

Case Report

Pathologically Complete Response to Camrelizumab and Apatinib in Advanced Cervical Cancer with PTEN, PIK3CA, MTOR, and ARID1A Mutations: A Case Report

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Keywords

Cervical cancer · PD-1 inhibitor · Camrelizumab · Apatinib · Case report

Abstract

Introduction: Limited treatment options are available for residual locally advanced cervical cancer after concurrent radio-chemotherapy. Pembrolizumab has been approved by the US Food and Drug Administration to treat patients with persistent, recurrent, and metastatic cervical cancer. However, it is expensive and not covered by medical insurance in China.

Case Description: A patient presented with stage IIIC1 cervical cancer characterized by PTEN, PIK3CA, MTOR, and ARID1A mutations, accompanied by low programmed cell death-ligand 1 expression (tumor cell proportion score 1% and combined positive score 1). The patient exhibited a residual cervical lesion after concurrent radio-chemotherapy but eventually achieved a pathologically complete response through a combination of the programmed cell death-1 (PD-1) inhibitor camrelizumab with the antiangiogenic drug apatinib (two medicines produced by Chinese Jiangsu Hengrui Pharmaceutical Co.). Surgical intervention confirmed the lack of residual tumor cells in the cervix. Regular follow-up confirmed that disease-free survival time was 41 months and overall survival time was 51 months. Adverse events, including cutaneous capillary endothelial proliferation, hepatic insufficiency, hemorrhoidal hemorrhage, and neutropenia, were manageable during treatment with camrelizumab and apatinib. **Conclusion:** Our findings suggest that the combination of camrelizumab and apatinib could offer a valuable therapeutic option for residual advanced cervical

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cancer patients after concurrent radio-chemotherapy. Camrelizumab is affordable, at just 10% of the price of pembrolizumab, although it is similarly not covered by medical insurance for cervical cancer in China. The PTEN, PIK3CA, MTOR, and ARID1A gene mutations hold the potential to serve as predictive biomarkers for cervical cancer patients treated by PD-1 inhibitors.

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Published by S. Karger AG, Basel

Introduction

Cervical cancer is a prevalent gynecological cancer in developing countries, with persistent human papillomavirus infection identified as a key pathogenic factor [1]. While cervical cancer screening is widely promoted, over 30% of cervical cancer cases are diagnosed at an advanced stage (stage IIB–IVA) [2], precluding the possibility of surgical intervention. For patients with local advanced cervical cancer, standard treatment involves concurrent radio-chemotherapy, but its 5-year survival rate remains disappointingly low at 40–50% [3]. Furthermore, limited treatment options have been developed for residual locally advanced cervical cancer after concurrent radio-chemotherapy. However, promising results have been seen in recent years with immune checkpoint inhibitors (ICIs) [4, 5].

KEYNOTE-028, a multicohort phase I clinical trial reported in 2017, first evaluated pembrolizumab monotherapy antitumor activity (objective response rate [ORR] 17%) in patients with recurrent or metastatic programmed cell death-ligand 1 (PD-L1)-positive cervical cancers [6]. In the subsequent phase II clinical trial, KEYNOTE-158, pembrolizumab monotherapy had 12.2% ORR for patients with previously treated advanced cervical cancer [5]. In 2020, the US Food and Drug Administration approved pembrolizumab use in PD-L1-positive cervical cancer patients with previous chemotherapy resistance [7]. Nevertheless, pembrolizumab monotherapy has demonstrated limited antitumor activity [5–7]. The KEYNOTE-826 trial found a median progression-free survival (mPFS) of 10.4 months and overall survival (OS) of 24 months for 50.4% of those with a combination of pembrolizumab and chemotherapy, with or without bevacizumab. This combination fared better than chemotherapy alone, with or without bevacizumab (mPFS: 8.2 months, OS: 24 months; 40.4%) [8]. However, pembrolizumab did not receive a recommendation from China's National Medical Products Administration, and it is not covered by Chinese medical insurance. Therefore, it is extremely expensive for Chinese patients to use pembrolizumab.

The Chinese CLAP study, a multicenter, single-arm, phase II trial, investigated the effectiveness and safety of combining the PD-1 inhibitor camrelizumab with the antiangiogenic drug apatinib (two medicines produced by the Chinese Jiangsu Hengrui Pharmaceutical Co.) in treating persistent, recurrent, or metastatic cervical cancer. Results revealed an impressive 55.6% ORR and an mPFS of 8.8 months with manageable toxicities. These findings suggest that the camrelizumab and apatinib combination demonstrates good antitumor activity with manageable adverse events, potentially offering a promising new treatment option for patients with persistent, recurrent, and metastatic cervical cancer [9].

