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Case Report

Choroid Metastasis in a Patient with Squamous Cell Carcinoma of the Uterine Cervix: A Case Report

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Keywords
Choroid · Metastasis · Cervix · Carcinoma

Abstract
We present the case of a 43-year-old woman with unilateral loss of vision who had a history of cervical cancer, staged as FIGO IIIB, and who had undergone previous chemotherapy and radiotherapy, but was not a surgical candidate. An examination revealed serous retinal detachment with an underlying choroidal mass in the left eye. We reviewed all available published case reports of uterine cervix metastases to the eye and adnexa and compiled all information into a table to present clinical and epidemiological findings. Unilateral choroidal metastasis arising from cervical cancer is extremely rare. In most cases, a history of cervical carcinoma is confirmed in the advanced stage of the disease. Ocular metastasis may be the presenting

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feature of primary cervical malignancy; therefore, to rule out malignancy in every woman who develops these clinical features, a cervical examination should be included in the workup.

Introduction

Cervical cancer is the only preventable malignancy. Eight out of 10 people will become infected with the human papillomavirus at some point in life. In 1 of 1,000 cases, the infection persists and progresses to cancer [1]. Also, cervical cancer is the eighth most common cancer in the world population [2]. Cervical cancer has been the second leading cause of death from malignancy in Mexican women since 2006. The estimated annual occurrence is 13,960 cases in women, with an incidence of 23.3 cases per 100,000 women [1, 2].

Cervical cancer infiltrates the adjacent organs, including the vagina, peritoneum, urinary bladder, ureters, rectum and paracervical tissue. It mainly metastasizes through direct regional spread and lymphatic drainage to the retroperitoneal lymph nodes [3]. Hematogenous spread, through thoracic or smaller venous channels, generally occurs in more advanced disease or with unusual cell types, such as adenoscopic or neuroendocrine tumors. Approximately 5% of cases of cervical neoplasms involve hematogenous spread; the lung (40%), bone (16%), and liver (8%) are the most affected organs [4].

Ocular metastases arising from primary cervical carcinoma are extremely rare, but they do occur. Some published studies have reported that the orbit, followed by the choroid, are the most common location of metastasis. The iris and subconjunctival tissue are the least common sites of metastasis.

Case Report

We present the case of a 43-year-old female patient who underwent gynecologic evaluation in November 2018 for an abundant transvaginal hemorrhage. She also mentioned pain in the waist that did not radiate to other areas. Upon examination, a tumor of approximately 4 × 4 cm that originated in the cervix was found, along with a bleeding lesion on palpation, with atypical vessels in the form of a coma involving both lips, parametria, and vaginal rectum septum. The physical examination indicated no further abdominal masses or palpable lymphadenopathy. An incisional biopsy was performed, which revealed a poorly differentiated, microinvasive, squamous cell carcinoma (Fig 1a, b).

Following the International Federation of Gynecology and Obstetrics (FIGO), the lesion was classified as stage IIB because of the invasion of the parameters. The patient completed five cycles of chemotherapy, based on carboplatin and gemcitabine, in addition to radiotherapy (50.4 Gy in 28 fractions).

During patient follow-up in July 2019, gynecologic examination revealed an increased tumor mass volume, now 6 × 6 cm, with a lesion that reached to the introitus, invading both the septa and parametria to the pelvic wall. It was reclassified as stage IIIB because of the involvement of the pelvic wall and pelvic lymph nodes. The patient was administered four

applications of cisplatin along with brachytherapy (30 Gy in five fractions), which was completed in September 2019.

At the beginning of November 2019, the patient began to experience a nonproductive cough, accompanied by headache and blurred vision in the left eye, which was painless and progressed rapidly.

Contrast tomography in axial acquisition with pulmonary window showed three solid, rounded lesions with poorly defined edges, located in the right lung, in relation to metastases (Fig. 2a; white arrows). Figure 2b–c shows hepatic (horizontal white arrows) and splenic metastases (vertical white arrow), para-aortic ganglionic conglomerate surrounding retroperitoneal vascular structures, and dilation of the left renal pelvis (oblique white arrow). Figure 2d–e shows cervical tumor infiltrating the posteroinferior bladder wall, as well as the anterior wall of the rectum.

Further evaluation by our service detected a right eye without alteration, left eye with a visual acuity of 1-m finger count, annexes, anterior segment, gonioscopy, and tonometry within normal parameters, left eye with clear vitreous on fundoscopy, papilla without alterations, vasculature without inflammation data, tortuosity in the upper temporal arch, serous retinal detachment in the upper temporal sector with abundant fluid involving the macular area, and a choroidal tumor projecting from the middle periphery to the macular area, with white-yellowish granular infiltrates. There were no detectable satellite lesions or extreme periphery involvement (Fig. 3a).

