Squamous cell carcinoma of the cervix with cranial metastasis: A case report*

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ABSTRACT

Squamous cell carcinoma is the most common female genital tract malignancy that typically spreads to the pelvic organs first by direct extension, and less commonly to distant sites through lymphangitic and hematogeneous spread. We report on a 47-year-old woman diagnosed with squamous cell carcinoma who underwent concurrent chemoradiation, presenting with a fronto-parietal scalp mass which on histopathologic examination also shows squamous cell carcinoma, likely metastatic.

Keywords: Cervical cancer, cranial metastasis, scalp metastasis

INTRODUCTION

Cervical cancer remains the most common malignancy of the female genital tract in the Philippines. Although the overall survival rate has greatly improved because of early detection and a wide range of treatment options, the development of and improved accessibility of more accurate diagnostic imaging modalities has led to higher detection of cervical cancer metastases in sites not previously reported.

The most common sites of metastatic disease are to the lungs, extrapelvic nodes and liver. Metastasis to the bone is uncommon – the exact frequency of which is not known but is estimated to be in the range of 0.8%-23% (Agarwal), depending on the diagnostic modality used for metastatic work up (Zilberlicht, Ferroir). A retrospective review by Kim, et al. found the incidence of bone metastasis to be 1.9%, most commonly in the vertebral column, with the lumbar spine being the most common site of bony involvement. The pelvis and long bones are also frequently affected, but spread to the cranium is rare, with only several cases reported worldwide. (Table 1)

Cervical malignancy is known to metastasize through several routes – 1) direct extension, 2) lymphangitic spread, and 3) hematogenous spread. In most of the cases reported, skull metastases developed after treatment for advanced stage primary disease. This is consistent with the tendency of cervical cancer to spread to the lymphatic system before hematogenous spread occurs. (Zilberlicht).

CASE REPORT

This is the case of squamous cell carcinoma of the cervix, Stage IIIB, in a 47-year-old gravida 3 para 3 (3003), who presented with a frontoparietal scalp mass during the first cycle of systemic chemotherapy for tumor persistence. She initially presented with heavy vaginal bleeding and urinary obstructive symptoms, reported as decreasing urine output. She consulted a provincial hospital where she was diagnosed to have cervical malignancy. The patient then opted for alternative medicine but persistence of the heavy vaginal bleeding prompted her to consult in a tertiary hospital. A punch biopsy of the cervical mass showed squamous cell carcinoma, large cell non-keratinizing, cervix.

At the time of initial consult, she had good functional capacity (ECOG 0) but was severely anemic and had acute kidney injury from obstructive uropathy. On clinical examination, she was diagnosed to be a FIGO Stage IIIB. She underwent hemodialysis, followed by cystoscopy, bladder biopsy and insertion of percutaneous nephrostomy tubes bilaterally. Biopsy of the edematous bladder mucosa was negative for malignancy.

She underwent pelvic external beam (5200 cGy) with parametrial boost (1000 cGy), concurrent with Carboplatin (AUC 2) as radiosensitizer. Total treatment time was 80 days due to recurring complicated urinary tract infections and the need for multiple blood transfusions due to persistent vaginal bleeding. Upon completion of the chemoradiation, tumor persistence was diagnosed based on failure of the cervical mass to regress in size. She was then started on systemic chemotherapy in the form of Carboplatin (AUC 5) and Paclitaxel (175mg/m2).

After giving the first cycle of systemic chemotherapy, the patient developed a 6 x 7 x 2 cm well-circumscribed gradually-enlarging non-tender soft tissue mass at the fronto-parietal area (Figure 1). On imaging, magnetic resonance imaging (Figure 2) showed a frontoparietal scalp soft tissue mass causing calvarial lytic changes and

Table 1. Case reports of cranial metastasis from primary cervical malignancy.