We used camrelizumab + apatinib to treat a stage IIC1 cervical squamous cell cancer patient who had persistent cancer after radical radio-chemotherapy and reached a pathologically complete response with a disease-free survival time of 41 months and OS time of 51 months. Here, we present the entire treatment process and analyze the genetic changes and their improvement to the therapeutic effect of camrelizumab.

Case Presentation

Diagnosis

In December 2019, a 53-year-old Chinese woman presented with abnormal heavy vaginal bleeding and was treated for hemostasis and removal of an intrauterine device in the outpatient clinic. However, the patient refused further examination and treatment. She continued to suffer from sporadic vaginal bleeding without consulting a doctor due to the coronavirus disease 2019 pandemic. On August 29, 2020, the patient again experienced heavy vaginal bleeding. A color Doppler ultrasonography examination showed a borderless and uneven hypoechoic mass in the cervix measuring approximately $7.9 \times 8.1 \times 8.7$ cm. On September 14, 2020, a cervical biopsy pathology revealed squamous cell carcinoma (Fig. 1a). A systemic positron emission tomography-computed tomography (PET-CT) with fluorodeoxyglucose as an imaging agent labeled by a radioactive isotope of fluorine-18 (18F-FDG) examination was performed on September 24, 2020, showing a cervical mass measuring $8.9 \times 9.7 \times 6.5$ cm (Fig. 2a1, a2), with observed bilateral extrailiac para-vascular lymph node metastasis and no metastatic lesions in other parts of the body. Based on the 2019 International Federation of Gynecology and Obstetrics staging system, the patient was diagnosed with stage IIIC1 uterine cervical cancer.

Radical Radiotherapy and Chemotherapy

On September 25, 2020, the patient was treated with albumin paclitaxel (260 mg/m^2) combined with carboplatin with an area under the concentration of $5 \text{ mg/mL}\cdot\text{min}$ on day 1, which successfully controlled vaginal bleeding after one cycle of chemotherapy (Fig. 3). Physical examination revealed a mass occupying the cervix with a cauliflower-like appearance, with no visible normal cervix and vaginal fornix. The mass surface displayed dark red rotten tissue growing into and occupying the upper half of the vagina. The tumor was growing on both sides of the cervix, reaching the pelvic wall. The patient then received pelvic intensity-modulated radiation therapy, brachytherapy, and concurrent chemotherapy. During intensity-modulated radiation therapy, 60 Gy in 25 fractions were applied for bilateral extrailiac para-vascular lymph node metastasis, and 45 Gy in 25 fractions were applied for bilateral common iliac, internal iliac, external iliac, the obturator, and anterior sacrum lymph node drainage area, cervix, uterine body, and the entire vagina. Brachytherapy used a uterine cavity tube and implantation needles with a dose of 7 Gy, 90% of the high-risk clinical target volume, for three fractions with iridium 192 as a radioactive source. Concurrent chemotherapy with cisplatin 30 mg/m^2 was administered once weekly for 4 weeks. However, the treatment was discontinued due to grade 4 neutropenia according to Common Terminology Criteria for Adverse Events (CTCAE) v4.0. The patient resumed treatment 37 days later, on January 11, 2021, after neutrophil counts returned to normal, and received the fourth brachytherapy with a prescription dose of 90% of the high-risk clinical target volume 7 Gy. One cycle of chemotherapy was conducted to make up for the treatment interruption with albumin paclitaxel (260 mg/m^2) combined with carboplatin (area under the concentration = $5 \text{ mg/mL}\cdot\text{min}$) on day 1. Pelvic magnetic resonance imaging (MRI) conducted on February 21, 2021, showed that the mass was $6.6 \times 5.7 \times 4.2$ cm (Fig. 2b), with partial response according to Response Evaluation Criteria in Solid Tumor (RECIST) after radical radiotherapy and chemotherapy.

