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Adenoid Cystic Carcinoma of the Breast and Uterine Cervix: Two Rare Extraglandular Presentations

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Abstract **Case Report**

Background: Adenoid cystic carcinoma is a rare malignant epithelial tumor most frequently arising in the salivary glands. Primary involvement of the breast or uterine cervix is exceptional. Although these tumors share similar histological features, their clinical behavior and therapeutic management differ substantially according to the primary site. ***Case presentations:*** We report two cases of primary adenoid cystic carcinoma occurring at unusual extraglandular sites. The first patient was a 78-year-old woman diagnosed with a 1.6-cm solid-variant adenoid cystic carcinoma of the breast. The tumor showed a triple-negative phenotype, a Ki-67 proliferation index of 50%, The patient underwent breast-conserving surgery consisting of a right partial mastectomy close surgical margin of less than 1 mm, and no sentinel lymph node involvement. The pathological stage was pT1cN0M0. She underwent breast-conserving surgery, adjuvant chemotherapy with three cycles of EC100 followed by three cycles of paclitaxel, and three-dimensional conformal radiotherapy to a total dose of 42 Gy in 15 fractions. The second patient was a 70-year-old woman diagnosed with a 3-cm adenoid cystic carcinoma of the uterine cervix. She underwent total colpohysterectomy with bilateral pelvic lymph node dissection. Final histopathological examination revealed full-thickness cervical stromal invasion, lymphovascular space invasion, positive surgical margins, and tumor involvement of the parametria and anterior vaginal cuff. None of the 17 removed pelvic lymph nodes showed metastatic involvement. The tumor was classified as FIGO stage IIB. Given the positive surgical margins, parametrial involvement, and the impossibility of further surgical resection, postoperative concomitant chemoradiotherapy was administered using volumetric modulated arc therapy to a total dose of 66 Gy, combined with weekly cisplatin at 40 mg/m². At 3 years of follow-up, both patients remained under satisfactory disease control, with no documented locoregional recurrence or distant progression. ***Conclusion:*** Adenoid cystic carcinoma of the breast and uterine cervix represents two exceptionally rare entities with distinct prognostic profiles. Breast adenoid cystic carcinoma is usually associated with favorable outcomes, although solid morphology, high proliferative activity, and close margins may justify treatment intensification. In contrast, cervical adenoid cystic carcinoma is generally locally aggressive and requires multimodal treatment. Accurate pathological diagnosis and individualized multidisciplinary management are essential.

Keywords: Adenoid cystic carcinoma; breast cancer; cervical cancer; rare tumor; radiotherapy; VMAT; cisplatin; case report.

INTRODUCTION

Adenoid cystic carcinoma (ACC) is a rare malignant epithelial neoplasm that arises most commonly from the major and minor salivary glands. It is characterized histologically by a biphasic proliferation of epithelial and myoepithelial cells arranged in tubular, cribriform, or solid architectural patterns [1,2]. Although ACC predominantly affects the salivary glands, primary tumors with similar morphological and molecular features may exceptionally develop in other glandular organs, including the breast and uterine cervix [3,4].

Primary ACC of the breast accounts for less than 0.1% of all breast malignancies [3,5]. It commonly occurs in postmenopausal women and frequently exhibits a triple-negative immunophenotype. Despite the absence of estrogen receptor, progesterone receptor, and HER2 expression, conventional breast ACC generally has a more favorable clinical course than common triple-negative invasive breast carcinomas, with a low incidence of axillary lymph node involvement and high long-term survival rates [5–8].

However, breast ACC is a heterogeneous entity. Predominantly solid or solid-basaloid morphology, high proliferative activity, necrosis, marked cytological atypia, and high-grade transformation have been associated with more aggressive behavior [9,10]. Alterations involving the MYB pathway, particularly the MYB–NFIB fusion, have also been identified in a substantial proportion of mammary ACCs and support their relationship with ACCs arising at other anatomical sites [11].

Primary ACC of the uterine cervix is even rarer, representing well below 1% of cervical malignancies [4,12]. It usually affects postmenopausal women and frequently presents with vaginal bleeding. Unlike conventional breast ACC, cervical ACC is regarded as an aggressive neoplasm characterized by deep stromal infiltration, lymphovascular and perineural invasion, parametrial extension, hematogenous dissemination, and a risk of late local or distant recurrence [12–15].

