tissue desmoid type fibromatosis approaching surgical margins with 24% central necrosis. Next-generation sequencing of the tumor showed a T41A CTNNB1 missense variant which may be associated with a lower risk of recurrence (Lazar, 2008; Kasper, 2016).

Informed consent was received from the patient prior to publication of this report.

### 3. Discussion

This case report presents the unique situation and fetal health-preserving multi-modality treatment of a patient with a pelvic desmoid tumor through eight months of pregnancy and 7 months of postpartum care. Between 8% and 18% of desmoid tumors are pregnancy related, typically arise from abdominal wall muscles either in the third trimester or postpartum period, reach maximum sizes of ~10 cm, and are treated via prompt surgical resection (Robinson et al., 2012). That said, due to an approximately 20% spontaneous remission rate for such masses, recent treatment guidelines accept observation instead of surgery for asymptomatic cases (Kasper et al., 2011). The pelvic floor muscles are a rare but well documented site of tumor origin (Kasper, 2016; Mariani et al., 2000). The tumor in this case report originates from an uncommon location and is atypical in presentation. It was diagnosed shortly before conception, not resected until after delivery, reached almost 3 times the size at diagnosis, and was treated with multiple modalities. Its location and rapid growth yielded significant mass effect on the adjacent bladder and rectum, respectively causing significant urinary retention and constipation.

Due to the estrogen responsive nature of desmoid tumors and the patient's decision to prioritize her fetus's health throughout treatment, tumor growth was aggressive, making neither conventional tumor resection nor observation tenable. Instead, a combination of cryoablation, chemotherapy, observation, and eventual surgery was implemented. Cryoablation was the first treatment modality. It was applied sparingly to minimize fetal risk; the induced central necrosis did not reach the mass periphery and consequently did not slow tumor growth. Next the patient received doxorubicin chemotherapy. Doxorubicin, as single drug therapy or in conjugation with dacarbazine, has been used to effectively reduce desmoid tumor size (Aznab, 2017; Gega, 2006; Garbay, 2012). Recent evidence identifies Sorafenib as another effective, albeit teratogenic, treatment of desmoid tumors (Gounder, 2018). Doxorubicin was used due to the relative safety profile and anecdotal and pharmacokinetic evidence of low fetal-risk, especially in the second trimester (Kerr, 2005). The tumor continued to grow throughout two doses of chemotherapy. Several weeks thereafter, tumor growth ceased, indicating delayed effectiveness of cryoablation, doxorubicin, stabilized hormones, or some combination therein. If cryoablation had been more aggressive or doxorubicin treatments continued for longer, growth might have been further limited. Interestingly, post-resection analysis identified the malignant tissue as progesterone-receptor positive but estrogen-receptor negative, an atypia for desmoid tumors but not relevant to initial management.

Once the mass stopped growing, treatment focused on observation and symptom management. Prior to delivery, managing the patient's mass-effect-induced urinary retention with self-catheterization was essential in allowing the fetus to grow until 35 weeks gestation. After delivery, tumor size was reduced and growth was limited, possibly due to postpartum prolactin, arguably the most effective phase of treatment prior to definitive resection. The patient's tumor was identified to have a T41A missense variation in the CTNNB1  $\beta$ -catenin gene. Missense mutations of CTNNB1, primarily in codons 41 or 45, occur in upwards of 87% of sporadic desmoid tumors and are a potential diagnostic feature of desmoid tumors (Le Guellec, 2012), with the 45F and 41A mutation having the poorest and best five-year recurrence-free-survival of 23% and 57% respectively, the latter nearly equivalent to outcomes of non-mutated tumors (Lazar, 2008; Kasper, 2016). Our patient's tumor is not within the high recurrence-risk group.

There exist few case reports offering guidance on the management of pregnancy-concurrent intra-abdominal desmoid tumors (Supplemental 1), and none detailing a pre-pregnancy diagnosis paired with a significantly post-delivery resection. Taken as a whole, this case report demonstrates the viability of carrying a pregnancy to term despite a large progressive pelvic desmoid tumor. Desmoid tumors, unlike adenocarcinomas or other sarcomas are, in cases such as this report details,

indolent enough to be effectively treated with approaches that preserve fetal life and fertility.