Fluorescein angiography showed homogeneous hypofluorescence during the arterial phase, which progressed to areas of hyperfluorescence in a multiple mottled pattern in the late phases. A temporal domain optical coherence tomography revealed a wedge-shaped, low-reflectivity lesion on the vitreoretinal interface, sensorineural retinal detachment with subretinal fluid, and pigmentary epithelium disruption (Fig. 3c).

Using ultrasonography mode AB axial projection, a vitreous cavity, occupied by a homogeneous, wedge-shaped hyperechogenic image in the upper sector, was noted, which enhanced the spikes of medium reflectivity. The optic nerve had a normal shape and trajectory (Fig. 3d). Furthermore, plain tomography of the orbit and adnexa showed no evidence of infiltrative injury to the adnexal structures (Fig. 3e)

The patient refused palliative chemotherapy. She died from respiratory complications 2 months after the ocular symptoms occurred.

Discussion

We performed a systematic PubMed search for ocular metastases from cervical cancer using the keywords “choroid metastases and uterine cancer”, “choroid metastases and cervical cancer,” “ocular metastases and uterine cancer,” and “ocular metastases and cervical cancer,” using operator Boolean “AND” to limit our search to obtain the greatest number of related posts. All publications in English were extracted and included for reference in our study.

In their case series of 28 patients, Bloch and Gartner [5] presented a case of metastatic cervical cancer. However, they did not specify whether the eye or orbit was affected, nor was the tumor histology reported. Similarly, Ferry and Font [6] presented a series of 227 cases of metastatic carcinoma of the eye and adnexa; 4 cases of orbital metastases of unknown primary

origin were reported in female patients, possibly with cervical cancer, although case documentation was lacking.

The first article on this topic was published in 1987 by Hertzanu et al. [7], who described the case of a 44-year-old woman with proptosis, diplopia, and blurred vision as presenting features; she was eventually diagnosed with squamous cell cervical cancer that metastasized to the orbit [7]. Since then, 20 additional cases, including this report, of well-documented ocular metastases from cervical cancer have been published; 5 were choroidal metastases, 3 were unilateral, and 2 involved both eyes. We present the sixth case of choroidal metastasis, and the first case in Mexico.

The most common site for ocular metastasis was the orbit, as observed in 50% of all cases (10/20), followed by the choroid in 30% (6/20). Other uveal tissue involved included the ciliary body and the iris, with a single report of each, in addition to subconjunctival tissue and metastases in the intraorbital portion of the optic nerve.

The median age of the 20 reported patients, including ours, was 51 years (range, 25–64 years), and the squamous cell subtype was the most frequent type reported (14/19). Only one article did not include the tumor subtype, although the authors mentioned cervical carcinoma of the uterus [8]. Most of the patients received chemotherapy and radiotherapy as first-choice treatment because of the tumor's advanced stage at the time of diagnosis.

Among all cases reported, the lungs were the most common target organ, with 44% (8/18) of the cases reporting lung involvement, followed by a tie between bone and liver lesions, each of which occurred in 22.2% (4/18) of patients.

In 4 cases, eye injury was the only site of metastasis. However, these reports did not include the details of the detection protocols for metastatic lesions and imaging test findings, such as computed tomography. Therefore, additional metastatic sites might have been missed.

It is important to keep in mind some differential diagnoses such as amelanotic choroidal tumor and choroidal hemangioma that have a vascular component that may help us to differentiate them from other tumors.

The treatment options available for these patients are generally limited. Thus, patient prognosis is unfavorable because there is a correlation between the duration of the diagnosis of ocular metastasis and the time of death. The median survival period after diagnosis of ocular metastasis is 3 months (range, 1–5 months; n = 11), based on the results of 11 of 20 well-documented publications, which indicates that metastasis to the eye generally heralds an ominous clinical course [9].

In the report by Gosslee et al. [10], the authors provided the first table to include variables such as age, the affected eye, histologic line, clinical stage, metastasis site, treatment, and clinical outcome. Subsequently, other authors [8] added new variables to complete this table which reviews all of the publications regarding ocular metastases of a primary cervical tumor. This review is shown in Table 1 and includes the present case.

