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Pregnancy-Associated Progression with Spontaneous Postpartum Regression in Metastatic Alveolar Soft Part Sarcoma- A Case Report and Literature Review

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Abstract

We report the case of a woman in her late thirties with metastatic alveolar soft part sarcoma (ASPS). Her pulmonary lesions increased in size after a miscarriage and during a subsequent pregnancy, prompting consideration for systemic treatment and potential enrollment in a clinical trial of tyrosine kinase inhibitor plus immunotherapy. At the time of trial screening, however, a baseline staging CT performed a few weeks postpartum unexpectedly demonstrated marked regression. Because enrollment required radiographic progression, she was excluded from trial participation, and no systemic therapy was initiated. Surveillance imaging over the following two years confirmed continued regression of the residual lesion. This case may reflect the influence of pregnancy-to-postpartum physiology on tumor behavior through hormonal, immune, and angiogenic pathways, and it emphasizes the importance of reassessment after delivery before systemic therapy is considered.

Keywords: alveolar soft part sarcoma; pregnancy-associated tumor progression; postpartum tumor regression; angiogenic and immune microenvironment

1. Background

ASPS is a rare soft tissue sarcoma with a paradoxical natural history, with slow growth at the primary site but a high risk of late metastases [1,2]. Progression during pregnancy has been reported, but postpartum regression is exceptionally rare [3–5]. This case may illustrate the potential influence of reproductive physiology on ASPS behavior.

2. Case Presentation

A woman now in her late thirties had been diagnosed in 2007, during her early twenties, with primary ASPS of her right lower limb. She underwent wide local excision followed by adjuvant radiotherapy. Her postoperative course was uneventful, and serial chest radiographs over the next decade showed no evidence of recurrence. She was subsequently discharged from routine oncologic surveillance.

In 2021, a spine MRI performed for unrelated neurological symptoms incidentally revealed pulmonary abnormalities. Dedicated chest CT confirmed three lung nodules measuring 3.2 cm, 2.4 cm, and 1.5 cm. Percutaneous biopsy established the diagnosis of metastatic ASPS. Immunohistochemistry demonstrated strong nuclear TFE3 positivity, while estrogen and progesterone receptors were negative. Mismatch repair proteins (MLH1, MSH2, MSH6) were intact. Due to limited tissue, β-hCG staining and next-generation sequencing were not performed. At that time, she remained asymptomatic. Follow-up CT imaging at short intervals demonstrated a slight interval decrease in size of the pulmonary lesions, and an observational strategy with radiographic surveillance was adopted.

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In mid-2022, she experienced a miscarriage. A chest CT performed shortly thereafter demonstrated interval enlargement of all three nodules, measuring approximately 3.6 cm, 2.8 cm, and 2.5 cm. Later that year, she became pregnant again. Cross-sectional imaging with ionizing radiation was deferred during gestation; a targeted thoracic ultrasound was attempted but proved nondiagnostic, and chest MRI was not pursued.

Following delivery in mid-2023, chest CT demonstrated multifocal progression: the dominant lesion measured approximately 5.6 cm, while the other two measured 2.7 cm and 2.4 cm (Figure 1). In light of this radiographic progression, she was referred for consideration of enrollment in a clinical trial evaluating a combination of a tyrosine kinase inhibitor and an immune checkpoint inhibitor (ICI).

