

Pancreatic metastasis from cervical cancer: A case report and literature review

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Abstract. Cervical cancer metastasis to the pancreas is rare, and the clinical manifestations are variable and contingent upon the location of the metastasis. Consequently, certain patients may be overlooked due to the absence of overt clinical symptoms. Nevertheless, there is no universally accepted treatment protocol for such patients. The present report describes a case of a 64-year-old woman with stage IIIB cervical squamous cell carcinoma (International Federation of Gynecology and Obstetrics 2009) who received definitive chemoradiation in March 2018 [intensity modulated radiation therapy (IMRT) + weekly paclitaxel + brachytherapy]. After 6 years, pancreatic metastasis was confirmed by MRI/PET-CT and endoscopic ultrasonography-guided fine-needle aspiration biopsy. Between January and May 2024, the patient underwent six cycles of paclitaxel/carboplatin/bevacizumab/programmed cell death protein 1 inhibitor therapy followed by IMRT (45 Gy with 55 Gy boost). Post-treatment imaging revealed a partial response (lesion reduction from 45x30 mm to 32x20 mm). As of November 2024, the latest data indicated that the patient was disease-free on pembrolizumab maintenance. Furthermore, a systematic review of 14 related cases described in previous studies to analyze the characteristics of metastatic pancreatic cancer (mPC) is presented. In total, 14 publications were identified for systematic review. Among these patients, 7 had squamous cell carcinoma. The median age of the patients at the time of initial diagnosis was 49.8 years, and the mean

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interval between the identification of the primary tumor and metastasis was 46 months. Several clinical manifestations were observed depending on the site of metastasis. Endoscopic ultrasonography-guided fine-needle aspiration was revealed as one of the most effective methods for diagnosing mPC. In conclusion, there is currently no consensus regarding subsequent treatment plans. Pancreatic metastases originating from cervical cancer are infrequent and necessitate careful consideration along with individualized treatment approaches.

Introduction

Cervical cancer is the fourth most common cancer in women worldwide. Among the pathological types of cervical cancer, squamous cell carcinoma (SCC) is the most common, accounting for 75-80% of cases (1). Moreover, cervical adenocarcinoma accounts for 10-25% of cases and adenosquamous carcinoma accounts for 3-5% of cases (2). Cervical cancer metastasis usually occurs in the pelvic region, which includes mainly the bladder, vagina and rectum. Other common sites of occurrence include the liver, lungs and bones, and metastasis to abdominal organs other than the liver is rare (3). The majority of pancreatic tumors are primary ductal adenocarcinomas, while metastatic pancreatic cancer (mPC) accounts for only 2-5% of all pancreatic malignancies (4,5). Such metastases are often accompanied by widespread systemic dissemination, with isolated pancreatic metastases being exceptionally rare $(\sim 2\%)$ (6). Tumors with the highest propensity for pancreatic metastasis include renal cell carcinoma, lung cancer, breast cancer and colorectal cancer, followed by melanoma and leiomyosarcoma (7). Notably, cervical cancer metastases to the pancreas have only been sporadically reported. Of particular significance is the median latency period of up to 9 years between primary tumor resection and pancreatic metastasis, with its asymptomatic nature often complicating early diagnosis (8). Currently, there is no established clinical treatment for mPC, and the selection of treatment primarily depends on the pathological type. A representative example is pancreatic metastasis from renal cell carcinoma. Compared with that following non-surgical management, the 10-year survival rate following surgical intervention shows improvement, suggesting that active surgical intervention may enable

Key words: cervical cancer, pancreatic, metastatic, squamous cell carcinoma, endoscopic ultrasonography-guided fine-needle aspiration

long-term survival in this subgroup (8). This phenomenon may be attributed to the unique biological behavior of renal cell carcinoma and its sensitivity to systemic therapies, highlighting the critical importance of tumor heterogeneity in clinical decision-making (8). The present report describes the rare case of metastasis of cervical cancer to the pancreas. Through a comprehensive search of the medical database, 14 documented cases of cervical carcinoma with pancreatic metastases were identified. Subsequent systematic review of these clinical case reports provided valuable insights into the clinicopathological characteristics of pancreatic metastatic tumors originating from cervical primary malignancies.

Case report

A 64-year-old woman presented to Peking Union Medical College Hospital (Beijing, China) 6 years after receiving radiotherapy and chemotherapy for cervical cancer and 6 months after a pancreatic head mass was identified.

A total of 6 years prior, the patient underwent a biopsy for abnormal postmenopausal vaginal bleeding (March 2018; Peking Union Medical College Hospital, Beijing, China). CT and MRI imaging suggested the presence of an abnormality in the cervical space (Fig. 1). Pathological examination (data obtained from medical records) revealed moderately differentiated SCC in the uterine cervix (data not shown). The disease was staged as IIIB SCC, per the 2009 International Federation of Gynecology and Obstetrics staging system (9). Intensity-modulated radiotherapy was initiated at a dose of 50.4 Gy in 28 fractions for the whole pelvis, 60.2 Gy for the pelvic lymph nodes, 70 Gy for the right posterior bladder lesion, and 60.4 Gy for the right parametrium, along with concurrent weekly paclitaxel treatment. The treatment regimen consisted of 50 mg/m² (body surface area) paclitaxel administered via intravenous infusion once weekly over 6 consecutive weeks. This was followed by intracavitary brachytherapy at a dose of 28.5 Gy in 5 fractions, which were delivered 2 days apart. Regular follow-up (abdominal contrast-enhanced CT, pelvic MRI and tumor marker analysis) at the end of treatment revealed no significant abnormalities.