ICIs and Vascular-Targeted Drug Treatment

In September 2020, the paraffin-embedded tissue from cervical biopsies was sent to Zhejiang Shaoxing Topgen Biomedical Technology Corporation for next-generation sequencing and immunohistochemical staining. Tumor mutation testing was conducted using the OncoDrug-Seq™ 603-gene panel assay on the DNBSEQ-T7 platform, employing an App-A

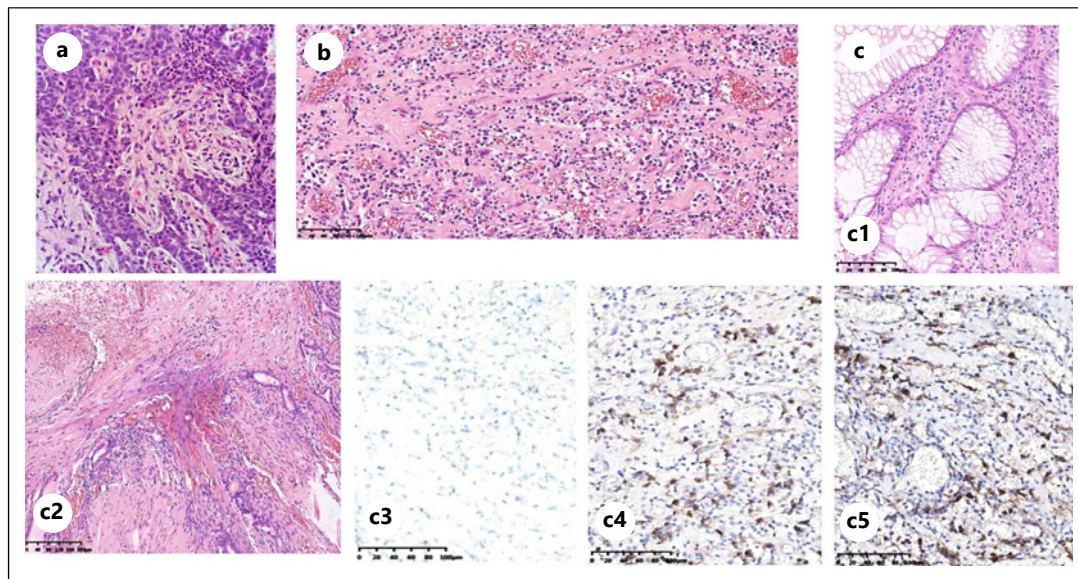


Fig. 1. Pathology results of cervical biopsy, colonoscopy biopsy, and surgical excision of cervical and rectal tissue. **a** The pathology of the cervical biopsy before treatment reveals squamous cell carcinoma (H&E stain. $\times 20$). **b** The pathology of the preoperative colonoscopy biopsy shows moderate chronic inflammation with lymphocytes, plasma cells, and neutrophil infiltration (H&E stain. $\times 20$). **c** The pathology of surgical excision of cervical and rectal tissue. **c1** Presence of cervical tissue hemorrhage, necrosis, inflammatory cell infiltration, fibroblastic proliferation, focal hemosiderin deposition, granulation tissue formation, and no observed tumor cells (H&E stain. $\times 20$). **c2** Chronic inflammation of the rectal mucosa, interstitial hemorrhage, hyperplasia of fibrous tissue, and focal serous suppurative inflammation (H&E stain. $\times 10$). **c3** Immunohistochemistry of cervical tissue: CK negative. **c4** Immunohistochemistry of cervical tissue: scattered CD38 positive. **c5** Immunohistochemistry of cervical tissue: scattered CD138 positive. H&E, hematoxylin and eosin; CK, cytokeratin; CD, cluster of differentiation.

FCL PE150 kit (cat. No. 940-000003-00). The PD-L1 IHC stain 22C3 pharmDx (Code SK006) was used to evaluate PD-L1 protein expression. The patient tested positive for PD-L1 and exhibited genetic mutations of PTEN, MTOR, ARID1A, PIK3CA, and FGFR2 (Table 1). Additionally, the tumor was microsatellite stable (MSS) with a low tumor mutational burden (TMB-L) and moderate tumor neoantigen burden (Table 1).

On February 22, 2021, the patient underwent treatment with Chinese-produced PD-1 inhibitor camrelizumab 200 mg intravenous infusion on the first day combined with targeted antiangiogenic drug mesylate apatinib 250 mg taken orally once daily, with 3 weeks per cycle. After six cycles of treatment, pelvic MRI showed that the cervical mass disappeared (Fig. 2c), and the treatment effect was evaluated as a clinically complete response according to RECIST on July 08, 2021. Gynecological examination indicated that the vaginal canal was narrow, the cervix presented with normal morphology and a rough surface of cervical mucosa, and no tumor was observed. The cervix was slightly tough, but there was no abnormal mass according to palpation examination. The patient was continued on the camrelizumab combined with apatinib treatment for two cycles. In August 2021, the oral administration of apatinib was stopped due to hemorrhoids and hematochezia, while camrelizumab was continued for three cycles. On October 12, 2021, grade 2 drug-induced hepatic insufficiency was diagnosed according to CTCAE v4.0. Camrelizumab treatment was discontinued, and bicyclol tablets and atomolan tablets (without glucocorticoid therapy) were administered orally. Camrelizumab treatment was administered one time after liver function returned to normal on November 8, 2021.

