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Atypical presentation of a cervical breast-cancer metastasis mimicking a dumbbell-shaped neurinoma

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ABSTRACT

INTRODUCTION: Spinal metastases are frequently encountered in patients with breast cancer. Because of recent improvements in oncologic therapies a growing incidence of symptomatic leptomeningeal metastases (LM) should be expected. The differential diagnosis of LM comprises a wide range of conditions, including neurinoma. The radiologic discrimination between metastases and neurinomas is primarily based on distinct neuroimaging features, particularly number, size and growth pattern.
PRESENTATION OF CASE: We report the first case of a solitary leptomeningeal metastasis of a cervical nerve-root, which mimicked a benign dumbbell-shaped neurinoma, using neuroimaging and visualized intraoperatively. The tumor was successfully treated with surgery followed by adjuvant radiochemotherapy (RCT).
DISCUSSION: While the patient history directs towards a metastasis, the localization, growth pattern and MRI signal were concordant with a cervical neurinoma. The current literature is not conclusive concerning the optimal choice of treatment; the therapy is strictly palliative and indications for surgery remain individual decisions. However, due to recent improvements in survival of patients with LM require reconsideration of established strategies.
CONCLUSION: The present case report and the reviewed literature point towards a growing clinical relevance of symptomatic LM in cancer patients and their possible atypical presentations and locations.

1. Introduction

In advanced stages, solid tumors can metastasize to various organs, including the central nervous system. In particular, breast, lung and prostate cancer metastases are frequently encountered in the spine.[1] Current operative concepts are focused on lesions to the vertebra, while metastases to non-osseous spinal structures are rare and usually associated with advanced disease.[2–5] The ongoing advancements in oncologic therapies have led to improvements in the life expectancy of cancer patients, even in palliative situations. Therefore, an increasing incidence of the formerly rare symptomatic leptomeningeal metastases (LM) should be expected.[1,2] LM cause obstruction of cerebrospinal fluid (CSF) circulation and compression of neurologic tissues.[6] The differential diagnosis of LM includes ruling out a wide range of malignant and benign conditions, such as congenital and degenerative lesions, infectious and autoimmune diseases and neurinoma.[7] The radiologic discrimination between metastases and neurinomas is primarily based on distinct neuroimaging features, particularly number, size and growth pattern.[7] Whereas LM are often encountered as multiple small nodules at ower spinal structures (e.g. the cauda equina), presumably due to gravity,[7] neurinomas appear as single lesions in the neuroforamen and might present at any height.[8] The clinical presentation of LM depends on the location and growth-pattern, often resulting in general symptoms such as nausea and head-aches due to interruption of the CSF flow and, later signs of myelopathy due to compression of the spinal cord.[7,9] On the other hand, neurinomas usually affect single nerve roots with typical clinical symptoms in the associated dermatomes and peripheral nerves.[10]

The present study reports the first case of a solitary leptomeningeal metastasis, mimicking a benign dumbbell-shaped neurinoma of a cervical nerve-root that was successfully treated with surgery and adjuvant radiochemotherapy (RCT).

Abbreviations: BC, breast cancer; CSF, cerebrospinal fluid; CK, cytokeratin; CT, computed tomography; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IRS, immunoreactive score; LM, leptomeningeal metastases; MRI, magnetic resonance imaging; PR, progesterone receptor; RCT, radiochemotherapy.

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2. Presentation of case

2.1. History

A 47-year-old woman was referred to our institution because of progressive unilateral arm elevation weakness with an onset 8 weeks prior. The patient did not complain of pain or numbness. She presented with a clearly visible atrophy of the biceps and triceps muscles and substantial reduction of both muscular strength in arm elevation and elbow flexion and extension. Neurological examination revealed hyperactive biceps and triceps tendon reflexes and hypesthesia confined to C5–7 dermatomes, indicating cervical myelopathy.

The patient was diagnosed with breast cancer (BC) 9 years earlier and underwent unilateral mastectomy (pT2m, pN3a, M0, G2, R0, estrogen receptor (ER) immunoreactive score (IRS) 12, progesterone receptor (PR) IRS 4, and human epidermal growth factor receptor 2 (HER2/neu) negative). She rejected adjuvant therapy while undergoing alternative therapeutic measures. Five years later, supraclavicular lymph node-metastases on her right side were found; again, the patient declined chemotherapy. Six months later, a brain metastasis was diagnosed and RCT was initiated (corticosteroids, bevacizumab and capecitabine). The patient rejected being treated with zoledronate for suspected bone metastasis, and she aborted RCT 14 months later. Until the occurrence of the current neurologic symptoms, regular follow-up examinations showed that the patient had stable disease.