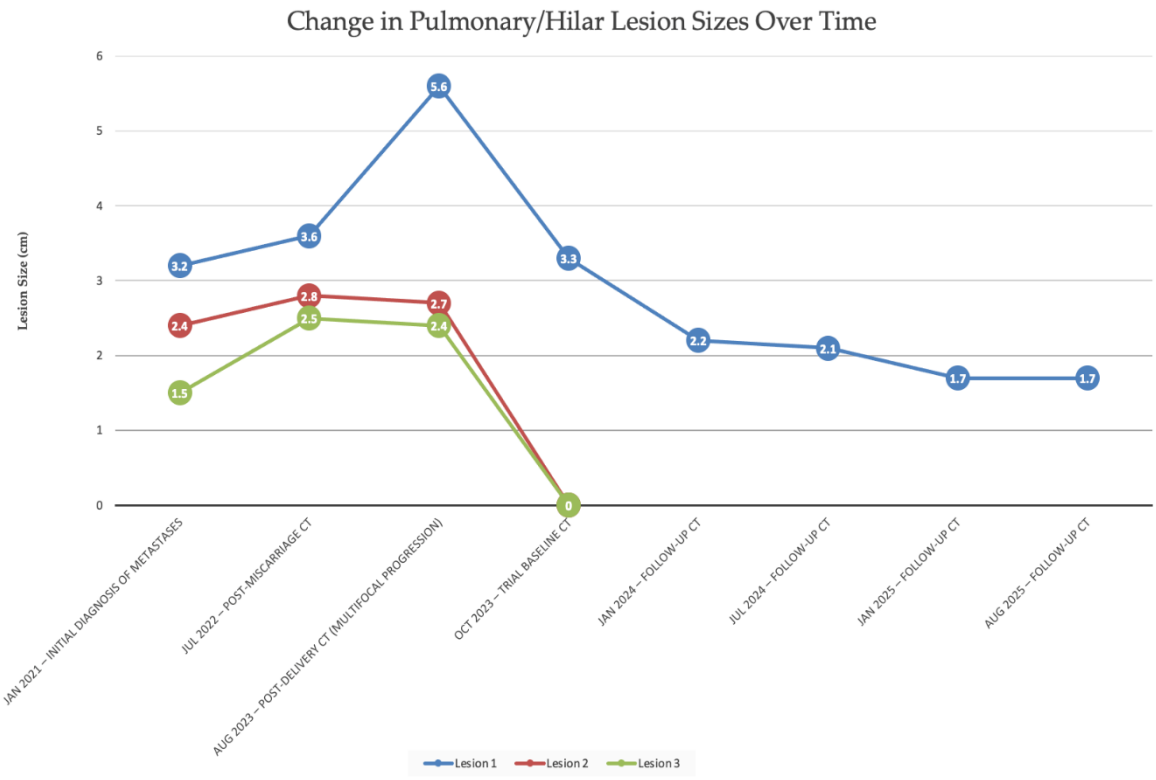

Figure 1. Line chart showing the longitudinal measurements of thoracic lesions from our patient with metastatic ASPS. Lesions enlarged after miscarriage in mid-2022 and peaked post-delivery in mid-2023 (largest 5.7 cm). Two smaller lesions resolved postpartum, and by August 2025 only one residual nodule (1.7 cm) remained stable without systemic therapy.

As stipulated by protocol, a baseline whole-body staging CT (head, chest, abdomen, pelvis) was required to confirm Response Evaluation Criteria in Solid Tumors (RECIST)–defined progression before enrollment. Unexpectedly, the screening CT performed a few weeks postpartum demonstrated spontaneous regression: two nodules had resolved completely, and the largest had decreased from 5.6 cm to 3.3 cm (Figure 1). Because the protocol mandated radiographic progression at baseline, she was deemed ineligible for trial participation, and no systemic therapy was initiated.

She continued on active surveillance. Serial chest CTs at 4–6-month intervals showed sustained regression of the residual dominant nodule, measuring 2.2 cm (January 2024), 2.1 cm (July 2024), and 1.7 cm (January and August 2024).

3. Discussion

ASPS is an ultra-rare malignancy, representing less than 1% of all soft-tissue sarcomas [1,2]. It typically arises in adolescents and young adults and demonstrates indolent local growth but a

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pronounced tendency for late metastases, most often to the lung, bone, and brain [1,2]. The relationship between reproductive physiology and ASPS remains poorly understood. Although progression during pregnancy has been reported in ASPS, postpartum regression is exceptionally rare, and durable regression has not been documented, highlighting the relevance of the present case [3–5].

In the present case, metastatic activity seems to fluctuate with reproductive events: pulmonary lesions increased in size after a miscarriage and during pregnancy, but decreased in the months following delivery. This unexpected clinical course could be related to physiologic transitions across pregnancy and the postpartum period, suggesting that reproductive states might affect the dynamics of metastatic ASPS.

After delivery, the staging CT performed for trial eligibility revealed that two pulmonary metastases resolved completely and the dominant lesion decreased in size without systemic therapy. This course remained stable on subsequent scans, and at the most recent follow-up in August 2025, almost two years later, the dominant lesion was stable with no evidence of progression. Because trial entry required evidence of radiological progression at baseline, she was not eligible for enrollment. Beyond its impact on eligibility for treatment, the durability of regression in the absence of treatment may reflect uncommon biologic behavior in ASPS and may highlight the importance of reassessing disease status in the peripartum setting before systemic therapy is considered.

Pregnancy and the postpartum period constitute opposing physiologic environments that may help explain the observed pattern of metastatic progression during gestation and regression after delivery. During gestation, rises in estrogen, progesterone, and human chorionic gonadotropin support maternal adaptation, angiogenesis is heightened, and maternal immune tolerance is established [6]. After childbirth, abrupt hormone withdrawal occurs, immune surveillance is re-established, and tissue involution remodels stromal, vascular, and lymphatic networks [7]. Taken together, these shifts may transiently create a microenvironment that is more permissive to tumor growth during pregnancy and less so after delivery. Evidence for such physiology–tumor interactions is strongest in breast cancer [6–8]; whether similar mechanisms operate in sarcoma, including ASPS, remains uncertain, but they may provide a biologic context for the postpartum regression observed in this case.