Conclusions

In general, ocular metastasis arising from uterine cervical carcinoma as a primary tumor is a poor prognostic risk factor for mortality, because the duration between the diagnosis of ocular metastasis and death varies from 2 to 5 months, regardless of whether the site is

intraorbital or intraocular. In women presenting with ocular metastases from an unknown primary tumor, cervical carcinoma screening is useful as part of the evaluation because visual symptoms can be the initial presentation. Cervical carcinoma represents a significant public health challenge in terms of awareness, vaccination programs and early detection, as well as access to, coverage of, and quality of the healthcare service.

Statement of Ethics

Oral and written informed consent were obtained from the patient's sister for publication of this case.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Angel García Vásquez, MD: conception of the paper, design of the paper, data analysis and interpretation, manuscript drafting, and literature search. Gabriela Thomassiny Bautista, MD: co-writing of the manuscript, design of the paper, literature search, manuscript editing and final approval. Oscar Solorzano Enriquez, MD: design of the paper, literature search, manuscript editing, and final approval. Erika de la Rosa Jaime, MD: design of the paper, literature search, manuscript editing, and final approval. María José Sardá Ramirez, MD: interpretation of image studies, design of the paper, literature search, manuscript editing, and final approval. Janet Amelia Moheno Lozano, MD: interpretation of histopathology studies, design of the paper, literature search, manuscript editing, and final approval. All authors state that they approve the paper. All authors attest that they meet the current ICMJE criteria for authorship.

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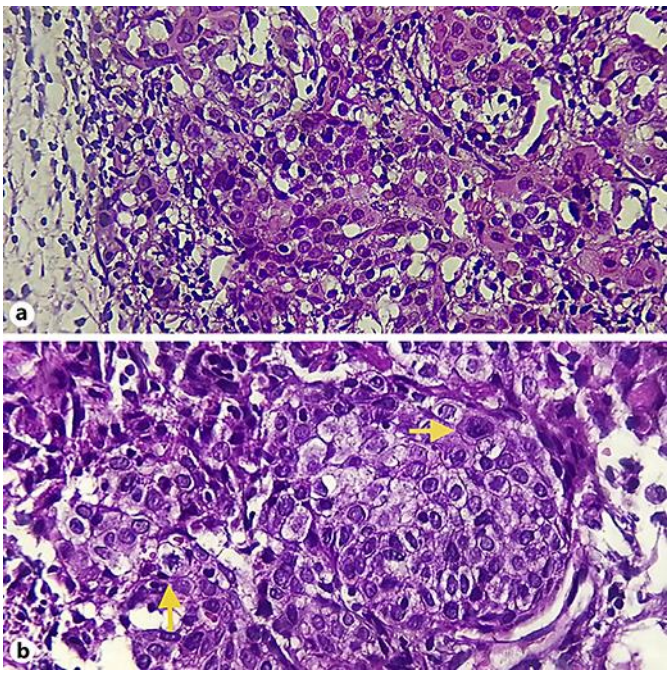

Fig. 1. Cervical biopsy micrographs. **a** Infiltration is shown below the submucosa due to squamous cell neoplasia. Hematoxylin and eosin (H&E), ×4. **b** Nonkeratinizing epithelial cell sheets with hyperchromatic nuclei, pleomorphism (horizontal yellow arrow), and high mitotic index (cell with atypical mitosis, vertical yellow arrow). H&E, ×40.