Because of the exceptional incidence of both entities, no prospective trials or universally accepted treatment guidelines are available. Management is therefore based mainly on retrospective series, population-based studies, isolated case reports, and extrapolation from the standard treatment of more common breast and cervical carcinomas [6–8,13–16].

We report two cases of primary ACC arising in the breast and uterine cervix. The aim of this report is to compare their clinicopathological characteristics, therapeutic management, and outcomes, while highlighting the markedly different biological behavior of ACC according to its primary anatomical site.

Case presentation 1: Adenoid cystic carcinoma of the breast

A 78-year-old woman presented with a right breast nodule. Breast ultrasonography and mammography revealed a lesion measuring approximately 22 × 18 mm.

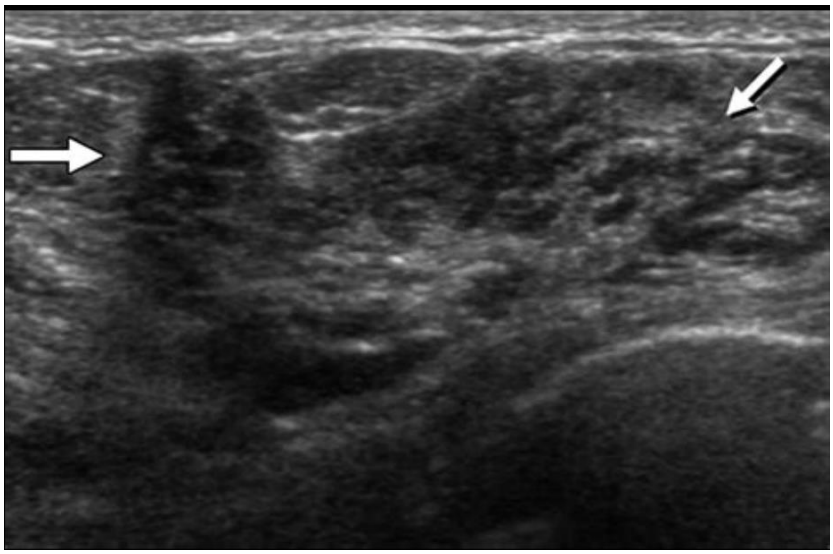

Figure 1. Breast ultrasound showing a 22 × 18 mm hypoechoic lesion in the right breast. Histopathological examination of a core needle biopsy was consistent with adenoid cystic carcinoma of the breast. Figure 1A. Breast ultrasound showing a 22 × 18 mm hypoechoic lesion in the right breast.

The patient underwent a partial lumpectomy as a breast-conserving surgical procedure, combined with sentinel lymph node biopsy. Histopathological examination of the surgical specimen revealed a 1.6-cm adenoid cystic carcinoma with a predominantly solid growth pattern.

The tumor showed a triple-negative immunophenotype, with negative estrogen receptor, progesterone receptor, and HER2 expression. The Ki-67 proliferation index was 50%.

The closest surgical margin measured less than 1 mm. The sentinel lymph node was negative for metastatic involvement. The staging assessment showed no evidence of distant metastasis. The final pathological stage was pT1cN0M0.

Given the predominantly solid morphology, elevated Ki-67 proliferation index, triple-negative phenotype, and close surgical margin, the multidisciplinary tumor board recommended adjuvant systemic and locoregional treatment.

The patient received three cycles of EC100 followed by three cycles of paclitaxel. Adjuvant breast radiotherapy was subsequently delivered using a three-dimensional conformal radiotherapy technique to a total dose of 42 Gy in 15 fractions.

At 3 years of follow-up, the patient remained free of documented locoregional recurrence and distant progression.

Case presentation 2: Adenoid cystic carcinoma of the uterine cervix

A 70-year-old multiparous woman presented with postmenopausal and postcoital bleeding. Cervical biopsy, supplemented by immunohistochemical assessment, supported the diagnosis of primary adenoid cystic carcinoma of the uterine cervix.

Pelvic magnetic resonance imaging demonstrated a cervico-isthmic tumor without radiologically detected pelvic lymphadenopathy. She underwent total colpohysterectomy with bilateral pelvic lymph node dissection.