2.2. Examination

After admission, total spine and cranial magnetic resonance imaging (MRI) scans were performed and revealed the previously diagnosed right parietal intracerebral metastasis and a solitary lesion in the cervical spinal canal. The spinal tumor was located in the right neural foramen between C3/4 with an extraforaminal extension, thereby compressing the cervical plexus at levels C3–5. The osseous structures showed no erosions. Thus, the neuroimaging findings were consistent with a dumbbell-shaped neurinoma (Fig. 1a–c).

An abdominal staging computed tomography (CT) scan and a three-phase bone scintigraphy showed no further lesions. The case was reviewed at an interdisciplinary tumor board, and according to the histological findings, resection followed by adjuvant therapy was recommended.

2.3. Operation

Surgery was performed under general anesthesia using a ventral approach to the cervical spine, with the patient in the supine position. After microsurgical exposure, the tumor presented as completely intradural with the characteristic appearance of a neurinoma (Fig. 2). Following resection of the intraspinal tumor and corpectomy, the vertebral bodies C3 and C4 were replaced (Pyramesh-Cage, Medtronic GmbH, Meerbusch, Germany) and ventral plate-stabilization (CSLP, Synthes GmbH, Umkirch, Germany) from C2–5 was performed (Fig. 3).

2.4. Pathological findings

Macroscopic pathological examination revealed a soft, yellow-gray tumor. The intraoperative rapid frozen section showed disorganized nerve root tissue with cell nests of unknown entity. The definitive histological examination of the tissue revealed epithelioid cells with irregular and hyperchromatic nuclei and scattered mitosis arranged in nests embedded in stroma rich in collagen fibers (Fig. 4a). Immunohistochemical staining revealed that the tumor cells were positive for cytokeratin (CK) 8 (Fig. 4b), 85% were positive for ER (Fig. 4c), 10% for HER2/neu (Fig. 4d) and 2% for PR. There were no CD3, CD20, S-100 or vimentin-positive cells. The Ki67 proliferation index was 20%. Fluorescence in situ hybridization showed no positive signals for HER2/neu. The final histopathology

