



Case Report

Skull Metastasis as a Primary Manifestation in Cervical Carcinoma

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Abstract

Cervical cancer (CC) is one of the most frequent malignant cancers in the female population. Skull and brain metastasis in CC is still a quite rare entity. We present the case of a 62-year-old woman with a primary manifestation of cervical carcinoma (FIGO IIIA) with two concurrent skull bone metastases. Because of increase in the size of the cranial tumors and new onset of neurological deterioration, a complete removal of one of the lesions with histological verification was performed. The microsurgical resection of the exophytic parietal lesion was achieved using a new visualization technique under the exoscope (Olympus Corporation, ORBEYE®). A multidisciplinary approach and combined treatment methods could ensure a better quality of life for patients with metastatic CC.

Introduction

CC is one of the most common cancers in women and affects mostly middle-age women (55-65 years) with increasing incidence after 30 years of age [1, 2]. In Germany, CC has a prevalence of about 1.9%, according to 2018 data [3]. CC spreads locally mainly via the lymphatic system, but hematogenous dissemination can just as easily occur in various organs such as lungs, pelvic and long bones. “Metastatic cascade” is referred to as a multistep process for the distant spread of cancer [4-7]. Metastasis to the brain usually occurs after a lung preparation [4, 8]. Development of both skull and brain metastasis at the same time is very rare [9]. For the first time we present the case of a patient with two skull bone metastases as a primary manifestation for malignancy and subsequent diagnosis of CC.

Case Report

A 62-year-old patient, para-2, after two spontaneous partus

presented in January 2022 with new onset of speech, gait, and tongue movement disturbances for 2 days. Additionally, she described hearing difficulties and an earache for about 2 weeks. Clinical examination revealed a large well-circumscribed lesion on the right parietal side of the head that was known to the patient for more than two months (Figure 1). Previously the described lesion was classified as an atheroma and observation was recommended due to the initial small size and negative history for malignancy.

Because of the rapid volume progression and the new onset of cranial nerve palsies (N. VI, VII, VIII and XII), further diagnostic was initiated at the department of neurology of a local hospital. Computed tomography (CT) demonstrated a right parietal cystic lesion with exophytic growth and bone destruction. An additional lesion was located in the temporal bone, which was responsible for the presented neurologic symptoms. Contrast-enhanced MRI offered better visualization of the tumor, which showed no evidence of other cranial lesions (Figure 1).

Past medical history was negative for malignancies. On primary consultation, the patient described additional blackish-brown vaginal discharge and intermittent bleeding per vaginam. Initial gynecologic examination revealed diffuse, slow bleeding from the entire portio vaginalis, without pelvic pain. The most likely clinical diagnosis turned out to be cervical carcinoma. After completion of radiological diagnostics with chest-abdomen-pelvis CT, the patient was referred to our department for further treatment.

According to multidisciplinary tumor board consensus the patient underwent resection of the exophytic lesion on the right parietal side to accomplish histological verification. The surgical procedure was performed under an exoscope (Figure 2). This technical method provided excellent visualization possibility for all staff members in the operating room, as all colleagues directly observed each step of the operation. A circumferential excision was made around the lesion and the skin was elevated. After detachment of the skin margins, the lesion and cystic lesion were visualized. One burr hole was made and a round bone flap was excised. The cystic component of the lesion appeared to have

connection to the periosteum. It was filled with viscous necrotic tissue, which was aspirated. The rest of the tumor capsule was elevated along with the bone flap, and the underlying dura mater became visible (Figure 2). The calvarial bone flap was eroded by the tumor from inside out, and the dura was found to be affected as well, so a complete dural excision, followed by duraplasty, was performed. The bone defect was replaced with a bone cement graft (PALACOS®+G). The pathomorphological examination revealed carcinoma metastasis with most probable origin from cervical cancer (Figure 3).