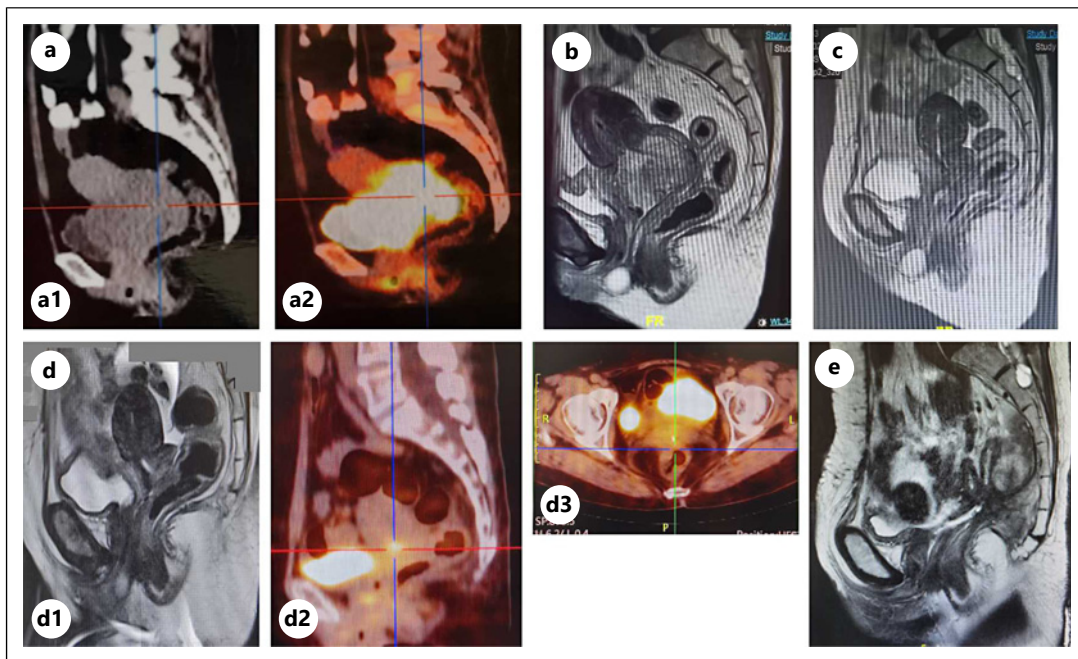


Fig. 2. Imaging pictures of patients before, during, and after treatment. **a** The systemic 18F-FDG PET-CT examination at the initial diagnosis. The CT image (**a1**) and PET-CT image (**a2**) show an abnormal mass in the cervix measuring $8.9 \times 9.7 \times 6.5$ cm with SUVmax of 14.5. **b** After radical radiotherapy and chemotherapy, a pelvic MRI T2-weighted image displays a high signal mass located at the cervix with a size of $6.6 \times 5.7 \times 4.2$ cm. The signal of mass is not homogeneous and has no distinct border with the uterine body. **c** Absence of a solid mass in the cervix after six cycles of camrelizumab and apatinib treatment. A T2-weighted pelvic MRI shows a patchy, slightly high signal with irregular uterine cervical morphology, and the cervical matrix is poorly displayed. **d1** Preoperative pelvic MRI T2-weighted image shows patchy, slightly high signal shadows in the posterior lip of the cervix with irregular cervical morphology. The boundary between the upper posterior wall of the cervix-vagina and the anterior wall of the rectum is unclear, with a loss of fat space between them. The local signal of the rectum is uneven, suggestive of possible rectum being invaded or adhered to by cervical lesion. **d2** Preoperative PET-CT shows focal increased 18F-FDG uptake in the cervical area, with an SUVmax of 4.9, and the lesion size is approximately 1.4×1.2 cm. **d3** Preoperative PET-CT showed adhesion between the cervix-vagina and rectum, with unclear demarcation and no accompanying increased 18F-FDG uptake. **e** Pelvic MRI T2-weighted images show an absence of uterus and bilateral appendages, observed residual lower rectum, and invisible sigmoid structure in the follow-up. 18F-FDG, fluorodeoxyglucose labeled by fluorine-18; PET-CT, positron emission tomography-computed tomography; CT, computed tomography; SUVmax, maximum standard uptake value; MRI, magnetic resonance imaging.