After 6 years of follow-up, in December 2023, the patient was diagnosed with pancreatic space-occupying lesions upon reexamination at the People's Hospital of Pingluo County (Shizuishan, China). Subsequently, the patient received treatment at the Cancer Hospital Chinese Academy of Medical Sciences (CAMS; Beijing, China). In December 2023, MRI revealed a peritoneal mass that was located posterior to the pancreas and was considered to have a high likelihood of malignancy, favoring a retroperitoneal origin (data not shown). Endoscopic ultrasonography (EUS)-guided fine-needle aspiration (FNA) biopsy of the pancreatic mass was performed in January 2024, and pathology (data obtained from medical records) revealed features suggestive of SCC (Fig. 2). The immunohistochemical results from CAMS (data obtained from medical records) indicated the following: P16 (3+) and P40 (+) (Fig. 3), and CK7 (-), CK20 (-), CK19 (2+), P63 (3+), PAX8 (-), GATA3 (+), CDX-2 (-), AE1/AE3 (3+), programmed death-ligand 1 (PD-L1): tumor proportion score, 60% and human papillomavirus [HPV (-)] (data not shown). Furthermore, a PET/CT examination in January 2024 revealed refined lymph nodes in the left parietal uterus and suggested that the mass behind the head of the pancreas may be a metastatic lesion (Fig. 4). On the basis of the imaging features and results of immunohistochemical staining, mPC from the cervical carcinoma was finally diagnosed.

In the Beijing Sixth People's Hospital (Beijing China), the patient received six cycles (21-day cycle) of intravenous infusion therapy consisting of paclitaxel (175 mg/m²), carboplatin (area under the curve=5), bevacizumab (7.5 mg/kg) and tislelizumab [an anti-programmed cell death protein 1 (PD-1) antibody; 200 mg], with the last administration occurring in May 2024. After the completion of treatment, an abdominal CT scan 16 days later indicated that the size of the pancreatic lesion had decreased compared with that in previous assessments, measuring ~32x20 mm (Fig. 5). Follow-up intensity-modulated radiotherapy was initiated for the pancreatic metastatic lesions and associated invasion, with a total dose of 45 Gy delivered in 25 treatment fractions. Additionally, the central region of the metastatic pancreatic lesions received a boost to a cumulative dose of 55 Gy. Following radiotherapy, the patient continued to receive 200 mg intravenous tislelizumab maintenance immunotherapy at Pingluo County People's Hospital. Multimodal surveillance comprising contrast-enhanced abdominal CT, pelvic MRI and serial serum tumor marker profiling conducted quarterly through November 2024 has yielded negative results across all modalities, confirming maintained disease-free status.

Discussion

The histopathology of cervical cancer is predominantly SCC, and the highest incidence is in the 40-59 year age group. In high-income nations, women aged 40-59 years exhibit stable age-standardized incidence rates, maintaining a consistently low range of 6.5-7.5 per 100,000 annually (10). This pattern sharply contrasts with the pronounced geographical disparities observed in low- and middle-income countries. India exemplifies this divergence, where incidence rates in this demographic have surged to 18-25 per 100,000, with rural regions experiencing even higher levels of 24-32 per 100,000 (11,12). Sub-Saharan Africa remains the global epicenter of disease burden, where countries such as Malawi and Zimbabwe report high rates persistently ranging between 40-56 per 100,000. Particularly in rural settings, these figures increase beyond 60 cases per 100,000 individuals (13). Irregular vaginal bleeding and abdominal pain are the main clinical symptoms, but certain patients have no symptoms at all (14). Cervical cancer metastasis typically occurs in the pelvic area, with the bladder, vagina and rectum being frequent sites of metastasis. Other common sites include the liver, lungs and bones. Early-stage cervical cancer is usually treated by means of surgery, with chemoradiotherapy used for inoperable lesions (15). The patient in the present case was 58 years old, presented with abnormal vaginal bleeding, diagnosed with stage IIIB SCC and was treated with concurrent chemoradiotherapy. Pancreatic metastases were found 6 years after treatment.

Pancreatic cancers (PCs) tend to be primary pancreatic ductal adenocarcinomas. mPC is rare, constituting 2-5% of all pancreatic malignancies. Moreover, renal cell carcinoma is the most likely tumor to metastasize to the pancreas (4). Patients

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Figure 1. Cervical lesion imaging. (A) The tumor was located in the sagittal

(C) The tumor was located in the transverse section on CT.

section on MRI. (B) The tumor was located in the transverse section on MRI.

with mPC present with symptoms related to the site of involvement: Obstructive jaundice may occur if the lesion is in the head of the pancreas, whereas there may not be any obvious symptoms in the early stages if the lesion is in the tail. The most common clinical symptoms are abdominal pain, jaundice and emaciation (16). In cases of cervical cancer, metastasis to the pancreas is very rare.