The biopsy specimen from the gynecologic examination of the cervix revealed poorly differentiated squamous cell carcinoma (G3) and confirmed the diagnosis of cervical cancer, FIGO IIIA, M1. Subsequent palliative stereotactic radiotherapy of both cranial lesions and concomitant radio-/chemotherapy with denosumab of the primary tumor disease was the recommended treatment plan. After completion of neurosurgical therapy, the patient was transferred to the department of obstetrics and gynecology for further treatment.

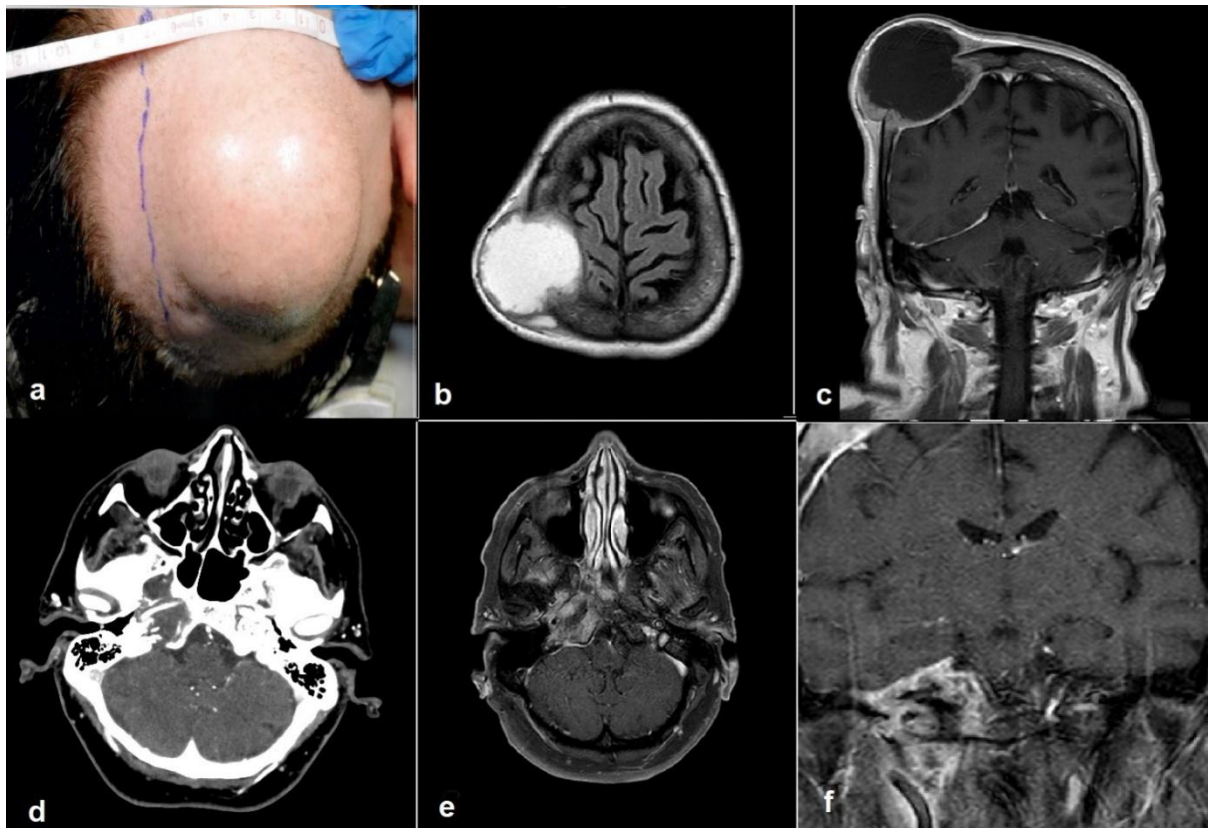


Figure 1: Exophytic subcutaneous lesion with size of approx. 7x7 cm (a); MRI-T1-weighted images (b), (c) in transversal and coronal sections: Exophytic lesion of the right parietal bone with osteolytic characteristics, contrast enhancement and no infiltration of brain parenchyma. CT (d) and MRI-T1-weighted images (e), (f) in transversal and coronal sections: Osteolytic lesion of the right temporal bone with contrast enhancement and almost no brain oedema.