Study	Age	Type	Stage	Therapy	Symptom	Site	Mgmt
Zilberlicht, A et al. (2015)	58	SCC	IIB	Chemo-radiation	Headache, tenderness	Parietal skull	Surgery, Radiotherapy
Ahmadloo, N et al., (2010)	65	SCC	IIIB	Chemo-radiation	Headache	Calvarium	Chemoradiation
Agarwal, et al. (2002)	60	SCC	IIIB	Radiotherapy + brachytherapy	Tenderness, vaginal bleeding	Temporo-parietal skill	Radiotherapy
Abhishek, et al. (2008)	53	Adenosquamous carcinoma	IIA	Surgery + radiotherapy	Tenderness, seizures	Frontal skull, superior sagitall sinus thrombosis	Chemoradiation
Mohanty, et al. (2010)	54	SCC	IIIB	Radiotherapy + brachytherapy	Tenderness	Occipital lobe	Radiotherapy
Takagi, H et al. (2010)	48	SCC	IIB	Surgery + Chemo-radiation	Scalp swelling		
Yanuk, et al (1991)	21		IV			Frontal bone	
Maheshawari, GK (2001)	45	SCC	IIB	Radiotherapy + brachytherapy		Scalp	Radiotherapy

Figure 1. Photographs showing frontoparietal mass increasing in size despite ongoing treatment.

intracranial extension impinging the superior sagittal sinus and indenting the subjacent brain, for which the main consideration was metastatic disease.

A biopsy of the cranial mass showed squamous cell carcinoma, likely metastatic. At this time, the cervical mass was also noted to increase in size and extent of vaginal involvement. The patient was referred to Neurology and Neurosurgery for co-management but she refused to have the cranial mass resected. She was then referred to Radiation Oncology for palliative radiotherapy of the cranial mass. Systemic chemotherapy was also shifted to Gemcitabine (800mg/m2) to be given on Days 1, 8 and 15 every 28 days. She received Day 1 of Gemcitabine and underwent 4 sessions of palliative radiotherapy (100 cGy/session) but succumbed to complications of multiple electrolyte imbalance (hypercalcemia, hypokalemia, hyperuricemia) from the persistent progressive cervical malignancy.

DISCUSSION

Metastasis to the skull is very rare, and its route of spread is believed to be hematogenous, as tumor emboli are theorized to reach the external carotid artery branches, and then are disseminated by local implantation. Most case reports describe skull metastases that developed after treatment for advanced stage primary disease. This is consistent with the theory that cervical malignancy spreads to the lymphatic system first before hematogenous spread occurs. (VItorino-Araujo).