Surgical Treatment

On November 18, 2021, a pelvic MRI was conducted; it was suspected that the rectum had been invaded or adhered to a cervical lesion (Fig. 2d1). On November 23, 2021, a colonoscopy showed mucosal depression 4 cm away from the anal margin with surrounding concentrated images of mucosal folds. The mucosal depression had a diameter of 2 cm, and two pieces of tissue were taken. Rectal mucous pathology indicated moderate chronic inflammation (Fig. 1b). The patient then underwent systemic 18F-FDG PET-CT on November 25, 2021, revealing elevated standard uptake value of the cervical focal mass and the cervix adhering to the rectum (Fig. 2d2, d3).

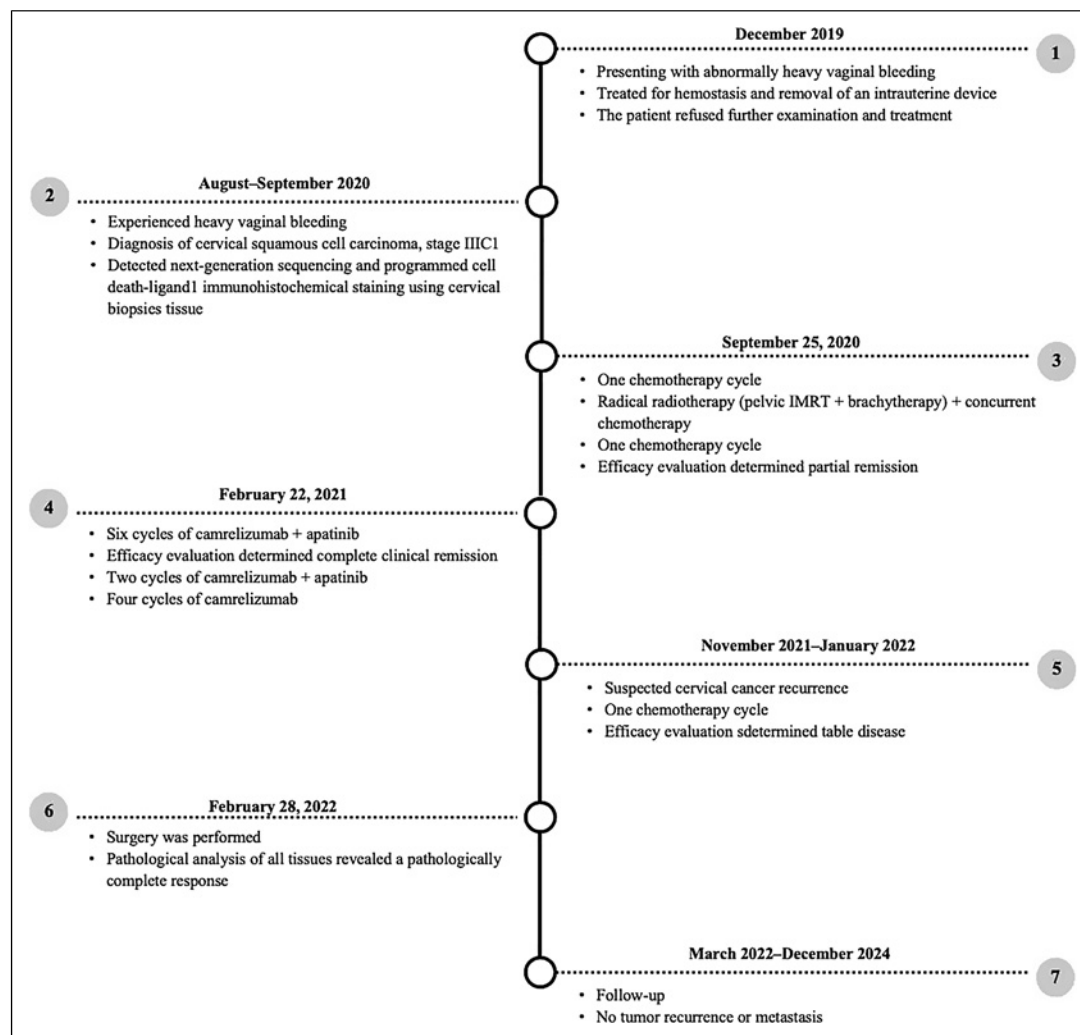


Fig. 3. Timeline summarizing the main events of the case.