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (17), a literature search was performed using the PubMed (https://pubmed. ncbi.nlm.nih.gov/), Metstr (https://www.metstr.com) and CNKI (https://www.cnki.net/) databases to identify all eligible articles published from January 1, 1964 to December 31, 2024. The following search strategy was used: 'Uterine Cervical Neoplasms' OR 'cervical cancer' OR 'cervix carcinoma') AND ('Pancreatic Neoplasms/secondary' OR 'pancreatic metastasis' OR 'metastases to pancreas' OR 'pancreatic metastasis'). In total, 173 studies (169 in English and 4 in Chinese) were retrieved for review, including 51 case reports. After the removal of duplicates, the titles and abstracts of the remaining papers were carefully screened, and 20 case reports were identified as being inconsistent with the findings presented in the present article. Finally, a total of 14 studies (12 articles in English and 2 articles in Chinese), published from 1966-2024, were included in the review (Table I) (6,17-30). Out of the studies, seven cases were histologically classified as SCC, two cases as adenocarcinoma, four cases as neuroendocrine carcinoma, and one case as small cell carcinoma. The median age of the patients was 49 years, ranging from 36-70 years. Most of the patients had heterochronic metastases (13/14), and one patient was found to have pancreatic metastases at the same time as the diagnosis of cervical cancer, which is rare (26). Among the remaining patients, the time interval between the initial diagnosis and metastasis ranged from 2 months to 8 years, with a mean interval of 46 months. In these patients, back pain and weight loss were the most common symptoms, and only two patients had no obvious symptoms. In addition, 11 patients had a single metastasis, and 3 patients had multiple metastases. The exact process through which cervical cancer spreads to the pancreas remains unclear. Typically, cervical cancer spreads locally and can metastasize to other organs once the lymphatic and vascular systems become involved (31). Among the documented cases of pancreatic metastasis, only four presented evidence of lymph node involvement; therefore, we hypothesize that hematogenous dissemination is a common route for the spread of cervical cancer to the pancreas.

mPC is difficult to distinguish from primary pancreatic lesions. The diagnosis of pancreatic metastases usually includes ultrasound, CT, MRI, EUS, PET and magnetic resonance cholangiography (27). On CT images, primary PC and mPC have similar enhancement patterns, except in cases of metastatic renal cell carcinoma. In a previous study, pancreatic metastases were observed on multi-slice CT images in 75% of patients with nonrenal cell carcinoma, presenting as solitary, heterogeneous, ill-defined nodules with persistent low attenuation, indistinguishable from primary PC (32). The increased use of EUS-FNA has made histopathological diagnosis possible. EUS-FNA is widely used for the evaluation of pancreatic lesions due to its higher accuracy in detecting small lesions and the higher availability of samples for cytological/histological diagnosis than for CT or MRI. The sensitivity of EUS-FNA for the diagnosis of pancreatic metastases has been reported to be 93.8%, with a specificity of 60% and a positive diagnosis rate of 89% (33). mPC was diagnosed by EUS-FNA in 9/14 patients previously reported (3,5,6,8-13).

The most prevalent pathological type of PC is adenocarcinoma. By contrast, primary SCC is very rare, constituting ~0.28% of all PCs (34). Most patients diagnosed with pancreatic SCC are aged >65 years and are predominantly male (35). Given its rarity, a diagnosis of primary pancreatic SCC should be considered only after ruling out the presence of a primary site for SCC elsewhere. P40 is one of the isoforms of the P63 protein, whose specificity in differentiating between SCC from adenocarcinoma is high. The sensitivity and specificity for SCC are 100 and 90%, respectively (36). Furthermore, P40 is rarely expressed in the pancreas, as this organ is predominantly affected by adenocarcinoma. The P16 gene is located at the chromosome 9p21 locus and functions as an oncogene. Diffuse positive immunostaining for p16 serves as a reliable surrogate marker for high-risk HPV positive cervical cancer. Notably, even among patients who are negative for HPV, the majority still demonstrate positive p16 expression (37). As early as 2012, the American Society for Colposcopy and Cervical Pathology recommended p16 as a diagnostic marker for cervical cancerous lesions (38). Furthermore, a study (39) has reported a notable association between the degree of squamous intraepithelial lesions of the cervix and both the distribution and intensity of p16 staining. Additionally, strong positive expression of p16 has been observed in distant metastatic lesions, indicating its specificity. By contrast, primary PC has reduced expression of p16. Research indicates that the level of p16 in PC is markedly lower than that in adjacent normal tissues, particularly in advanced-stage patients (40,41).

There is no standard treatment for mPC, and chemotherapy is the most common treatment. 5-fluorouracil, leucovorin,



Figure 2. E US-FNA results of the target lesion. (A) Histological findings of EUS-FNA material from the pancreatic mass (hematoxylin and eosin stain). (B) Cytological and (C) histological findings of EUS-FNA material from the peritoneal mass (hematoxylin and eosin stain). EUS-FNA, endoscopic ultrasonography-guided fine-needle aspiration.



Figure 3. Immunohistochemical analysis. (A) P16 (3+) and (B) P40 (+).

irinotecan and oxaliplatin (FOLFIRINOX) and nab-paclitaxel + gemcitabine (AG) are frequently recommended as first-line treatment regimens for mPC; however, there is currently no international consensus on the progression-free survival and overall survival (OS) of patients receiving these two chemotherapy regimens (42). Notably, FOLFIRINOX is associated with a greater toxic response and is not recommended for patients with an Eastern Cooperative Oncology Group performance status of 2 or with comorbidities, where the risk of complications due to chemotherapy outweighs the expected benefit of prolonging OS (43,44). Therefore, when deciding on the first-line chemotherapy, clinicians must consider not only the extent of mPC but also the general condition of the patient and the presence of comorbidities. Moreover, immunotherapy has changed the treatment landscape for numerous solid tumors. In a clinical trial using toripalimab (anti-PD-1) + AG as a first-line treatment for patients with locally advanced PC or mPC, a favorable response and manageable toxicity were reported (45). Multiple clinical studies have also reported that the combination of anti-PD-1/PD-L1 antibodies with chemo-therapy can improve mPC outcomes, with a manageable safety profile (46,47). Thus, immunotherapy may be effective in the treatment of PC but can be used as part of a multiagent strategy rather than as monotherapy.