ASPS biology offers a plausible link between these physiologic shifts and the radiographic changes observed. The defining genetic alteration in ASPS is the ASPSCR1::TFE3 fusion, which functions as a chimeric transcription factor that reprograms transcriptional control and upregulates angiogenesis-linked programs, contributing to the tumor's highly vascular phenotype [9,10]. During pregnancy, pro-angiogenic signaling is physiologically enhanced, with sex-steroid–dependent regulation of VEGF-A/VEGFR2 and Tie2 pathways shaping uterine vasculature [11]; by contrast, the postpartum period features involution with vascular and stromal remodeling [7,8]. In this context, the postpartum reduction in tumor burden in this case could be explained by a transient shift toward a less angiogenic environment that is less permissive for ASPS metastases. Consistent with this interpretation, VEGFR tyrosine-kinase inhibitors show activity in ASPS: pazopanib improved overall disease control and produced radiographic responses in a randomized trial of metastatic soft-tissue sarcoma [12]; sunitinib achieved objective tumor shrinkage in a progressive ASPS series with responses regained on rechallenge [13]; and cediranib showed greater tumor shrinkage and objective responses than placebo in a randomized, double-blind ASPS study [14].

Immune changes offer another explanatory layer. Pregnancy is associated with maternal immune tolerance, characterized by expansion of regulatory T cells, a shift toward Th2 cytokine profiles, and engagement of PD-1/PD-L1 at the feto-maternal interface, which protects the semi-allogeneic fetus but may attenuate antitumor immunity [15–17]. After delivery, this tolerance diminishes, with effector T-cell recruitment and restoration of immune surveillance [16,18]. Human transcriptomic studies show increased immune infiltration and distinct inflammatory signatures in postpartum breast cancers compared with non-pregnancy–associated disease [19]. In ASPS, immune checkpoint inhibitors (ICI), which block PD-1/PD-L1 signals so T cells can recognize and attack tumor

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cells, have shown clinically meaningful benefit: in a prospective trial of atezolizumab, about one third of patients had measurable tumor shrinkage with responses that often persisted for many months [1,20], and a worldwide registry has reported responses in more than half of evaluable patients, with durable benefit observed broadly among those treated with ICIs [1,21]. Taken together, postpartum immune reactivation may transiently resemble physiologic checkpoint inhibition and could help explain the regression observed in this case.

The interplay between angiogenesis and immunity may provide a further biologic framework for this case. VEGF signaling not only sustains tumor vasculature but also suppresses antitumor immunity by impairing dendritic cell maturation, expanding regulatory T cells and myeloid-derived suppressor cells, and reducing adhesion molecules required for lymphocyte trafficking [2,15]. In contrast, VEGF blockade can normalize aberrant vasculature, enhance immune infiltration, and potentiate checkpoint inhibition [2,15]. These mechanisms have been demonstrated clinically in ASPS, where combinations such as axitinib plus pembrolizumab achieved acceptable response rates, underscoring the therapeutic synergy of vascular inhibition and immune activation [22]. Physiologically, the postpartum period may reproduce a similar interplay, in which endocrine withdrawal, vascular involution, and immune restoration act together to create a microenvironment less permissive for metastasis.

The unexpected finding on trial screening CT of spontaneous postpartum regression became the turning point in both management and interpretation of the disease course in this patient. Because systemic therapy was not initiated, surveillance alone showed that physiologic transitions after delivery may, in rare cases, coincide with tumor regression resembling the effects of targeted or immune-based treatments. Although causality cannot be established, the durability of this course suggests that natural regressions, though rare in ASPS, should be recognized when they occur. Taken together, this case highlights the importance of reassessment after delivery before systemic therapy is considered in reproductive-age patients, and suggests that carefully observed natural regressions may provide valuable insights into the interaction between reproductive physiology and sarcoma biology.

4. Conclusions

Reproductive physiology may meaningfully influence the clinical behavior of alveolar soft part sarcoma, with potential acceleration of metastatic activity during pregnancy and regression in the early postpartum period. The abrupt hormonal withdrawal, vascular involution, and restoration of immune surveillance that occur after delivery may together create a transient biologic environment that is less permissive for ASPS progression.