Our gynecologic-oncology multiple-disciplinary team discussed the patient's case, concluding that cervical tumor recurrence caused the invaded rectum anterior wall. Ulcers had formed in the anterior wall of the rectum; a vaginal-rectal fistula was about to occur. Camrelizumab treatment was stopped, and radical surgery was recommended. However, surgery was not performed because the patient would not accept a colostomy. On January 4, 2022, the patient received one cycle of liposomal doxorubicin (25 mg/m^2) + cisplatin (75 mg/m^2) on day 1 of every 3 weeks, achieving stable disease status after chemotherapy based on pelvic MRI and rectal and perianal color Doppler ultrasonography results. Therefore, "total hysterectomy + bilateral adnexectomy + radical resection of rectal cancer (Hartman) + sigmoidostomy + pelvic abdominal adhesion lysis + intestinal adhesion lysis" were performed on February 28, 2022 (Fig. 3). The postoperative pathology revealed no tumor cells in the entire uterine cervix, endometrium and myometrium, bilateral fallopian tubes and ovaries, vaginal stump, rectum, and part of the colon. The cervical and rectal tissue exhibited chronic inflammation (Fig. 1c1, c2). No residual tumor cells were detected by immunohistochemistry, which was negative for cytokeratin (Fig. 1c3) and positive for cluster of differentiation (CD)38 (Fig. 1c4) and CD138 (Fig. 1c5).

Table 1. Next-generation sequencing genetic and immunohistology testing results

	Gene name	Variation	Variation frequency, %
Targeted therapy-related genes	PTEN	Exon 8 T319X	15.60
	PTEN	Exon 2 P30Qfs*24	24.10
	PIK3CA	Exon 3 G118D	13.90
	MTOR	Exon 47 S2215F	16.90
	ARID1A	Exon 15 R1276X	20.80
	FGFR2	Exon 13 E565A	35.70
Other tumor-related genes	WT1 E143 × 19.90%	NM_024426:exon1:c.427G>T: p.Glu143Ter, somatic mutation	
	BLM N515Kfs*2 10.90%	NM_000057:exon7:c.1544dup: p.Asn515Lysfs*2, somatic mutation	
Clinical significance unknown variation	SOX17 M270L, RECQL4 P310S, EP300 A179V, KDR T1258M, FAT1 R1506S, ESR1 A546T, CRTC2 R379C, MYOF T1032I, NUP107 R307W, FGFR3 E320D, GLI1 R418Q, CREBBP A2419V, ZC3H7B M379L, WNK1 Q1032K, CLMN R517H, PTPRD A1664T, TIMM8B T82A, PDE1C P42R, MTMR3 I737_Q741del		
	Biomarker name	Biomarker status	
Predictive biomarkers of ICIs	Microsatellite instability status	10.69%, MSS	
	Tumor mutational burden	7.33 muts/Mb, TMB-L	
	Tumor neoantigen burden	10.67 neo-peptides/Mb, tumor neoantigen burden moderate	
	Type I HLA heterozygosity	Moderate	
	PD-L1 IHC staining	TPS: 1%, CPS: 1, PD-L1 positive	
TPS, tumor cell proportion score; CPS, combined positive score; mut/Mb, mutation per megabase; PD-L1, programmed cell death-ligand 1.			

Follow-Up

No postoperative antitumor therapy and no tumor recurrence or metastasis were found during systemic reviews every 3 months until December 2024 (Fig. 2e). The disease-free survival time was 41 months from the complete response on July 08, 2021. The OS time was 51 months from diagnosis in September 2020.

Adverse Events

During treatment, the main adverse events were grade 2 reactive cutaneous capillary endothelial proliferation, grade 2 hepatic insufficiency, grade 2 hemorrhoidal hemorrhage, and grade 4 neutropenia, according to CTCAE v4.0.

Discussion

We present the case of a stage IIIC1 cervical cancer patient with a persistent residual lesion after radio-chemotherapy and reaching a pathological complete response to a combination of camrelizumab + apatinib. The patient's biomarkers of ICIs showed non- and low

sensitivity, including microsatellite stability, low tumor mutational burden, 1% tumor cell proportion score, and combined positive score 1. The good response to camrelizumab was likely derived from the patient's genetic mutations.