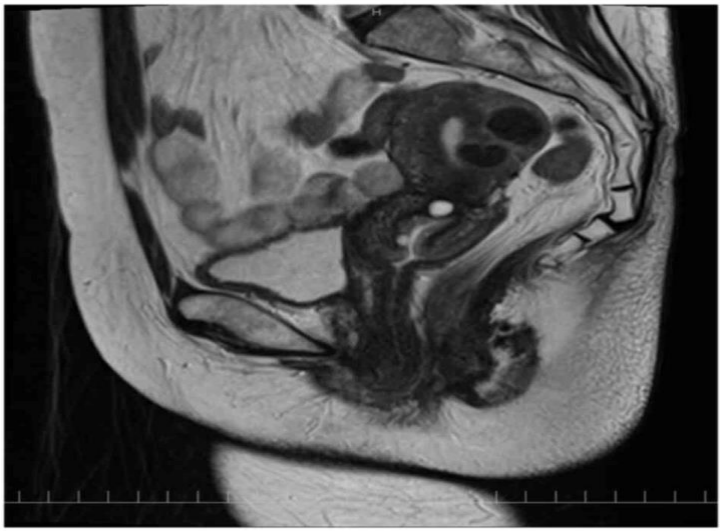

Figure 2: Sagittal T2-weighted pelvic magnetic resonance image showing the cervical tumor with extensive stromal involvement

Histopathological examination revealed full-thickness cervical stromal invasion, lymphovascular space invasion, positive surgical margins, and tumor involvement of the parametria and anterior vaginal cuff. None of the 17 removed pelvic lymph nodes showed metastatic involvement.

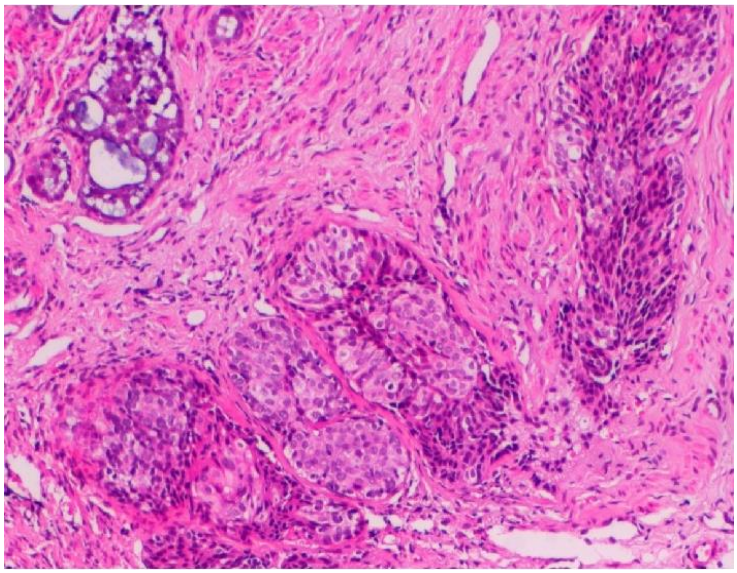

Figure 3: Histological examination of the cervical tumor showing infiltrative nests with cribriform architecture and pseudoglandular spaces containing basement membrane-like material (hematoxylin and eosin staining, ×200)

The tumor was classified as FIGO stage IIB. Given the positive surgical margins, parametrial involvement, and the impossibility of further surgical resection, postoperative concomitant chemoradiotherapy was administered using volumetric modulated arc therapy to a total dose of 66 Gy, combined with weekly cisplatin at 40 mg/m².

At 3 years of follow-up, the patient remained free of documented locoregional recurrence and distant progression.

DISCUSSION

Adenoid cystic carcinoma is defined by a characteristic biphasic proliferation composed of luminal epithelial cells and basal or myoepithelial cells, arranged in tubular, cribriform, or solid patterns. Although breast and cervical adenoid cystic carcinomas share this morphological designation, their clinical course, prognostic factors, and therapeutic management differ substantially according to the primary site.

The comparison with previously published studies is summarized in Table 1.