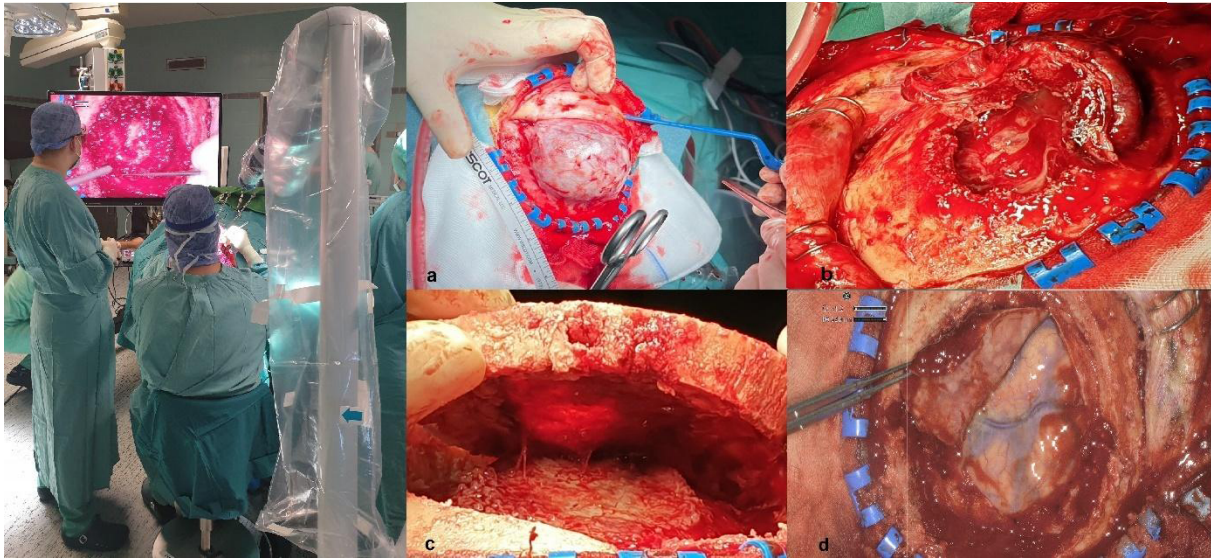


Figure 2: Macroscopic images and intraoperative findings: a) Tumour lesion after elevation of the skin flap. Exophytic growth with periosteal elevation and vascularisation can be observed; b) opening of the cystic lesion with necrotic fluid and osteolytic bone edges; c) Craniotomy and bone elevation with a view of the lower tumour-membrane and dura with tissue hyper-proliferation; d) ORBEYE-Exoscope intraoperative findings: Opening of dura mater with normal underlying brain surface. Front-left: Operators' view and technical positioning.