#### CRedit authorship contribution statement

**Brennan Marsh-Armstrong:** Writing – original draft, Writing – review & editing, Visualization, Data curation, Conceptualization. **Jula Veerapong:** Writing – review & editing, Investigation. **Michael Tad-donio:** Writing – review & editing, Investigation. **Sarah Boles:** Writing – review & editing, Investigation. **Jason K. Sicklick:** Writing – review & editing, Investigation. **Pratibha Binder:** Writing – review & editing, Investigation, Supervision, Project administration, Funding acquisition, Data curation, Conceptualization.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gore.2021.100901>.

#### References

Aznab, M. Triple Therapy with Doxorubicin, Imatinib and Tamoxifen in Recurrence Desmoids Tumor Associated with Pregnancy: Case Report and Literature Review. *Iran. J. Cancer Prev. In Press*, (2017).

- de Bree, E., Keus, R., Melissas, J., Tsiftsis, D., van Coevorden, F., 2009. Desmoid tumors: need for an individualized approach. *Expert Rev. Anticancer Ther.* 9, 525–535.
- Fiore, M., et al., 2014. Desmoid-Type Fibromatosis and Pregnancy: A Multi-institutional Analysis of Recurrence and Obstetric Risk. *Ann. Surg.* 259, 973–978.
- Garbay, D., et al., 2012. Chemotherapy in patients with desmoid tumors: a study from the French Sarcoma Group (FSG). *Ann. Oncol.* 23, 182–186.
- Gega, M., et al., 2006. Successful Chemotherapeutic Modality of Doxorubicin Plus Dacarbazine for the Treatment of Desmoid Tumors in Association With Familial Adenomatous Polyposis. *J. Clin. Oncol.* 24, 102–105.
- Gounder, M.M., et al., 2018. Sorafenib for Advanced and Refractory Desmoid Tumors. *N. Engl. J. Med.* 379, 2417–2428.
- Kasper, B., et al., 2016. Correlation of CTNNB1 Mutation Status with Progression Arrest Rate in RECIST Progressive Desmoid-Type Fibromatosis Treated with Imatinib: Translational Research Results from a Phase 2 Study of the German Interdisciplinary Sarcoma Group (GISG-01). *Ann. Surg. Oncol.* 23, 1924–1927.
- Kasper, B., Ströbel, P., Hohenberger, P., 2011. Desmoid Tumors: Clinical Features and Treatment Options for Advanced Disease. *The Oncologist* 16 (5), 682–693.
- Kerr, J.R., 2005. Neonatal Effects of Breast Cancer Chemotherapy Administered During Pregnancy. *Pharmacotherapy* 25 (3), 438–441.
- Lazar, A.J.F., et al., 2008. Specific Mutations in the  $\beta$ -Catenin Gene (CTNNB1) Correlate with Local Recurrence in Sporadic Desmoid Tumors. *Am. J. Pathol.* 173, 1518–1527.
- Le Guellec, S., et al., 2012. CTNNB1 mutation analysis is a useful tool for the diagnosis of desmoid tumors: a study of 260 desmoid tumors and 191 potential morphologic mimics. *Mod. Pathol.* 25, 1551–1558.
- Mariani, A., Nascimento, A.G., Webb, M.J., Sim, F.H., Podratz, K.C., 2000. Surgical Management of Desmoid Tumors of the Female Pelvis. *J Am Coll Surg* 191, 9.
- Reitamo, J.J., Häyry, P., Nykyri, E., Saxen, E., 1982. The Desmoid Tumor. I: Incidence, Sex-, Age- and Anatomical Distribution in the Finnish Population. *Am. J. Clin. Pathol.* 77, 665–673.
- Robinson, W.A., McMillan, C., Kendall, A., Pearlman, N., 2012. Desmoid Tumors in Pregnant and Postpartum Women. *Cancers* 4 (1), 184–192.
- Zhang, Z., Shi, J., Yang, T., Liu, T. & Zhang, K. Management of aggressive fibromatosis (Review). *Oncol. Lett.* 21, 1–1 (2021).