Radiotherapy always requires histological (or cytological) confirmation of the pathology of the tumor, and the sensitivity and complete remission rate of SCC to radiotherapy are generally higher than those of other histological types (48). In a previous study, a combination of radiotherapy and PD-L1 blockade improved survival and reduced tumor volume in patients with PC, compared with a single modality. PD-L1 expression was also reported to be increased in tumor cells





Figure 4. A multipanel PET-CT fusion imaging study showing the mass behind the head of the pancreas, with multiplanar reconstructions (axial, coronal and sagittal) delineating the metabolically active tumor mass.



Figure 5. The patient received a course of chemotherapy and immunotherapy, and subsequently underwent a follow-up examination via abdominal CT.

following radiotherapy (49). Moreover, a phase II randomized study by Chen *et al* (50) reported that the disease control rates of radiotherapy combined with nabumab/ipilizumab and nabumab/ipilizumab alone were 37.2 and 17.1%, respectively, indicating that stereotactic body radiation therapy combined with nabumab/ipilizumab has a good safety profile and antitumor activity.

With respect to targeted therapies, the randomized, double-blind study, Pancreas Cancer Olaparib Ongoing, reported that the addition of olaparib to first-line platinum-based chemotherapy improved the outcomes of patients with germline breast cancer gene 1 and 2 mutations and mPC (51). The use of entrectinib was included in the American Society of Clinical Oncology guidelines for the first time in 2020 (52) and studies have reported that this drug induces durable and clinically significant responses in patients with

Case	First author/s, year	Age at diagnosis of PT, year	Age at discovery of metastatic disease, year	Time period between PT and metastasis, months	Histology	Stage	PT treatment	Metastasis symptoms	Other site	Lymph nodes	Diagnostic means	Metastasis treatment	Survival, months	(Refs.)
1	Wastell <i>et al</i> , 1966	66	12	60	SCC	Ш	RT	Back pain; weight loss; anorexia; dark urine; and pale stools	1	I	Postoperative pathology	Surgery	0.5	(18)
7	Chung <i>et al</i> , 2007	45	53	06	SCC	B	Surgery and CCRT	Acute renal failure; nausea; vomiting; and anorexia	Liver; lumbar spine; and scalp	ı	CT	ı	ς	(19)
З	Kuwatani <i>et al</i> , 2008	38	39	11	Small cell carcinoma	IIB	Chemotherapy	No symptoms		I	EUS-FNA	Chemotherapy	5	(20)
4	Ogawa <i>et al</i> , 2011	43	45	24	SCC	Not mentioned	Not mentioned	Back pain and weight loss	ı	I	Postoperative pathology and IHC	Surgery and RT	ε	(9)
S	Mahajan <i>et al</i> , 2017	54	57	36	Adeno- carcinoma	AIII	Surgery and CCRT	No symptoms		I	EUS-FNA	Chemotherapy	I	(21)
9	Lee <i>et al</i> , 2019	36	36	0	SCC	IB2	CCRT	Nausea and vomiting	Both breasts; both adrenal glands; and peritoneum	+	EUS-FNA	Chemotherapy	1	(22)
٢	Gupta <i>et al</i> , 2019	55	58	36	SCC	IIIB	CCRT	Hematemesis melena		+	Postoperative pathology	Surgery	I	(23)
~	Kim et al, 2019	68	70	20	Adeno- carcinoma	IIB	CCRT	Back pain		I	EUS-FNA	I	I	(24)
6	Datta <i>et al</i> , 2022	51	53	24	SCC	IIIC	CCRT	Back pain; anorexia; and weight loss	ı	I	EUS-FNA	Chemotherapy	ı	(25)
10	Kopke Túlio <i>et al</i> , 2018	56	56	0	SCENC	IVB	Chemotherapy	Epigastric pain	Liver and bilateral retroperitonea	+	EUS-FNA	Chemotherapy	I	(26)
11	Nishimura <i>et al</i> , 2013	36	44	96	MANEC	IB	Surgery and CCRT	Back pain	I	I	EUS-FNA	Surgery	I	(27)
12	Liu <i>et al</i> , 2018	49	51	22	SCENC	ΙB	CCRT	No symptoms	I	·	EUS-FNA	RT	I	(28)
13	Nakajima <i>et al</i> . 2023	50	48	24	SCC	IIB	CCRT	Abdominal pain	I	ı	EUS-FNA	RT	I	(29)

Table I. Comparative analysis of literature-reported patient profiles.



neurotrophic tyrosine receptor kinase fusion-positive solid tumors (53,54). Furthermore, according to the National Comprehensive Cancer Network 2023 guidelines, individuals with mPC who have distinctive KRAS gene mutations (KRAS G12C) may be able to extend their survival through the use of molecular therapeutics, including sotorasib or adagrasib (55).