Table 1: Comparison of the present cases with selected published studies on adenoid cystic carcinoma of the breast and uterine cervix

Study	Primary site	Number of patients	Main clinicopathological characteristics	Treatment	Outcome or principal finding
Arpino *et al.,*[1]	Breast	28	Predominantly localized and node-negative tumors; frequent triple-negative phenotype	Surgery with variable use of radiotherapy and systemic therapy	Five-year disease-free survival of 100% and overall survival of 85%; no local recurrence reported
Khanfir *et al.,*[2]	Breast	61	All assessed patients had pN0 disease; heterogeneous surgical approaches	Breast-conserving surgery or mastectomy; postoperative radiotherapy in approximately two-thirds of patients	Five-year overall survival 94%, disease-free survival 82%, and locoregional control 95%
Kim *et al.,*[3]	Breast	6	Median-aged population with mostly localized disease	Surgery; adjuvant treatment individualized	No disease-related death during reported follow-up; generally favorable course
Treitl *et al.,*[4]	Breast	6	Rare tumors representing approximately 0.1% of breast cancers treated at the institution	Predominantly surgical management; selective radiotherapy	Indolent course and very low incidence of axillary nodal metastasis
Zhang *et al.,*[5]	Breast	14	Most patients postmenopausal; tumors generally localized	Breast-conserving surgery or mastectomy; variable radiotherapy and chemotherapy	Favorable long-term oncological outcomes; surgery remained the main treatment
Zhang *et al.,*[6]	Breast	7	Predominantly triple-negative tumors with generally low proliferative activity	Surgery with selective chemotherapy and radiotherapy	Most patients remained disease-free; authors emphasized individualized treatment
Present breast case	Breast	1	Age 78 years; 1.6-cm predominantly solid ACC; triple-negative; Ki-67 50%; margin <1 mm; pT1cN0M0	Breast-conserving surgery, 3 cycles of EC100 followed by 3 cycles of paclitaxel, then 3D conformal radiotherapy, 42 Gy in 15 fractions	Satisfactory disease control at the latest assessment
Hoskins *et al.,*[7]	Uterine cervix	6	Mostly older women; marked local aggressiveness and frequent advanced presentation	Surgery and/or radiotherapy according to disease extent	High recurrence risk; authors emphasized the aggressive behavior of cervical ACC
Prempree *et al.,*[8]	Uterine cervix	6	Five invasive tumors and one in situ lesion;	Surgery, radiotherapy, or combined treatment	Combined treatment proposed because of the

			predominantly elderly patients		high risk of local and distant failure
Elhassani *et al.,*[9]	Uterine cervix	1	Age 68 years; locally advanced cervical ACC	Concomitant chemoradiotherapy	Complete clinical and radiological response after treatment; disease control documented at 12 months
Kaur *et al.,*[10]	Uterine cervix	1	Age 55 years; postmenopausal bleeding and locally advanced cervical lesion	Multimodal treatment including radiotherapy and chemotherapy	Authors recommended aggressive multimodal management because of the high metastatic and recurrence risk
Sinaa *et al.,*[11]	Uterine cervix	2	Two younger women, including one aged 36 years; unusual age of presentation	Surgery and adjuvant treatment according to stage	Demonstrated that cervical ACC can also occur in younger women; prolonged monitoring recommended
Benhayoune *et al.,*[12]	Uterine cervix	2	Two 80-year-old women presenting with postmenopausal bleeding; advanced disease	Treatment adapted to stage and performance status	Poor clinical course highlighting the aggressive nature of cervical ACC
Liu *et al.,*[13]	Uterine cervix	Population-based cohort	Cervical ACC and adenoid basal carcinoma analyzed using registry data	Surgery, radiotherapy, chemotherapy, or combined treatment	Radiotherapy and chemotherapy appeared relevant in selected high-risk or advanced cases
Present cervical case	Uterine cervix	1	Age 70 years; 3-cm tumor; full-thickness cervical invasion; lymphovascular invasion; parametrial and anterior vaginal cuff involvement; 0/17 nodes; FIGO IIB	Surgery followed by VMAT to 66 Gy with weekly cisplatin 40 mg/m²	Satisfactory disease control at the latest assessment

ACC: adenoid cystic carcinoma; 3D: three-dimensional; VMAT: volumetric modulated arc therapy.