This case illustrates the importance of short-interval reassessment following childbirth, as unexpected spontaneous regression can alter decisions regarding systemic therapy and clinical trial eligibility. Although natural regression in ASPS is rare, careful observation of such events offers valuable insights into the interaction between reproductive states, angiogenic signaling, and immune modulation.

These findings underscore the need for individualized management strategies for reproductive-age patients with metastatic ASPS and suggest avenues for future translational research exploring the mechanistic links between pregnancy physiology and sarcoma biology.

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Abbreviations

The following abbreviations are used in this manuscript:

ASPS	Alveolar soft part sarcoma
ASPSCR1::TFE3	ASPSCR1–TFE3 fusion gene
β-hCG	Beta–human chorionic gonadotropin
COX-2	Cyclooxygenase-2
ICI	Immune checkpoint inhibitor
MLH1	MutL homolog 1
MSH2	MutS homolog 2
MSH6	MutS homolog 6
PD-1	Programmed cell death protein 1
PD-L1	Programmed death-ligand 1
RECIST	Response Evaluation Criteria in Solid Tumors
TFE3	Transcription factor E3
Th2	T helper 2
VEGF-A	Vascular endothelial growth factor A
VEGFR2	Vascular endothelial growth factor receptor 2

References

1. Fujiwara T, Kunisada T, Nakata E, Nishida K, Yanai H, Nakamura T, Tanaka K, Ozaki T. Advances in treatment of alveolar soft part sarcoma: an updated review. *Japanese Journal of Clinical Oncology*. 2023;53(11):1009–1018. https://doi.org/10.1093/jjco/hyad102.
2. Suto H. Advances in alveolar soft part sarcoma treatment in the era of immunotherapy. ESMO Rare Cancers. 2025;1(C):100002. https://doi.org/10.1016/j.esmorc.2025.100002.
3. Wang Y, Cui J, Yan X, Jin R, Hong X. Alveolar soft part sarcoma with multiple brain and lung metastases in pregnancy: a case report and literature review. Medicine (Baltimore). 2017;96(46):e8790. https://doi.org/10.1097/MD.0000000000008790.
4. BaniHani MN, Al Manasra AR. Spontaneous regression in alveolar soft part sarcoma: case report and literature review. World Journal of Surgical Oncology. 2009;7:53. https://doi.org/10.1186/1477-7819-7-53.
5. Carsuzaa F, Fieux M, Piguel X, Frouin E. Recurrent peripartum alveolar soft-part sarcoma: Case report using CARE methodology. European Annals of Otorhinolaryngology, Head and Neck Diseases. 2023;140(3):231–233. https://doi.org/10.1016/j.anorl.2023.04.005.
6. Crump LS, Kines KT, Richer JK, Lyons TR. Breast cancers co-opt normal mechanisms of tolerance to promote immune evasion and metastasis. American Journal of Physiology - Cell Physiology. 2022;323(6):C1475–C1495. https://doi.org/10.1152/ajpcell.00189.2022.
7. Lyons TR, O'Brien J, Borges VF, Conklin MW, Keely PJ, Eliceiri KW, Marusyk A, Tan A-C, Schedin P. Postpartum mammary gland involution drives ductal carcinoma in situ progression through collagen and COX-2. Nature Medicine. 2011;17(9):1109-1115. Available from: https://doi.org/10.1038/nm.2416.
8. Jindal S, Gao D, Bell P, Albrektsen G, Edgerton SM, Ambrosone CB, Thor AD, Borges VF, Schedin P. Postpartum breast involution reveals regression of secretory lobules mediated by tissue-remodeling. *Breast Cancer Research*. 2014;16(2):R31. https://doi.org/10.1186/bcr3633.
9. Dickson BC, Chung CTS, Hurlbut DJ, Marrano P, Shago M, Sung YS, Swanson D, Zhang L, Antonescu CR. Genetic diversity in alveolar soft part sarcoma: A subset contain variant fusion genes, highlighting broader molecular kinship with other MiT family tumors. Genes Chromosomes Cancer. 2020;59(1):23-29. https://doi.org/10.1002/gcc.22803.