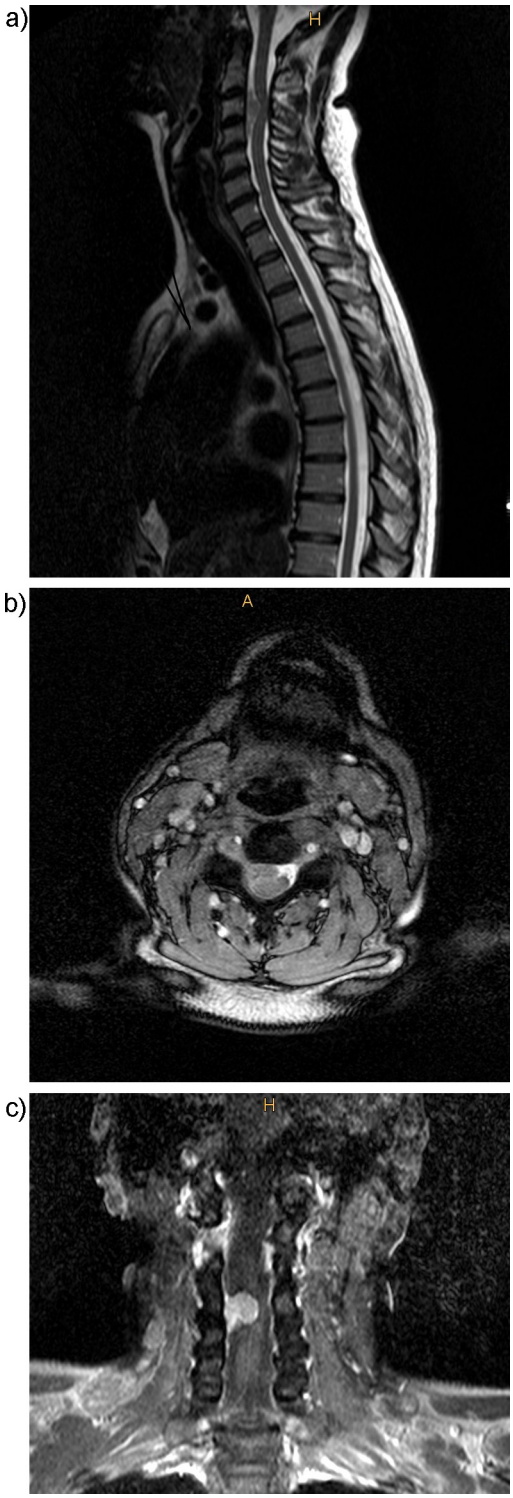

Fig. 1. (a)–(c) MRI of the cervical spine with the tumor (a) mid-sagittal plane T2/TSE; the tumor is compressing the spinal cord in a triangular shape, expanding from the second to the fourth cervical vertebral body (C2–C4), (b) axial plane B-TFE/TRA; the dumbbell-shaped intra-neuroforaminal growth of the tumor on the right side is depicted. The spinal cord is shifted and compressed and (c) coronal plane T1/TSE. The tumor is visible at the right side, located at the height of the third and fourth cervical vertebral body (C3–C4).

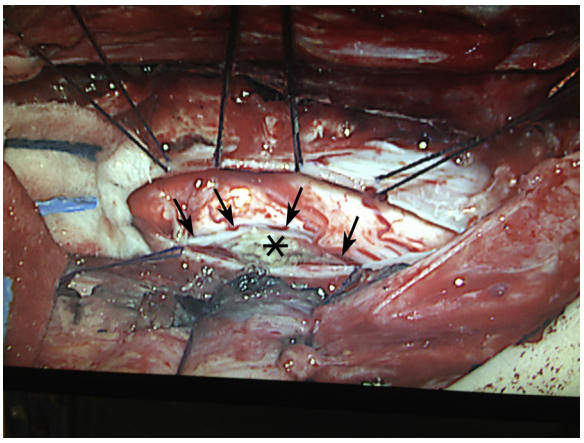

Fig. 2. Intraoperative photograph of the operation site. Left is cranial (with a sponge inserted). Threads hold the longitudinally opened dura mater; the spinal cord (star) is compressed by the intradural tumor (arrow).

report specified the tumor as a metastatic lesion originating from the previously diagnosed BC.

2.5. Postoperative course

Postoperatively, the patient presented with minor dysphagia, which was treated effectively by logopedic therapy. While the muscular weakness of the arm showed no significant changes during the inpatient stay, there was a clear improvement in the hypesthesia at the C5–7 dermatomes. The patient was transferred to a medical oncology service and received combined RCT.

At the last follow-up, 3 months after the operation, the neurologic symptoms were unaltered, and a spinal MRI showed no signs of local recurrence (Fig. 5).

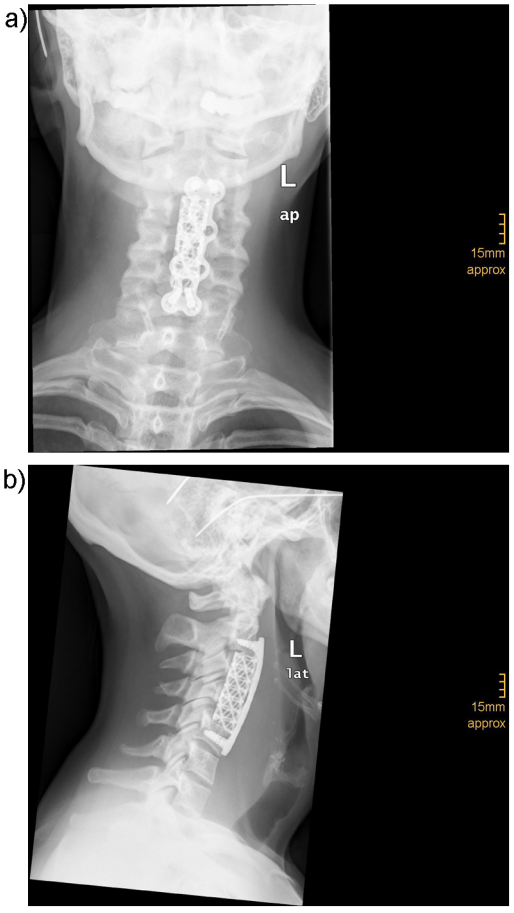

Fig. 3. Conventional postoperative plain X-rays of the cervical spine in two planes: (a) anteroposterior and (b) lateral view. A ventral plate osteosynthesis spanning from C2 to C5 with a ventral intervetebral pyramesh-cage replacing C3 and C4 are depicted.