The phosphatase and tensin homolog (PTEN) gene is a tumor-suppressor gene undergoing alterations in approximately 8% of cervical cancer cases [10]. Impaired PTEN function triggers the activation of phosphoinositide 3-kinase (PI3K) and subsequent downstream signaling through serine-threonine kinase AKT/mammalian target of rapamycin (mTOR), which regulates key processes such as cell growth, survival, and proliferation, contributing to aggressive cancer phenotypes [11]. Mouse cancer models confirmed that the activation of the PTEN-PI3K-AKT-mTOR signal pathway was related to the overexpression of PD-L1 [12], and evidence suggests that the PTEN-PI3K-AKT-mTOR signal pathway activation also promotes antitumor adaptive immunity response [13]. PTEN loss of function includes mutations, deletions, transcriptional silencing, or protein instability [11]. Additionally, phosphoinositide-3-kinase, catalytic, and alpha polypeptide (PIK3CA) mutation can activate the PI3K pathway, resulting in the overexpression of PD-L1 [14]. Table 2 shows our patient's mutations in PTEN (two-point mutations), PIK3CA, and MTOR. The patient's active PTEN-PI3K-AKT-mTOR signal pathway may have promoted sensitivity to the PD-1 inhibitor camrelizumab treatment. Previous research indicated that cervical cancer patients treated with camrelizumab plus apatinib had improved PFS outcomes when they had mutations in PIK3CA and PTEN [15].

The AT-rich interaction domain (ARID) family has a highly conserved ARID domain, which can recognize DNA sequences with specific AT-rich features. The ARID family participates in the process of genetic duplication and expression, cell growth, differentiation, and development [16]. ARID1A is a member of this family, and patients with the ARID1A mutation could benefit more from ICIs treatment than do those with ARID1A wild type. The ARID1A mutation is associated with a higher abundance of CD4+T and CD8+T cells in malignant tumors as well as increased expression of PD-L1. ARID1A was a compelling biomarker to predict the therapeutic effect of ICIs [16]. Our patient carried 20.80% exon 15 of the ARID1A variation (Table 2), which promoted the therapeutic effect of camrelizumab.

Apatinib is a vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase inhibitor [17]. Apatinib has the function of selective combination with the receptor endocellular ATP-binding domain and inhibition of endothelial cells' proliferation, migration, and tube formation, thus inhibiting VEGFR-2-mediated angiogenesis [18]. Apatinib plays an antitumor role by controlling tumor angiogenesis. Additionally, low-dose apatinib (250 mg/day) can regulate the tumor immunosuppression microenvironment, which is helpful for increasing the sensitivity of PD-1 or PD-L1 inhibitor therapy. A mouse model experiment of lung cancer found that low-dose apatinib can relieve hypoxia, improve the recruitment of CD8+T cells, and decrease the infiltration of tumor-related macrophages. The use of anti-PD-L1 and low-dose apatinib delayed tumor cell growth, decreased the number of metastatic lesions, and prolonged life duration [19]. We believe that low-dose apatinib improved our patient's sensitivity to camrelizumab treatment.

ICI monotherapy is recommended for tumors with PD-L1-positive expression, microsatellite instability-high, or deficient mismatch repair [20, 21]. Antiangiogenic agents can increase the efficacy of ICIs in PD-L1-negative expression, MSS, or proficient mismatch repair (pMMR) tumors. For example, the use of pembrolizumab and lenvatinib in MSS/pMMR endometrial cancer has improved the treatment's efficacy, providing new treatment options to patients with MSS/pMMR endometrial cancer after progress has been made in the first-line treatment [22, 23]. The combination of ICIs and antiangiogenic agents broadens the application scope of ICIs in multiple solid tumors; in particular, it brings new therapeutic innovations for renal cell carcinoma and hepatocellular carcinoma [24]. A phase I study of the

Table 2. Lymphocyte subset alteration during treatment course

Abbreviation	Entry name	Reference range, cells/ μ L	Date (before camrelizumab)					Date (camrelizumab in use)			Date (after camrelizumab) January 11, 2022	Change as compared to before camrelizumab
			November 18, 2020	February 22, 2021	April 07, 2021	May 24, 2021	July 09, 2021	August 01, 2021	September 30, 2021			
CD3	Total T lymphocytes count	723–2,737	345.07	172.77	492.63	434.09	722.51	647.35	658.85	654.76	Increase	
CD8+/CD3+	T8 lymphocyte count	220–1,129	166.11	77.67	332.26	186.49	360.53	340.62	335.58	347.59	Increase	
CD4+/CD3+	T4 lymphocyte count	404–1,612	166.77	91.31	125.53	226.09	299.79	245.3	287.21	264.75	Increase	
CD3+/CD4+/CD8+	Double-positive T lymphocyte count	6–56	1.81	3.08	0.68	0.64	2.92	1.81	0.85	1.66	Decrease	
CD16+/CD56+	NK lymphocyte count	150–1,100	47.74	40.36	289.62	56.2	446.53	348.75	291.45	303.19	Increase	
CD19+	B lymphocyte count	90–560	8.23	7.99	37.56	34.28	53.45	87.64	97.58	147.45	Increase	
CD45+	Total lymphocyte count (CD45+)		409.61	229.1	830.3	535	1,248.7	1,091.8	1,061	1,110.7	Increase	
H/S	H/S	0.68–2.47 (ratio)	1	1.8	0.38	1.12	0.83	0.72	0.86	0.76	Decrease	