10. Tanaka M, Chuaychob S, Homme M, Yamazaki Y, Lyu R, Yamashita K, Ae K, Matsumoto S, Kumegawa K, Maruyama R, Qu W, Miyagi Y, Yokokawa R, Nakamura T. ASPSCR1::TFE3 orchestrates the angiogenic program of alveolar soft part sarcoma. Nature Communications. 2023;14:1957. https://doi.org/10.1038/s41467-023-37049-z.
11. Kim M, Park HJ, Seol JW, Jang JY, Cho YS, Kim KR, Choi Y, Lydon JP, DeMayo FJ, Shibuya M, Ferrara N, Sung HK, Nagy A, Alitalo K, Koh GY. VEGF-A regulated by progesterone governs uterine angiogenesis and vascular remodelling during pregnancy. EMBO Molecular Medicine. 2013;5(9):1415–1430. https://doi.org/10.1002/emmm.201302618.
12. van der Graaf, W.T.A.; Blay, J.-Y.; Chawla, S.P.; et al. Pazopanib for Metastatic Soft-Tissue Sarcoma (PALETTE): A Randomised, Double-Blind, Placebo-Controlled Phase 3 Trial. Lancet 2012, 379, 1879–1886. https://doi.org/10.1016/S0140-6736(12)60651-5.
13. Stacchiotti, S.; Negri, T.; Zaffaroni, N.; et al. Sunitinib in Advanced Alveolar Soft Part Sarcoma: Evidence of a Direct Antitumor Effect. Ann. Oncol. 2011, 22, 1682–1690. https://doi.org/10.1093/annonc/mdq644.
14. Judson, I.; Morden, J.P.; Kilburn, L.; et al. Cediranib in Patients with Alveolar Soft-Part Sarcoma (CASPS): A Double-Blind, Placebo-Controlled, Randomised, Phase 2 Trial. Lancet Oncol. 2019, 20, 1023–1034. https://doi.org/10.1016/S1470-2045(19)30215-3.
15. Tsuda S, Nakashima A, Shima T, Saito S. New paradigm in the role of regulatory T cells during pregnancy. Front Immunol. 2019;10:573. https://doi.org/10.3389/fimmu.2019.00573.
16. Abu-Raya B, Michalski C, Sadarangani M, Lavoie PM. Maternal immunological adaptation during normal pregnancy. Front Immunol. 2020;11:575197. https://doi.org/10.3389/fimmu.2020.575197.
17. Veras E, Kurman RJ, Wang TL, Shih IM. PD-L1 expression in human placentas and gestational trophoblastic diseases. Int J Gynecol Pathol. 2017;36(2):146–53. https://doi.org/10.1097/PGP.0000000000000305.
18. Tamburini BAJ, Elder AM, Finlon JM, Winter AB, Wessells VM, Borges VF, Lyons TR. PD-1 blockade during post-partum involution reactivates the anti-tumor response and reduces lymphatic vessel density. Front Immunol. 2019;10:1313. https://doi.org/10.3389/fimmu.2019.01313.
19. Jindal S, Pennock ND, Sun D, Horton W, Ozaki MK, Narasimhan J, Bartlett AQ, Weinmann S, Goss PE, Borges VF, Xia Z, Schedin P. Postpartum breast cancer has a distinct molecular profile that predicts poor outcomes. Nat Commun. 2021;12:6341. https://doi.org/10.1038/s41467-021-26505-3.
20. Chen AP, Sharon E, O'Sullivan-Coyne G, Moore N, Foster JC, Hu JS, Van Tine BA, Conley AP, Read WL, Riedel RF, Burgess MA, Glod J, Davis EJ, Merriam P, Naqash AR, Fino KK, Miller BL, Wilsker DF, Begum A, Ferry-Galow KV, Deshpande HA, Schwartz GK, Ladle BH, Okuno SH, Beck JC, Chen JL, Takebe N, Fogli LK, Rosenberger CL, Parchment RE, Doroshow JH. Atezolizumab for advanced alveolar soft part sarcoma. N Engl J Med. 2023;389(10):911–21. https://doi.org/10.1056/NEJMoa2303383.
21. Hindi N, Razak A, Rosenbaum E, Jonczak E, Hamacher R, Rutkowski P, Bhadri VA, Skryd A, Brahmi M, Alshibany A, Jagodzinska-Mucha P, Bauer S, Connolly E, Gelderblom H, Boye K, Henon C, Bae S, Bogefors K, Vincenzi B, Martinez-Trufero J, Lopez-Martin JA, Redondo A, Valverde C, Blay JY, Moura DS, Gutierrez A, Tap W, Martin-Broto J. Efficacy of immune checkpoint inhibitors in alveolar soft-part sarcoma: results from a retrospective worldwide registry. ESMO Open. 2023;8(6):102045. https://doi.org/10.1016/j.esmoop.2023.102045.
22. Wilky, B.A.; Trucco, M.M.; Subhawong, T.K.; Florou, V.; Park, W.; Kwon, D.; Wieder, E.D.; Kolonias, D.; Rosenberg, A.E.; Kerr, D.A.; et al. Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: A single-centre, single-arm, phase 2 trial. Lancet Oncol. 2019, 20, 837–848. https://doi.org/10.1016/S1470-2045(19)30153-6.