Previous studies have reported the prospective benefits of pancreatic metastasectomy, including improved patient survival and quality of life (56). Akashi et al (57) analyzed the surgical outcomes of 15 patients with mPC and reported that surgical resection of the pancreas resulted in longer survival in those with primary renal cell carcinoma, whereas those with primary nonrenal cell carcinoma had a worse prognosis. Thus, surgery may be justified for localized metastasis to the pancreas in the absence of broad metastatic disease if the surgical risk is tolerable and resection with no remaining malignancy can be performed. A total of 1/13 of the aforementioned patients with cervical mPC underwent concurrent surgery, chemotherapy and radiotherapy; nonetheless, the patient developed liver metastases 3 months after the operation and died 8 months after surgery. Among the remaining patients, three underwent surgery alone; one died 16 days after the procedure from an abdominal infection; and the other two patients were still alive at 6 and 7 months of follow-up, with no evidence of local progression. After receiving chemotherapy, five patients had no signs of cancer progression at 4-16 months of follow-up; however, one patient developed numerous brain metastases at 16 months of follow-up. After receiving radiotherapy in addition to surgery or chemotherapy, two patients developed liver metastases 9 months after treatment, and one patient died 7 months after treatment due to brain metastases. A total of one patient underwent surgery combined with chemotherapy and recovered well. Furthermore, one patient received no treatment, whilst the course of treatment of one patient was unknown. In the absence of a consensus treatment model, the patient described in the current report was treated with multiple adjuvant therapies.

According to previous studies, platinum (cisplatin or carboplatin) combined with paclitaxel remains the first-line protocol for advanced cervical cancer and can effectively reduce the risk of metastasis (58,59). The emergence of pancreatic metastases in patients with cervical cancer is typically associated with systemic spread, and chemotherapy can systematically eliminate potential micrometastases, thereby delaying disease progression (60). As indicated by prior studies, the use of anti-PD-1/PD-L1 antibodies in combination with chemotherapy has improved therapeutic outcomes in patients with mPC (49,50). Therefore, tislelizumab was incorporated into the treatment regimen in the present case. Given that VEGF-driven angiogenesis is a primary driver of cervical cancer progression, antiangiogenic therapy has emerged as a promising strategy for treating persistent, metastatic or recurrent cervical cancer. Bevacizumab blocks the VEGF signaling pathway, inhibits tumor angiogenesis and reduces the blood supply to metastatic lesions. Additionally, it enhances vascular permeability within the tumor microenvironment, improving chemotherapy drug penetration and immune cell infiltration, thus synergizing with chemotherapy and immunotherapy (61). A phase III trial (GOG240) evaluating the efficacy of chemotherapy

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2 2 2	etastatic r sase, year	netastasis, months	Histology	Stage	PT treatment	Metastasis symptoms	Other site	Lymph nodes	Diagnostic means	Metastasis treatment	Survival, months	(Refs.)
9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	91	SCC	IIIB	CCRT	Obstructive jaundice		+	Postoperative pathology	Surgery and chemotherapy	ı	(30)

small-cell neuroendocrine; MANEC, mixed adenoneuroendocrine carcinoma

(topotecan/paclitaxel or cisplatin/paclitaxel) with or without bevacizumab reported that this targeted therapy markedly improved OS (62). The pathological type of the patient reported in the present study was SCC, which is sensitive to radiotherapy. Radiotherapy can effectively control local disease progression and induce the release of tumor antigens and anti-inflammatory factors, thereby improving the immune microenvironment and enhancing the immune response (63).

The present study describes a unique case of cervical SCC metastasizing to the pancreas. Treatment for a 58-year-old patient, who was in the high-incidence age category for cervical cancer, involved concurrent radiotherapy and chemotherapy. Irregular vaginal bleeding led to the diagnosis of stage IIIB SCC of the cervix, and 6 years after treatment, a review of a pelvic MRI revealed a pancreatic mass without any clinical signs. Pancreatic tissue was obtained through EUS-FNA, and immunohistochemical analysis revealed P16 (3+) and p40 (+). This, in conjunction with the patient's history of SCC, led to a diagnosis of secondary pancreatic adenocarcinoma originating from cervical cancer. A novel therapeutic approach combining chemotherapy, immunotherapy, targeted therapy and radiotherapy, which is previously unreported in the literature, to the best of our knowledge, may prove beneficial in enhancing patient outcomes.

In conclusion, for patients with a previous history of cervical cancer, when imaging suggests the presence of a pancreatic mass, even if there are no clinical symptoms, the possibility of mPC should not be ignored, and EUS-FNA is feasible for definitive diagnosis. Currently, there is no uniform standard for the treatment of mPC of cervical origin. Classical chemotherapy has been shown to be the baseline method for improving the survival rate among patients with mPC, and early genetic testing and appropriate supplementation with immune and targeted therapies may further prolong the survival period. However, at present, it is difficult to evaluate the prognosis and survival time of patients, as there are few cases of cervical cancer complicated with pancreatic metastasis, resulting in the lack of large-sample clinical studies. The existing evidence is mostly based on case reports or small-sample retrospective analysis, and the statistical efficacy is insufficient. Furthermore, the biological behavior of the tumor (such as pathological type and differentiation degree), the number of metastases (single or multiple) and whether it is combined with metastasis of other organs (such as liver and lung) are notably different among different patients, making it difficult to establish a unified prognostic model. In addition, there is currently no guideline for the first-line treatment of this metastatic site, and the treatment mainly depends on case experience, and the efficacy of different programs varies significantly. Therefore, more data are required for patients with cervical cancer and pancreatic metastasis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

HL, XC, XH and FZ contributed to the study conception and design. Material preparation, data collection and analysis were performed by XC. The first draft of the manuscript was written by HL and XC, and all authors commented on previous versions of the manuscript. XH and FZ confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present case report was approved by the Ethics Committee of Peking Union Medical College Hospital Chinese Academy of Medical Sciences & Peking Union Medical College (Beijing, China; approval no. K24C3515).

Patient consent for publication

The patient provided written consent for the publication of the data and images included in this case report.

Competing interests

The authors declare that they have no competing interests.