combination of camrelizumab and apatinib was first published in 2019, and the dosage of apatinib was determined to be 250 mg once a day when it was used in combination with camrelizumab [25]. The combination of camrelizumab and apatinib has been studied in many tumor species, including hepatocellular carcinoma, NSCLC, SCLC, colorectal carcinoma, cervical cancer, breast cancer, osteosarcoma, esophageal squamous cell carcinoma, gastric cancer, acral melanoma, nasopharyngeal carcinoma, and oral squamous cell carcinoma [26–32]. This combination is most commonly used in hepatocellular carcinoma, and has been researched in a dozen clinical studies, providing an ORR of 28%, mPFS of 5.87 months, and mOS of 19.35 months [26]. Immunotherapy biomarkers do not need to be detected in the clinical application study of the combination of camrelizumab and apatinib; microsatellite instability-high/deficient mismatch repair certainly has better efficacy than MSS/pMMR [33]. The CLAP study was published in 2020, almost 1 year before we used this regimen with our patient. It was a phase II trial and the only study to investigate the effectiveness and safety of combining camrelizumab with apatinib in treating persistent, recurrent, or meta-static cancer [9]. The phase III trial is anticipated. At present, practitioners are exploring the application of camrelizumab and apatinib in more kinds of cancers as well as their therapeutic potential in different stages of cancer treatment in order to achieve results without chemotherapy and ensure the quality of life of patients.

In our patient, imaging manifestations of pelvic MRI and PET-CT revealed that the rectum had been invaded or adhered to by cervical lesions in the process of using camrelizumab. Our MDT member, lacking experience in using PD-1 inhibitors, misinterpreted these imaging manifestations of inflammatory reactions as tumor recurrence. Pathological findings from the colonoscopy biopsy revealed moderate chronic inflammation in the rectal mucosa, with no cancer cells present. This pathological finding was initially deemed as false negative as our MDT member assessed the cervical tumor as not having fully penetrated the rectal wall into the mucosa. If the inflammatory reaction in the cervix had been accurately identified, it could have obviated the need for the patient to undergo surgery. However, the operation yielded evidence of a pathologically complete response, whereas the Chinese CLAP study merely presented clinical treatment outcomes.

In our patient, the total number of peripheral blood lymphocytes, including T lymphocytes, B lymphocytes, and NK cells, significantly increased after treatment with camrelizumab plus apatinib (Table 2), indicating our treatment's efficacy for advanced cervical cancer patients. On February 22, 2021 (following radical chemo-radiotherapy), reduced counts of T lymphocytes, B lymphocytes, and NK cells were noted compared to the counts observed on November 18, 2020 (during chemo-radiotherapy). Thus, we think that radical chemo-radiotherapy did not improve our patient's immune status.

Conclusion

Our findings suggest that the camrelizumab and apatinib combination could offer a valuable therapeutic option for residual advanced cervical cancer patients after concurrent radio-chemotherapy. Camrelizumab is affordable, costing 10% as much as pembrolizumab, although it is also not covered by medical insurance for cervical cancer in China. The PTEN, PIK3CA, MTOR, and ARID1A gene mutations could serve as predictive biomarkers for cervical cancer patients treated by PD-1 inhibitors, which need to be approved by prospective clinical studies. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000545068>).

Acknowledgment

We would like to thank Editage (www.editage.cn) for English language editing.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective review of patient data did not require ethical approval in accordance with national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was not supported by any sponsor or funder.

Author Contributions

Z.P.L. and S.H.L. treated the patient and were responsible for the conceptualization of the present study and wrote the manuscript. H.Z. and F.Y.R. were responsible for analyzing the patient's genetic test results and prepared the original draft. B.X. and D.X.Z. treated the patient and were responsible for editing and performing critical review of the manuscript. All authors read and approved the final manuscript for publication.

Data Availability Statement

The data of next-generation sequencing and immunohistochemical staining of the cervical biopsies tissue are openly available in the Genome Sequence Archive (Genomics, Proteomics & Bioinformatics, 2021) in National Genomics Data Center (Nucleic Acids Res, 2022) at <https://bigd.big.ac.cn/gsa-human/browse/HRA006695>. Further inquiries can be directed to the corresponding author.

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