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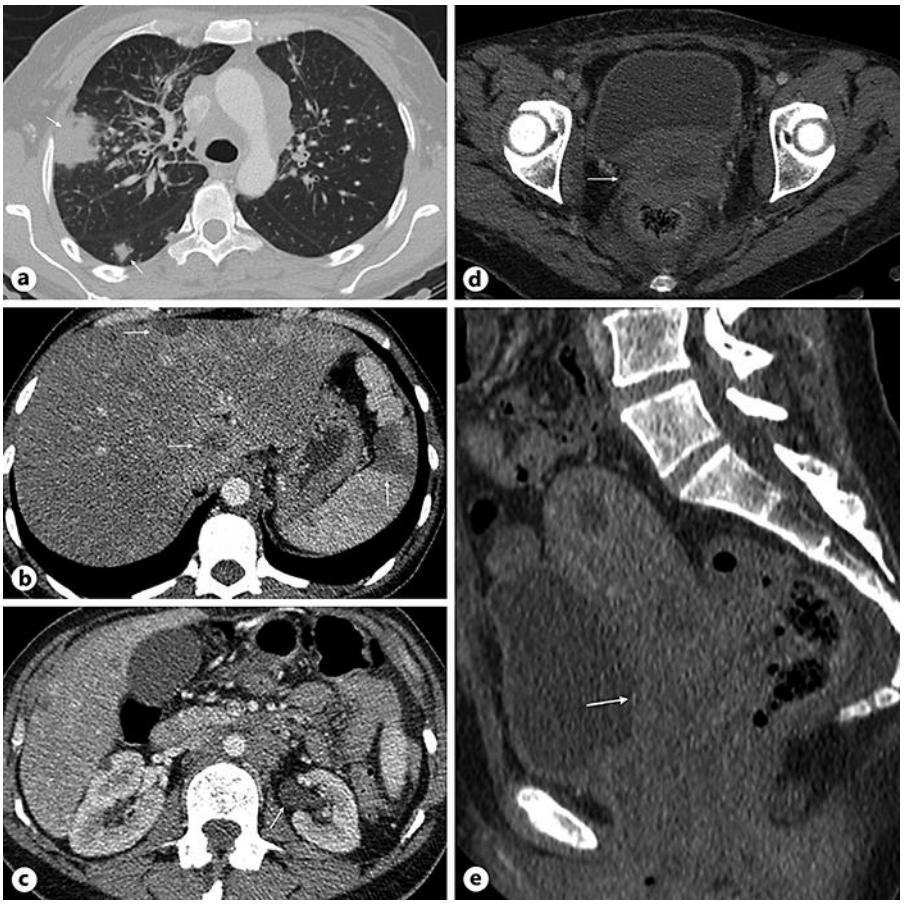

Fig. 2. Contrast axial tomography with the pulmonary window. **a** Metastatic lesions in the right lung and the mediastinum. Soft-tissue window. **b**, **c** Metastatic lesions in the liver, spleen, para-aortic lymph node conglomerate, and dilatation of the left renal pelvis. Axial (**d**) and (**e**) sagittal tomography of contrast pelvis shows a tumor of the cervix with extension to adjacent organs.

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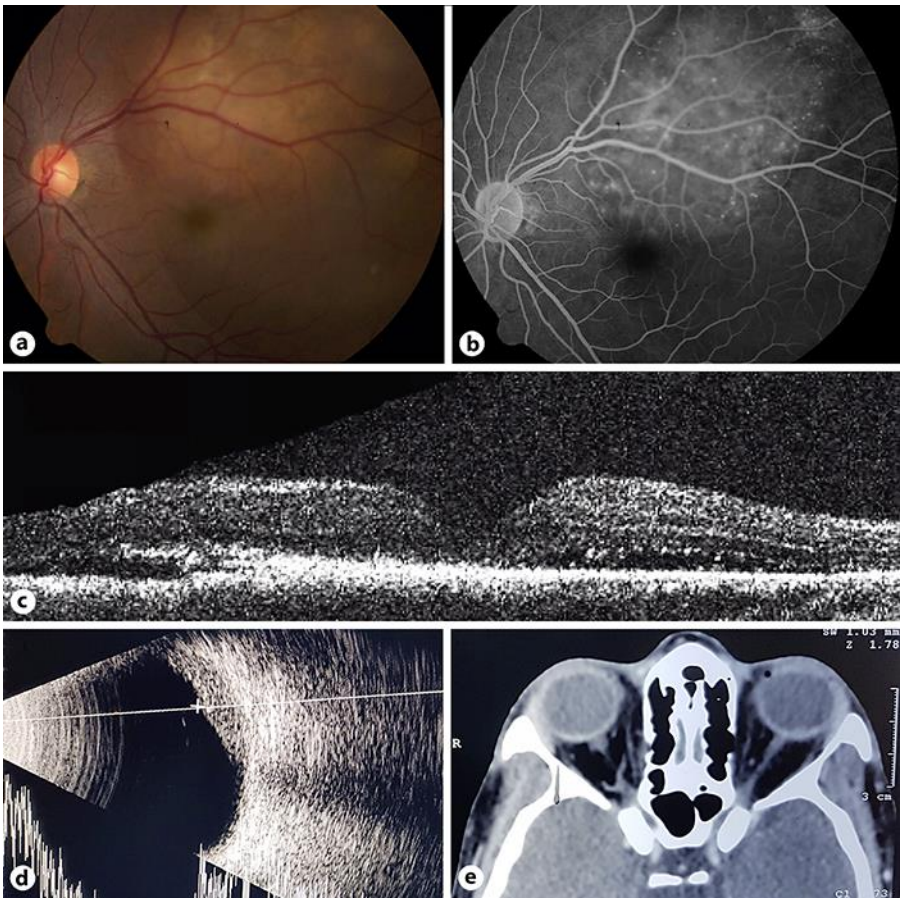

Fig. 3. **a** Clinical picture of the left eye fundus. **b** Fluorescein angiography of the left eye. **c** Temporal domain optical coherence tomography. **d** Ultrasonography mode AB of the left eye. **e** Simple tomography of the orbit and axial projection of the annexes.