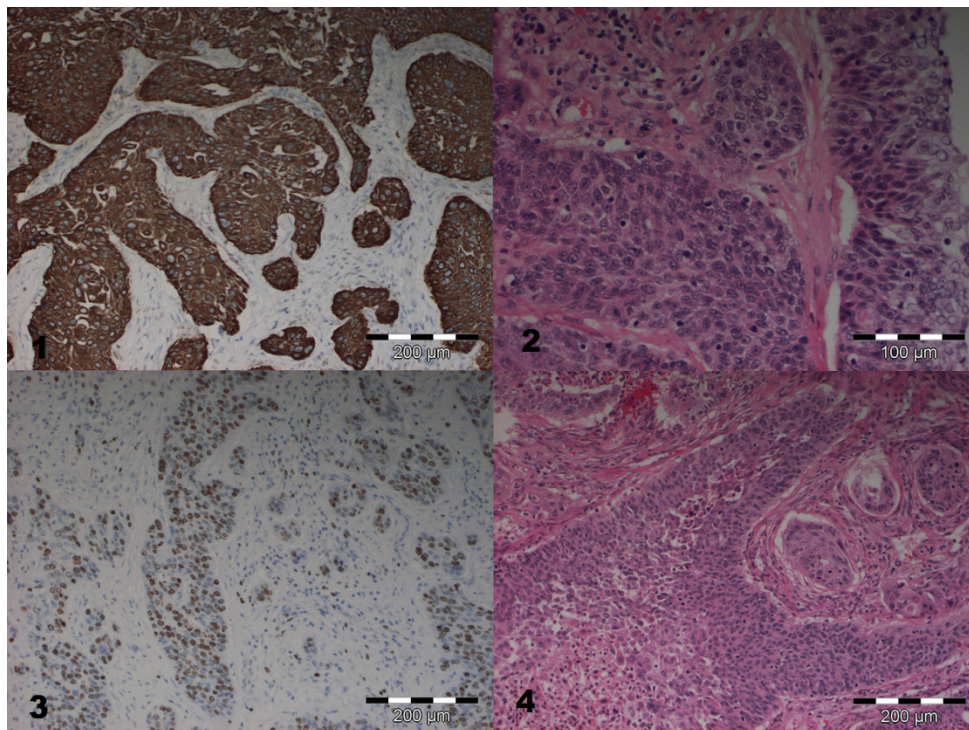


Figure 3: Microscopic images of histopathological sample from the cranial skull lesion: 1. Pan-Cytokeratin immune-stain with cyto keratin positive epithelial cells; 2. Squamous cell proliferation with multiple atypical mitoses, H&E stain x100; 3. Immunohistochemistry with Ki67 stain as a cell proliferation marker; 4. malignant glands with several giant cells, H&E stain x200.

Discussion

CC is one of the most common cancers in women especially in developing countries [10]. The vertebrae and pelvic bones are the most frequent sites for skeletal metastases in CC [11, 12]; however, metastasis in CC is generally rare and is associated with a poor prognosis [12, 13]. Multiple cutaneous metastases are indicative of likely uncontrolled and widespread metastatic disease with a poor overall prognosis [14].

Hematogenous spread of CC occurs only in advanced stages of the disease, particularly involving the lungs, liver, bones, and non-regional lymph nodes [1, 9, 15, 16].

Matsuyama et al. described a series of 713 patients with bone metastases, of which only six were in the cranial region [17]. Zilberlich et al. reported a case with a total of 20 months progression-free survival with isolated cranial metastasis from previously treated cervical cancer. Patients with bone metastasis from cervical cancer have a poor prognosis and a prognosis of life expectancy of less than one year [12].

Cisplatin-based combination chemotherapy can be considered in patients with good general health and good renal function [9]. Morgan et al. suggest that denosumab may also be used as second-line immunotherapy for bone metastases because of its bone-stabilizing properties [18].

Table 1 provides an overview list all published in literature cases of patients with cervical carcinoma and secondary diagnosed skull bone metastases. In comparison to this, our patient was primary diagnosed with two cranial metastases because of the neurological manifestation and only after further clinical work-up and gynecological biopsy verification the diagnosis of CC was confirmed.

Brain metastases from cervical cancer are extremely rare, with an incidence of 0.57% and diagnosed in up to 96.3% of cases after the diagnosis of CC [19]. The symptoms of brain metastasis in CC are not different from those of other brain metastases. Typical Symptoms present raised intracranial pressure with headache, nausea, and vomiting, followed by local symptoms such as seizures and paralysis, and cranial nerve palsies [19-21]. Brain metastases in CC have poor survival; the mean and median survival periods after diagnosis have been reported to be 7 and 4.6 months, respectively [4, 22].

Multidisciplinary approach should be the treatment strategy for patients with brain metastases from CC. After surgical resection of the metastasis, the preferred therapy choice is whole brain radiotherapy (WBRT) followed by chemotherapy [19].

In accordance with multidisciplinary team consensus, after neurosurgical resection of the skull metastasis, our patient received stereotactic radiotherapy of the brain metastasis followed by chemotherapy with denosumab.