Breast adenoid cystic carcinoma

Primary adenoid cystic carcinoma of the breast is extremely rare and represents approximately 0.1% of breast malignancies. It usually affects postmenopausal women and commonly presents as a localized, node-negative tumor. Although most mammary ACCs lack estrogen receptor, progesterone receptor, and HER2 expression, their biological behavior is generally more favorable than that of conventional triple-negative invasive breast carcinoma [1–6].

The Rare Cancer Network study by Khanfir *et al.,* included 61 patients and remains one of the most informative retrospective series. At a median follow-up of 79 months, the five-year overall survival, disease-free survival, and locoregional control rates were 94%, 82%, and 95%, respectively [2]. These results confirm the generally indolent course of conventional mammary ACC. Similarly, the institutional experiences reported by Kim *et al.,* Treitl *et al.,* and Zhang *et al.,* demonstrated low rates of nodal involvement and favorable long-term outcomes following adequate surgical excision [3–6].

However, mammary ACC is histologically heterogeneous. The conventional tubular and cribriform forms are usually associated with favorable outcomes, whereas the predominantly solid or solid-basaloid pattern may be associated with increased mitotic activity, necrosis, a higher proliferation index, greater genomic complexity, and a higher risk of recurrence or metastasis [14,15].

The present breast case differs from the majority of conventional low-grade mammary ACCs because of its predominantly solid architecture and Ki-67 proliferation index of 50%. Although the tumor was small and node-negative, the close surgical margin of less than 1 mm, high proliferative activity, and solid morphology were considered adverse features. These findings supported the multidisciplinary decision to administer adjuvant anthracycline- and taxane-based chemotherapy followed by breast irradiation.

Complete surgical excision remains the cornerstone of treatment. Breast-conserving surgery is appropriate when negative margins can be obtained.

Mastectomy should not be considered mandatory solely on the basis of the ACC histological subtype [2–6].

The role of axillary staging remains debated because lymph node metastases are uncommon. Sentinel lymph node biopsy may nevertheless be reasonable when the diagnosis is uncertain before surgery, in large tumors, in solid-basaloid variants, or when another invasive component cannot be excluded.

The value of postoperative radiotherapy has not been established through randomized trials. Retrospective population-based studies and multicenter analyses suggest that radiotherapy may improve locoregional control or survival, particularly following breast-conserving surgery [2,16–18]. The absolute benefit may be limited in completely excised, small, conventional low-grade tumors. Conversely, radiotherapy appears particularly justified in the presence of close or positive margins, a solid-basaloid pattern, high-grade transformation, or other unfavorable features.

In the present case, adjuvant three-dimensional conformal radiotherapy was administered to a total dose of 42 Gy in 15 fractions. This hypofractionated regimen provided effective whole-breast treatment while limiting the overall treatment duration.

The benefit of chemotherapy remains uncertain in conventional mammary ACC. Large retrospective studies have not demonstrated a consistent survival advantage from routine chemotherapy in unselected patients [18,19]. Nevertheless, systemic therapy may be considered in patients with a solid-basaloid phenotype, high proliferative activity, high-grade transformation, nodal involvement, large primary tumors, or metastatic disease. Therefore, the use of chemotherapy in our patient should be interpreted as an individualized decision based on adverse pathological characteristics rather than as a standard requirement for all breast ACCs.

Cervical adenoid cystic carcinoma

Primary ACC of the uterine cervix is substantially rarer than mammary ACC and accounts for less than 1% of cervical malignancies. Most reported patients are postmenopausal, although occasional cases have been described in younger women [7–13].

Cervical ACC is believed to originate from reserve cells of the endocervical epithelium. Its differential diagnosis includes adenoid basal carcinoma, basaloid squamous cell carcinoma, poorly differentiated squamous carcinoma, neuroendocrine carcinoma, and other biphasic cervical tumors. Adenoid basal carcinoma must be carefully distinguished from ACC because it usually has a more indolent course, whereas cervical ACC is characterized by deep infiltration and a higher metastatic potential.

Compared with mammary ACC, cervical ACC has markedly more aggressive behavior. Historical series described frequent full-thickness stromal invasion, parametrial extension, lymphovascular and perineural invasion, local recurrence, and hematogenous metastases [7,8]. Pulmonary, hepatic, osseous, and cerebral metastases have been documented, occasionally after prolonged disease-free intervals.