References

- 1. Xie H, Kong B and Duan T: Obstetrics and Gynaecology. 1st edition. People's Health Press, Beijing, p298, 2018.
- Gadducci A, Guerrieri ME and Cosio S: Adenocarcinoma of the uterine cervix: Pathologic features, treatment options, clinical outcome and prognostic variables. Crit Rev Oncol Hematol 135: 103-114, 2019.
- Shen J, Feng XS, Wen H, Zhou C, Mo M, Wang Z, Yuan J, Wu X and Zheng Y: Metastatic characteristics and survival analysis of 572 patients with distant metastases of cervical cancer: A hospital-based real-world study. Chin J Cancer 34: 361-367, 2024.
- 4. Ballarin R, Spaggiari M, Cautero N, De Ruvo N, Montalti R, Longo C, Pecchi A, Giacobazzi P, De Marco G, D'Amico G, *et al*: Pancreatic metastases from renal cell carcinoma: The state of the art. World J Gastroenterol 17: 4747-4756, 2011.
- Tsitouridis I, Diamantopoulou A, Michaelides M, Arvanity M and Papaioannou S: Pancreatic metastases: CT and MRI findings. Diagn Interv Radiol 16: 45-51, 2010.
- Ogawa H, Tsujie M, Miyamoto A, Yasui M, Ikenaga M, Hirao M, Fujitani K, Mishima H, Tsujinaka T and Nakamori S: Isolated pancreatic metastasis from uterine cervical cancer: A case report. Pancreas 40: 797-798, 2011.
- 7. Geraizadeh B, Kashkooe A, Nikeghbalian S and Malek-Hosseini SA: Metastatic tumors to the pancreas: A single center study. Arch Iran Med 22: 50-52, 2019.
- Reddy S, Edil BH, Cameron JL, Pawlik TM, Herman JM, Gilson MM, Campbell KA, Schulick RD, Ahuja N and Wolfgang CL: Pancreatic resection of isolated metastases from nonpancreatic primary cancers. Ann Surg Oncol 15: 3199-3206, 2008.
- Pecorelli S: Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynecol Obstet 105: 103-104, 2009.





- National Cancer Institute. SEER: Cancer Stat Facts: Cervical Cancer. https://seer.cancer.gov/statfacts/html/cervix.html. Accessed 4/5/25.
- Sathishkumar K, Chaturvedi M, Das P, Stephen S and Mathur P: Cancer incidence estimates for 2022 and projection for 2025: Result from national cancer registry programme, India. Indian J Med Res 156: 598-607, 2022.
- Budukh AM, Dikshit R and Chaturvedi P: Outcome of the randomized control screening trials on oral, cervix and breast cancer from India and way forward in COVID-19 pandemic situation. Int J Cancer 149: 1619-1620, 2021.
- Stelzle D, Tanaka LF, Lee KK, Khalil AI, Baussano I, Shah ASV, McAllister DA, Gottlieb SL, Klug SJ, Winkler AS, *et al*: Estimates of the global burden of cervical cancer associated with HIV. Lancet Glob Health 9: e161-e169, 2021.
- Han SY and Kong WM: Pathological characteristics and changes of cervical cancer. Hebei Medical Journal 42: 1414-1417+1421, 2020 (In Chinese).
- Crafton SM, Venkat PS and Salani R: A review of the state of cervical cancer: Updates from prevention to recurrent disease. Curr Opin Obstet Gyencol 36: 28-33, 2023.
- Jaén-Torrejimeno I, López-Guerra D, Rojas-Holguín A, De-Armas-Conde N and Blanco-Fernández G: Resection of isolated pancreatic metastases from pulmonary neoplasia: A systematic review. Updates Surg 74: 1817-1825, 2022.
 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, MCKENZE M, COMPARISON CONTRACT, Comparison of the systematic review.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, *et al*: The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 372: n71, 2021.
- Wastell C: A solitary secondary deposit in the pancreas from a carcinoma of the cervix. Postgrad Med J 42: 59-61, 1966.
- Chung JJ, Namiki T and Johnson DW: Cervical cancer metastasis to the scalp presenting as alopecia neoplastica. Int J Dermatol 46: 188-189, 2007.
- 20. Kuwatani M, Kawakami H, Asaka M, Marukawa K, Matsuno Y and Hosaka M: Pancreatic metastasis from small cell carcinoma of the uterine cervix demonstrated by endoscopic ultrasonography-guided fine needle aspiration. Diagn Cytopathol 36: 840-842, 2008.
- Mahajan S and Pandit-Taskar N: Uncommon metastasis to the pancreas from adenocarcinoma of the cervix detected on surveillance 18F-FDG PET/CT imaging. Clin Nucl Med 42: e511-e512, 2017.
- 22. Lee EJ, Hwang J and Kim DW: Small-cell neuroendocrine carcinoma of the uterine cervix with pancreatic metastasis: A case report and a review of the literature. J Obstet Gynaecol 39: 573-575, 2019.
- 23. Gupta PK, Lal P and Tiwari A: A case report of carcinoma of uterine cervix throwing heterochronous metastasis to the skin, spleen, and pancreas: The role of multimodality treatment approach. J Egypt Natl Cancer Inst 31: 8, 2019.
- 24. Kim DJ, Park JM, Kim JH, Nam K, Kang CD, Lee SJ, Lee K and Jeon YH: Pancreatic metastasis from adenocarcinoma of the uterine cervix. Korean J Gastroenterol 73: 182-185, 2019.
- 25. Datta D, Aggarwal D, Balakrishnan S, Varshney VK and Kumar R: Metastasis from cervical cancer presenting as a pancreatic head mass-an unexpected diagnosis! J Gastrointest Canc 54: 300-303, 2022.
- 26. Kopke Túlio MACB, Horta MSF, BispoMCS, Costa TSNBE and Chagas CMDBR: Pancreatic Metastases as the Initial Manifestation of a Neuroendocrine Carcinoma of the Uterine Cervix. Pancreas 47: e4-e5, 2018.
- 27. Nishimura C, Naoe H, Hashigo S, Tsutsumi H, Ishii S, Konoe T, Watanabe T, Shono T, Sakurai K, Takaishi K, *et al*: Pancreatic metastasis from mixed adenoneuroendocrine carcinoma of the uterine cervix: A case report. Case Rep Oncol 6: 256-262, 2013.
- Liu AL, Feng Y and Zhao Y: Pancreatic metastasis of complex small cell neuroendocrine carcinoma of cervix: A case report and literature review. Gastroenterology 23: 638-640, 2018.
- 29. Nakajima Y, Iwasaki E, Kayashima A, Machida Y, Kawasaki S, Horibe M, Kawaida M, Masugi Y, Iwata T and Kanai T: Successful radiotherapy for recurrent obstructive pancreatitis secondary to pancreatic metastasis from cervical squamous-cell carcinoma. Clin J Gastroenterol 16: 755-760, 2023.
- Ye H, Yi XL and Li XH: A case report of obstructive jaundice due to pancreatic metastasis from squamous cervical carcinoma. J Clin Hep Dis 38: 646-648, 2022.
- Akers A, Read S, Feldman J, Gooden C and English DP: Diagnostic challenges and individualized treatment of cervical adenocarcinoma metastases to the breast: A case report. World J Clin Cases 12: 412-417, 2023.