3. Discussion

Neurinoma and fibroblastoma constitute the majority of dumbbell-shaped tumors. These intraforaminal lesions are usually amenable to microsurgical resection with excellent local disease control and good clinical outcome.[8] Differential diagnosis comprises eliminating a multitude of conditions, including primary malignant neoplasms and metastatic disease to the leptomeninges. A range of primary solid malignancies is known to spread into the spine and mimic the growth pattern of intraforaminal tumors. [11] While the incidence of neurinoma reaches 0.3–0.5/100,000 persons per year,[8] LM of solid tumors are rare and most of them occur in advanced BC.[3,4,6,9,12–14] Still, LM represents an important neurologic complication of systemic BC[3,13] with an estimated frequency of 3–43%, based on clinical research and autopsies.[2,11,15] However, only 0.8–3.9% are symptomatic.[14] Interestingly, the incidence of LM is on the rise, supposedly because of more effective therapies and therefore, longer survival of BC patients.[2,11,15]

In neurinomas, a dumbbell-shaped growth pattern accounts for approximately 6% of the cases and these most often affect the cervical followed by the lumbar spine.[8] In contrast, in neuroimaging and autopsy, LM usually occurs as multiple small nodules.[7,9] Yet, with MRI they present with a signal similar to nerve sheath tumors, which tend to be greater in size and occur as solitary masses.[4,7] While neurinomas are usually located close to cervical and lumbar nerve roots, LM are most frequently found in the lumbar and sacral regions among the conus and cauda equina.[3,4,7,16] This might be explained by the possible mechanisms of metastasis: besides direct transdural invasion, hematogenous or lymphatic dissemination, the most likely route is tertiary spreading from brain tumors via the CSF[2,3,11,15] and the effect of gravity might explain the caudal location of the LM.[3] Therefore, localization and growth pattern are the most important indicators for the differential diagnosis. Still, in the present case, the localization, growth pattern and MRI signal were concordant with a cervical neurinoma.

Typical clinical signs of spinal neurinomas are segmental pain, root pain and motor deficits with varying onset and course, usually progressing slowly.[8] LM on the other hand are typically associated with headaches and nausea due to disruption of the CSF circulation and neurologic deficits of sensory and motor function in the case of compression of the spinal cord or nerve roots.[3,12,13,17] The majority of motor sensory dysfunction caused by LM is found to be of a myelopathic pattern rather than the effect of a single nerve root,[18] and most often affects the lower extremities.[16,17] While the initial manifestation of LM can occur between several weeks and 17 years following the primary diagnosis of BC,[6] rapid deterioration after the clinical diagnosis is common and the prognosis is poor.[6,11,19,20] Mean survival after diagnosis of LM is about 7.5 months[4,11] and one-year survival is 10–22%.[13] The described case presented with an atypical clinical presentation, consistent with a large neurinoma affecting the cervical plexus.

The objective of neurinoma treatment is to cure by surgical resection. LM therapy is palliative and aims to prevent further neurologic deterioration and improve the quality of life.[5,19,21] For LM, radiotherapy is widely accepted, yet has not been proven to affect overall survival,[20] and systemic as well as local chemotherapy are the focus of recent studies.[20] Until now, surgical treatment