In the series reported by Hoskins *et al.,* and Prempree *et al.,* local and distant failures occurred despite surgical treatment, leading the authors to recommend an aggressive combined approach [7,8]. Subsequent case reports have similarly supported the use of surgery followed by radiotherapy or concomitant chemoradiotherapy when adverse pathological factors are present [9–12].

The present cervical case had several major risk factors: invasion of the entire cervical wall, lymphovascular tumor emboli, parametrial involvement, and extension to the anterior vaginal cuff. Although all 17 pelvic lymph nodes were negative, the absence of nodal disease did not eliminate the risk related to the extensive local involvement.

The tumor was classified as FIGO stage IIB. Because further surgical excision was not feasible, postoperative concomitant chemoradiotherapy was selected. VMAT was delivered to a total dose of 66 Gy, combined with weekly cisplatin at 40 mg/m². The use of VMAT enabled conformal coverage of pelvic and high-risk target volumes while limiting the dose delivered to the bladder, rectum, bowel, and other organs at risk.

No specific prospective chemotherapy regimen has been established for cervical ACC. Weekly cisplatin is generally selected by extrapolation from the management of locally advanced squamous cell carcinoma and adenocarcinoma of the cervix. Registry-based analyses suggest that radiotherapy and chemotherapy may provide a benefit in selected patients, particularly in locally advanced or high-risk disease, although interpretation remains limited by small numbers and retrospective selection bias [13].

Comparison between the two primary sites

Despite sharing a common histological name, mammary and cervical ACC should not be regarded as a single clinical entity.

Mammary ACC is generally localized at diagnosis, has a very low incidence of lymph node metastasis, and is associated with high long-term survival. Treatment can therefore be relatively conservative in patients with conventional low-grade tumors and adequate surgical margins.

In contrast, cervical ACC frequently demonstrates deep local invasion, lymphovascular or

perineural spread, and a high risk of distant relapse. This behavior generally justifies a more aggressive multimodal approach, especially when parametrial involvement, positive margins, or locally advanced disease is present.

The present observations illustrate this site-dependent heterogeneity. The breast tumor was small and node-negative but had adverse histological features that led to intensified adjuvant treatment. The cervical tumor was also node-negative but showed extensive local invasion, requiring dose-escalated postoperative chemoradiotherapy.

Follow-up considerations

Long-term surveillance is essential for both tumor sites because ACC may recur after prolonged intervals.

For breast ACC, follow-up should include regular clinical breast examination and appropriate mammographic or cross-sectional imaging. Particular attention should be paid to local recurrence and pulmonary metastasis, especially in solid or high-grade variants.

For cervical ACC, pelvic examination and imaging should be performed according to symptoms and initial disease extent. Because hematogenous dissemination is relatively common, thoracic and abdominopelvic assessment should be considered when clinically indicated.

After 3 years of follow-up, both patients remained under satisfactory disease control. Although this intermediate-term outcome is encouraging, longer surveillance remains necessary because adenoid cystic carcinoma may recur after prolonged disease-free intervals, particularly at distant sites.

Strengths and limitations

The principal strength of this report is the comparative presentation of two histologically related but clinically distinct rare tumors, treated using individualized multidisciplinary strategies.

The main limitations are inherent to the case-report design. Detailed molecular testing, including assessment of MYB or MYBL1 alterations, was not available. Furthermore, the exact duration of follow-up was not documented in the available anonymized records. Consequently, the current report demonstrates satisfactory disease control at the latest assessment but cannot establish long-term remission.

CONCLUSION

Adenoid cystic carcinoma of the breast and uterine cervix comprises two exceptionally rare malignancies with distinctly different clinical behavior.

Breast ACC generally has a favorable prognosis and can often be treated with conservative surgery. Nevertheless, solid morphology, a high Ki-67 index, and close margins may support the use of chemotherapy and postoperative radiotherapy in selected patients.

Cervical ACC is more aggressive and is associated with deep local invasion and a substantial risk of late local or distant recurrence. Multimodal treatment combining surgery, radiotherapy, and cisplatin-based chemotherapy should be considered in patients with locally advanced or high-risk disease.

The satisfactory disease control observed in both patients after 3 years of follow-up supports the relevance of individualized multidisciplinary treatment. Nevertheless, prolonged surveillance remains essential because late recurrence and distant metastasis are well-recognized features of adenoid cystic carcinoma.

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