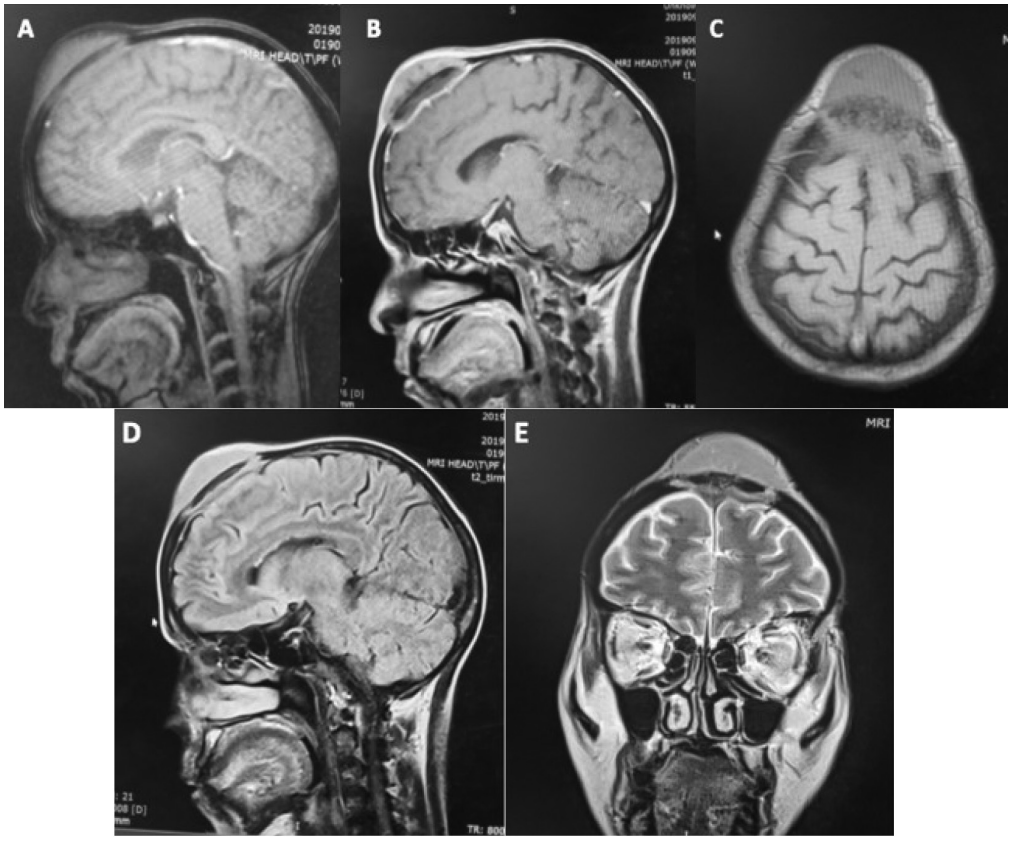

Figure 2. Plain and Contrast MRI of the brain in multiplanar views: There is a T1W and T2W isointense enhancing scalp soft tissue mass in the frontoparietal region with associated lytic erosion of the subjacent bone and indentation of the adjacent brain parenchyma which shows mild FLAIR hyperintensity, representing edema. The mass measures about 4.2 x 4.4 x 3.2 cm. The mass impinges the superior sagittal sinus. On contrast study, there is thickened abnormal meningeal enhancement at the anterior falx and frontal convexities the rest of the brain shows normal parenchymal signal. (A) T1 weighted sagittal view, (B) T1 weighted contrast enhanced sagittal view, (C) T1 weighted contrast enhanced axial view, (c) T2 weighted contrast enhanced FLAIR, (E) T2 weighted coronal view.

In the cases reported, the most common presenting symptom for scalp metastases from a primary cervical malignancy were headache or a palpable mass in the calvarium. These masses may mimic sebaceous cysts or lipomas, but a rapid swelling and growth should raise suspicion even in clinically tumor-free patients remote from primary treatment (Kapali). Ferroir, et al. reports a case of cranial metastasis presenting as paresthesia and palsy over the nape area. Chung, et al. reports of a similar case presenting initially as patches of alopecia. It is thus necessary for the clinician to be aware of this metastatic entity and its clinical presentation in order to address the patient's tumor progression adequately and in a timely manner.

In our index patient, she presented with a rapidly enlarging frontoparietal mass which initially appeared to only involve the soft tissue, but on imaging was seen to cause osteolytic changes on the underlying skull. Despite its rapid increase in size and aggressive osteolysis, the patient did not develop neuologic symptoms or signs of increased intracranial pressure.

Metastatic cervical cancer is usually treated by systemic chemotherapy with targeted radiotherapy, and median survival in the most recent reports is about 13.3 months (Zilberlicht). Incorporation of bevacizumab to chemotherapy significantly improved the median overall survival to 17 months (Tewari et al., 2014). According to Pasricha, patients with bone metastasis that is solitary, adequate and aggressive local treatment in the form of surgical resection can sometimes result in prolonged survival.

For all cases presenting with skull metastasis, the intent of treatment should be palliative. Local control was most often achieved with the use of radiotherapy (Vitorino-Araujo). Surgical management may be considered in patients who are amenable and can tolerate the procedure (Pasricha). Surgery aims to reduce neurologic complications by alleviating intracranial pressures and tumor burden in the hopes of improving response to adjuvant radiotherapy (Takagi). Since this is an uncommon metastatic site with only several cases reported worldwide, there is no single standard of care. Treatment should thus be individualized, to consider the patient's current status, her wishes and preferences, with the primary intent of symptom control and maintenance, if not improvement, of quality of life.

Tumor progression from a primary cervical malignancy, in itself, carries a poor prognosis. When the tumor progression is to the skeletal system from cervical carcinoma, life expectancy is less than twelve months after diagnosis, regardless of the duration of disease free interval (Ziberlicht). Due to this dismal prognosis, the attitude towards treatment should be directed toward palliation, rather than drastic therapeutic measures.

SUMMARY

This case highlights the need to address unusual symptoms in patients that have been treated for primary cervical cancer as this disease may spread to unusual sites. Moreover, it demonstrates that selected patients can achieve a long term disease free survival following radical therapy for an isolated bone recurrence. ■

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