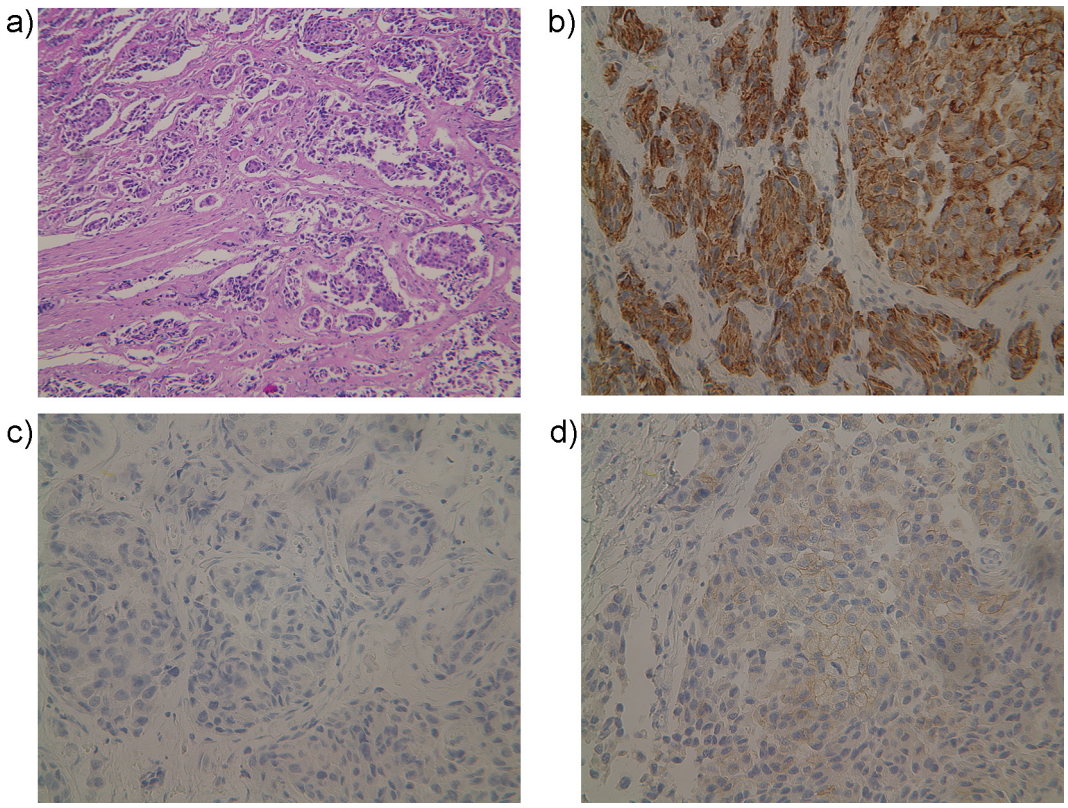

Fig. 4. (a)–(d) Histopathological images of the tumor (all 250× original magnification). (a) Hematoxylin-Eosin-staining: multiple cell nests embedded in the stroma with traces of nerve tissue. (b) Cytokeratin 8 immunohistochemical staining: positive in the cell nests indicating epithelial origin (i.e. breast cancer). (c) Progesterone immunohistochemical staining: positive. (d) HER2/neu immunohistochemical staining: positive for scattered cells.

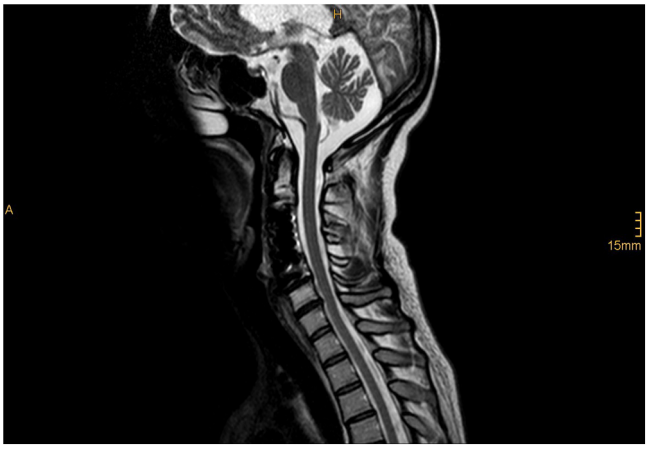

Fig. 5. Post-operative MRI of the cervical spine; sagittal plane T2/TSE. The tumor has been removed, the spinal cord is without compression, cerebrospinal fluid is visible around the cervical spinal cord. Metallic artifacts indicate the location of the ventral plate and pyramesh cage in C3–C5.

has been reserved for singular metastases and has been strictly palliative.[15,19] Indications for surgery remain individual decisions to be taken between physician and patient.

4. Conclusion

The present case report emphasizes the importance of the differentiation between benign neurinomas and solitary LM in cancer patients. Surgical treatment combined with adjuvant or neoadjuvant therapy can improve neurologic function and lessen pain. However, a literature search shows that no conclusive optimal treatment has yet been put forth.

Considering the growing number of medium- and long-term cancer survivors, future studies should focus on the improvement of diagnostic and therapeutic measures for patients with LM.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflict of interests statement

The authors declare that they have no competing interests. We have no personal or financial conflicts of interest related to the preparation and publication of this manuscript.

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Ethical approval

Following the statutes of the local ethics committee of the University hospital of cologne, no judgment is necessary for case reports with retrospective data-collection of clinical data when the informed consent of the patient is available.

Authors' contribution

C.K.B. was involved in conception and design of the study, interpretation of the data, and writing of the manuscript. P.L. was involved in the literature analysis and writing of the manuscript. J.B., NaM, P.E. and T.K. were involved in the literature analysis and critical review of the manuscript; P.E. and T.K. were involved in conception and design of the study. All authors read and approved the final manuscript. All authors approved the final version of the manuscript.

Key learning points

- Recognizing the importance of the differentiation between benign neurinomas and solitary leptomeningeal metastasis in cancer patients.
- Recognizing, that surgical treatment combined with adjuvant or neoadjuvant therapy can improve neurologic function and lessen pain.
- A literature search shows that no conclusive optimal treatment has yet been put forth.
- Considering the growing number of medium- and long-term cancer survivors, future studies should focus on the improvement of diagnostic and therapeutic measures for patients with leptomeningeal metastasis.

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