Table 1. Clinical and epidemiological findings of available reports on cervical cancer metastases to eyes and adnexa

Author/ year of publication	Age	OD/ OS	Vision	Presenting Symptoms	Location of mets	Primary tumor subtype	Staging of tumor subtype	Other sites of mets	Was ocular mets the presenting feature of cervical cancer?	Treatment	Final outcome	Duration between diagnosis of ocular mets and death
Hertzanu et al., 1987	44	OD	NA	Proptosis, diplopia, blindness	Orbit	Squamous cell	PU	None	Yes	Chemotherapy	NA	NA
Kurosawa et al., 1987	54	OD	20/100	Reduced vision, pain	Iris	Squamous cell	IV B	Lung	No	Radiation	DOD	NA
Wiegel et al., 1995	25	OS	NA	Reduced vision	Choroid	Adenocarcinoma	I B	Lung	No	Chemotherapy, radiation	NA	NA
Ortiz et al., 1995	28	OD	20/20	Conjunctival mass	Subconjunctival tissue	Squamous cell	IV B	Lung	No	Chemotherapy	DOD	4 months
Lee et al., 1997	46	OS	20/80	Proptosis	Orbit	Squamous cell	II B	None	No	Radiation	DOD	4 months
Inoue et al., 2000	55	OU	20/20	Educed vision	Choroid – both eyes	Squamous cell	III B	Lung, cerebellum	No	Chemotherapy, radiation	DOD	3 months
McCulley et al., 2002	29	OD	20/20	Proptosis, diplopia	Orbit	Unknown subtype	NA	Bone, liver	No	Chemotherapy radiation	DOD	NA
Park et al., 2005	57	OD	NLP	Proptosis, blindness	Orbit	Adenocarcinoma	I B	Lymph nodes	No	Chemotherapy	DOD	NA
Gosslee et al., 2009	36	OS	20/30	Ptosis, swelling, pain	Orbit	Squamous cell	II B	Lymph node	No	Chemotherapy, radiation, surgery	DOD	3 months
Singh et al., 2009	50	OS	20/80	Diplopia	Orbit	Squamous cell	PU	None	Yes	Chemotherapy, radiation	NA	NA
Sareen et al., 2012	59	OS	20/20	Proptosis, epiphora	Orbit	Squamous cell	III A	Lung, liver, bone, adrenals and scalp	No	Radiation	DOD	4 months
Shieeb et al., 2014	52	OU	CF at 1 m	Reduced vision	Choroid – both eyes	Squamous cell	PU	Liver, bone	Yes	Radiation	DOD	3 months
Nair et al., 2015	45	OD	CF at 1 m	Reduced vision	Choroid	Adenocarcinoma	PU	Lung, lymph node, bone	Yes	None	DOD	2 months
Uhinak et al., 2015	53	OS	NA	Ocular pain	Choroid	Adenosquamous	III B	Lung	No	Chemotherapy, radiation and brachytherapy	DOD	5 months
Tunion et al., 2014	61	OS	NA	Reduce vision/ocular pain	Optic nerve	Squamous	IV A	None	No	Chemotherapy	NA	NA
Arthur et al., 2016	27	OS	20/20	Proptosis/ptosis, reduce vision	Orbit	Squamous	IIB	NA	No	Chemotherapy, radiation, brachytherapy	NA	NA
Nash et al., 2017	55	OS	20/20	Left eyelid redness, pain	Orbit	Adenocarcinoma	PU	NA	Yes	None	DOD	1 month
Gupta et al., 2018	56	OS	NLP	Ocular pain	Ciliary body	Squamous	IIB	Bone	No	Chemotherapy, radiation	NA	NA
Kagusa et al., 2019	64	OD	NA	Proptosis/ocular pain	Orbit	Squamous	NA	Left hypochondrial	No	Chemotherapy, radiation	Peritonitis by perforation and died	2 months
Current case	43	OS	CF at 1 m	Reduced vision	Choroid	Squamous	IIIB	Lung, lymph node, liver, spleen.	No	Chemotherapy, radiation, brachytherapy	DOD	2 months

OD, right eye; OS, left eye; ND, not available; NPL, no light perception; CD, finger count; PND, previously undiagnosed; PE, own disease.