N	Author	Year	Age	Histology	Initial Stage	Primary Treatment	DFP	Treatment of metastasis	Metastatic lesion control	Country
1	Shimizu et al. [23]	1983	59	SCC	IIIB	RT + BT	5 m	none	died after 3 m	Japan
2	Böhme et al. [24]	1990	52	SCC	IIIB	Biopsie + RT	2 m	Biopsie + RT (60Gy/33Fx)	died after 2 m	Germany
3	Yanuck et al. [25]	1991	21	SCC	IV	none	PD	Biopsy + RT (30Gy/10Fx) + QT	died after 1 m	USA
5	Maheshwari et al.[15]	2001	45	SCC	IIB	RT (50Gy/25Fx) + BT	8 m	RT (45Gy/15Fx)	4 m	India
6	Agarwal et al. [9]	2002	60	SCC	IIIB	RT (45Gy/20Fx) + BT	2 m	Biopsy + RT (20Gy/5Fx)	-	India
7	Chung et al. [26]	2007	45	SCC	IB1	TAH + RT + QT	7 a	None	died after 3 m	Japan
8	Abhishek et al. [27]	2008	53	adenocarcinoma	IIA	TAH + RT (28Gy/14Fx)	4 m	Biopsy + RT (30Gy/10Fx) + QT	- (stable at discharge)	India

9	Takagi et al. [16]	2010	48	SCC	IIB	TAH + RT (45Gy/20Fx) + QT	8 m	RT (45Gy/15Fx); without QT	-	Japan
10	Dimitrakopoulos et al. [28]	2010	37	SCC	-	TAH + RT + QT	20 m	Biopsy + RT + QT	6 m	Greece
11	Mohanty et al. [12]	2010	54	SCC	IIIB	RT (50Gy/25Fx) + BT + QT	2 m	Biopsy + RT (30Gy/10Fx) + QT	- (good local control at discharge)	India
12	Vitorino-Araujo et al. [10]	2013	55	SCC	IIIB	-	-	Resection	- (stable at discharge)	Brazil
13	Zilberlicht et al. [29]	2014	58	SCC	IIB	TAH + RT + BT + QT	7 m	Resection + RT	20 m	Israel
14	Rao et al. [30]	2015	62	SCC	IV	-	PD	RT alone	4 m	India
15	Diaz, J F et al. [1]	2019	41	SCC	IIIB	RT (50Gy/25Fx) + BT + QT	18 m	Resection + RT (51Gy/17 Fx)	18 w	Peru
16	Saffarieh et al. [31]	2020	50	SCC	IIB	RT + BT + QT	2 a	Resection + RT + QT	2 a	Iran
17	Morgan et al. [18]	2021	56	SCC	IB2	TAH + RT + QT	1 w	Biopsy + RT (55Gy/25Fx) + QT	8 m	USA
18	Current case	2022	62	SCC	IIIA	Biopsie + RT + QT	PD	Resection + WBRT	3 m (until date of publication)	Germany

Table 1: Overview of all case reports on cervix carcinoma in the literature.

SCC - Squamous cell carcinoma; TAH - Total abdominal hysterectomy; RT - Radiotherapy; BT - Brachytherapy; QT - Concurrent chemotherapy; DFP - Metastasis free period; PD - Primary manifestation with skull metastasis; “-“ no published data; w - Weeks; m - Months; a - Years.

Conclusion

Skull and brain metastases from cervical cancer remain a challenging medical issue. The development of modern technology has the potential to achieve earlier diagnosis and a better management for these tumors. Nevertheless, the overall prognosis of this progressive disease remains relatively poor. Metastatic dissemination represents an aggressive and already advanced tumor stage that limits the overall life expectancy of the affected patients. Surgical resection in combination with radiotherapy and chemotherapy remains the preferred treatment recommendation. The exoscope provides a good intraoperative visualization, so that all members of the surgical team can follow every surgical step simultaneously. This enables also a better teaching technique for the trainee neurosurgeons.

Conflict of interest

The authors do not have any conflicts of interest involved in this research.

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