- 32. Choi TW, Kim SH, Shin CI, Han JK and Choi BI: MDCT findings of pancreatic metastases according to primary tumors. Abdom Imaging 40: 1595-1607, 2015.
- 33. Ardengh JC, Lopes CV, Kemp R, Venco F, de Lima-Filho ER and dos Santos JS: Accuracy of endoscopic ultrasound-guided fine-needle aspiration in the suspicion of pancreatic metastases. BMC Gastroenterol 13: 63, 2013.
- 34. Tella SH, Kommalapati A, Yadav S, Bergquist JR, Truty MJ, Durgin L, Ma WW, Cleary SP, McWilliams RR and Mahipal A: Survival and prognostic factors in patients with pancreatic squamous cell carcinoma. Eur J Surg Oncol 45: 1700-1705, 2019.
- 35. Makarova-Rusher OV, Ulahannan S, Greten TF and Duffy A: Pancreatic squamous cell carcinoma: A population-based study of epidemiology, clinicopathologic characteristics and outcomes. Pancreas 45: 1432-1437, 2016.
- 36. Kim NI and Lee JS: Greater specificity of p40 compared with p63 in distinguishing squamous cell carcinoma from adenocarcinoma in effusion cellblocks. Cytojournal 17: 13, 2020.
- 37. Bao H, Zhao Y, Zhang X, Bi H, Cong S, Fang L, Wang HJ and Wang L: HPV-negative high-grade cervical precancerous lesions or invasive cancer in China: A post hoc analysis of a multicentric clinical study. Int J Gynecol Obstet 161: 159-167, 2022.
- Paya A, Alenda C, Perez-Carbonell L, Rojas E, Soto JL, Guillén C, Castillejo A, Barberá VM, Carrato A, Castells A, *et al*: Utjlity Of p16 immunohistochemistry for the identification of Lynch syndrome. Clin Cancer Res 15: 3156-3162, 2009.
 Shafique M, Shoaib I, Aslam B, Khalid R, Tanvir I, Rasool MH,
- 39. Shafique M, Shoaib I, Aslam B, Khalid R, Tanvir I, Rasool MH, Shah TA, Almaary KS, Bourhia M and Qamar MU: Detection of high-risk human papillomavirus infected cervical biopsies samples by immunohistochemical expression of the p16 tumor marker. Arch Microbiol 206: 17, 2023.
- Mou H, Yu L, Zheng X, Liao Q, Hou X and Wu Y: p16 gene expression in pancreatic cancer tissue and its importance in diagnosis. J Biol Regul Homeost Agents 31: 1043-1047, 2017.
- 41. Zińczuk J, Zaręba K, Guzińska-Ustymowicz K, Kędra B, Kemona A and Pryczynicz A: p16, p21, and p53 proteins play an important role in development of pancreatic intraepithelial neoplastic. Ir J Med Sci 187: 629-637, 2018.
- 42. Pacheco-Barcia V, Custodio-Cabello S, Carrasco-Valero F, Palka-Kotlowska M, Mariño-Mendez A, Carmona-Bayonas A, Gallego J, Martín AJM, Jimenez-Fonseca P and Cabezon-Gutierrez L: Systemic inflammation response index and weight loss as prognostic factors in metastatic pancreatic cancer: A concept study from the PANTHEIA-SEOM trial. World J Gastrointest Oncol 16: 386-397, 2023.
- 43. Yang L, Su J, Wang W and Zhou F: The efficacy and safety of Nab-paclitaxel plus gemcitabine versus mFOLFIRINOX in the first-line treatment of metastatic pancreatic cancer: A retrospective study. World J Surg Oncol 21: 19, 2023.
- 44. Wainberg ZA, Melisi D, Macarulla T, Cid RP, Chandana SR, De La Fouchardière C, Dean A, Kiss I, Lee WJ, Goetze TO, *et al*: NALIRIFOX versus nab-paclitaxel and gemcitabinein treatment-naive patients with metastaticpancreatic ductal adenocarcinoma (NAPOLI 3): A randomised, open-label, phase 3 trial. Lancet 402: 1272-1281, 2023.
- 45. Shui L, Cheng K, Li X, Shui P, Zhou X, Li J, Yi C and Cao D: Study protocol for an open-label, single-arm, phase Ib/II study of combination of toripalimab, nab-paclitaxel, and gemcitabine as the first-line treatment for patients with unresectable pancreatic ductal adenocarcinoma. BMC Cancer 20: 636, 2020.
- 46. Wainberg ZA, Hochster HS, Kim EJ, George B, Kaylan A, Chiorean EG, Waterhouse DM, Guiterrez M, Parikh A, Jain R, et al: Open-label, phase I study of nivolumab combined with paclitaxel plus gemcitabine in advanced pancreatic cancer. Clin Cancer Res 26: 4814-4822, 2020.
- 47. Cheng K, Lv WR, LI X, Tian B and Cao D: Toripalimab with nabpaclitaxel/gemcitabine as first line treatment for advanced pancreatic adenocarcinoma: Updated results of a single arm, open label, phase Ib/II clinical study. J Clin Oncol 39 (Suppl 15): e16213, 2021.
- Perez CA and Brady LW (eds): Perez and Brady's Principles and Practice of Radiation Oncology. 7th edition. Lippincott Williams & Wilkins, Philadelphia, PA, 2018.
- 49. Azad A, Lim SY, D'Costa Z, Jones K, Diana A, Sansom OJ, Kruger P, Liu S, McKenna WG, Dushek O, *et al*: PD-L1 blockade enhances response of pancreatic ductal adenocarcinoma to radiotherapy. EMBO Mol Med 9: 167-180, 2017.

- 50. Chen IM, Johansen JS, Theile S, Hjaltelin JX, Novitski SI, Brunak S, Hasselby JP, Willemoe GL, Lorentzen T, Madsen K, *et al*: Randomized phase II study of nivolumab with or without ipilimumab combined with stereotactic body radiotherapy for refractory metastatic pancreatic cancer (CheckPAC). J Clin Oncol 40: 3180-3189, 2022.
- 51. Golan T, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, *et al*: Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. N Engl J Med 381: 317-327, 2019.
- National Comprehensive Cancer Network-NCCN: Guidelines for Non-Small Cell Lung Cancer. Version 2.2020. Available from: https://www.nccn.org. Accessed July 15, 2024.
- 53. Yılmaz F, Yaşar S, Mandel NM, Kaçan T, Özdemir M, Doğu GG, Şengül N, Meydan N, Başal FB, Tolunay PK, *et al*: Real-Life experience with entrectinib in neurotrophic tyrosine receptor kinase fusion-positive solid tumors: A multicenter retrospective trial. Target Oncol 19: 957-964, 2023.
- Yue S, Zhang Y and Zhang W: Recent advances in immunotherapy for advanced biliary tract cancer. Curr Treat Option Oncol 25: 1089-1111, 2023.
- 55. Pajewska M, Partyka O, Czerw A, Deptała A, Cipora E, Gąska I, Wojtaszek M, Sygit K, Sygit M, Krzych-Fałta E, *et al*: Management of metastatic pancreatic cancer-comparison of global guidelines over the last 5 years. Cancers (Basel) 15: 4400, 2023.
- 56. Sperti C, Pasquali C, Liessi G, Pinciroli L, Decet G and Pedrazzoli S: Pancreatic resection for metastatic tumorsto the pancreas. J Surg Oncol 83: 161-166, 2003.
- Akashi Y, Saiura A, Kishi Y, Koga R, Morimura R, Yoshioka R, Yamamoto J and Yamaguchi T: Outcome after surgical resection of isolated metastases to the pancreas. Hepatogastroenterology 57: 1549-1552, 2010.

- 58. Lou H, Cai H, Huang X, Li G, Wang L, Liu F, Qin W, Liu T, Liu W, Wang ZM, *et al*: Cadonilimab combined with chemotherapy with or without bevacizumab as first-line treatment in recurrent or metastatic cervical cancer (COMPASSION-13): A phase 2 study. Clin Cancer Res 30: 1501-1508, 2023.
- 59. Lan C, Lu H, Zhou L, Liao K, Liu J, Xie Z, Liang H, Zou G, Yang T, Xu Q and Huang X: Long-term survival outcomes and immune checkpoint inhibitor retreatment in patients with advanced cervical cancer treated with camrelizumab plus apatinib in the phase II CLAP study. Cancer Commun (Lond) 44: 654-669, 2023.
- 60. Wlodarczyk JR and Lee SW: New frontiers in management of early and advanced rectal cancer. Cancers (Basel) 14: 938, 2022.
- 61. Kumar L, Harish P, Malik PS and Khurana S: Chemotherapy and targeted therapy in the management of cervical cancer. Curr Probl Cancer 42: 120-128, 2018.
- 62. Godoy-Ortiz A, Plata Y, Alcaide J, Galeote A, Pajares B, Saez E, Alba E and Sánchez-Muñoz A: Bevacizumab for recurrent, persistent or advanced cervical cancer: Reproducibility of GOG 240 study results in 'real world' patients. Clin Transl Oncol 20: 922-927, 2017.
 63. Choi C, Yoo GS, Cho WK and Park HC: Optimizing radiotherapy
- Choi C, Yoo GS, Cho WK and Park HC: Optimizing radiotherapy with immune checkpoint blockade in hepatocellular carcinoma. World J Gastroenterol 25: 2416-2429, 2019.

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