Primary Myoepithelial Carcinoma of the Cervical Spine

A Case Report

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Investigation performed at Dr BAM Hospital, Mumbai, India

Abstract

Case: A 36-year-old man presented with a subacute onset left upper limb weakness. Further investigation revealed a myoepithelial carcinoma arising from the C3-C5 vertebrae. He underwent 2-stage surgery with tumor excision and post-operative radiotherapy. An improvement in power was noted, and no recurrence was observed at the 1-year follow-up.

Conclusion: Myoepithelial tumors are rare at skeletal locations and require a high degree of suspicion. Immunohistochemistry plays a vital role in establishing the diagnosis. A complete resection is paramount for a favorable outcome.

Myoepithelial tumors of the soft tissues are rare neoplasms of uncertain histogenesis and are currently classified as mixed tumors, myoepithelioma, and myoepithelial carcinoma. Although most arise in the salivary glands and skin, they have also been reported in breast, lung, upper airway, gastrointestinal tract, and soft tissues. Involvement of the skeletal system is rare, especially origin in the spinal column[1]. Only a handful of primary myoepithelial tumors have been reported in the spine and none having been reported in the cervical spine[1-4].

We present a case of a primary myoepithelial carcinoma arising in the cervical spine. We have discussed the clinical, radiological, and pathological characteristics, and the diagnostic and management dilemma faced and reviewed the pertinent literature. This narrative has been written as per the Case Report (CARE) guidelines for case reports[5].

The patient was informed that data concerning the case would be submitted for publication, and he provided consent.

Case Report

A 36-year-old right-hand dominant man presented with gradually progressive weakness of the left upper limb of 3 months duration, which was more significant in the C4 and C5 myotomes. Plain radiographs were inconclusive, but computed tomography (CT) of the cervical spine revealed an osteolytic lesion of the C3, C4, and C5 vertebral bodies along with the destruction of the left pedicle of C4 (Fig. 1). Magnetic resonance imaging (MRI) showed a heteroge-

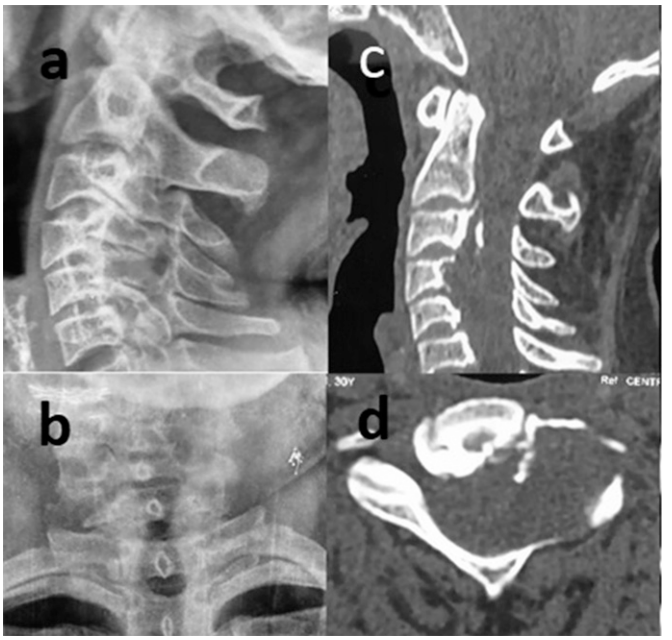

Fig. 1

Plain radiography and computed tomography of the cervical spine. (**Figs. 1-A** and **1-B**) Lateral and anteroposterior plain radiographs showing no obvious abnormality. (**Figs. 1-C** and **1-D**) Sagittal and axial sections of CT showing an osteolytic lesion of the C3-C5 vertebrae involving the vertebral bodies, left pedicle, and lateral masses.

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Keywords: myoepithelial carcinoma; immunohistochemistry; cervical; spine tumors; rare tumors

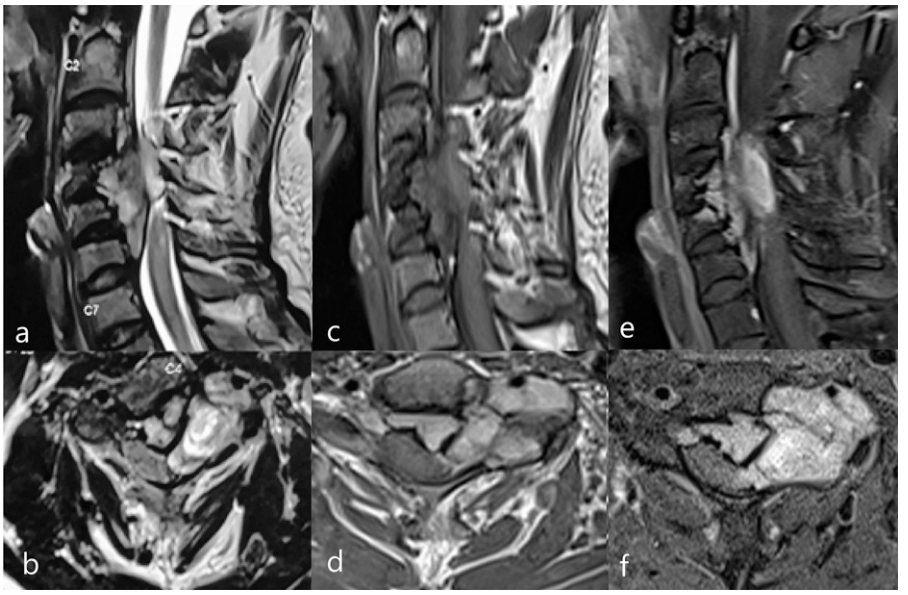

Fig. 2

MRI of the cervical spine. (**Figs. 2-A** and **2-B**) Sagittal and axial sections of T2-weighted MRI showing an extradural mass compressing the cord anteriorly at C3-C6. Myelomalacia can also be seen. (**Figs. 2-C** and **2-D**) Sagittal and axial sections of T1-weighted MRI confirming the above findings. (**Figs. 2-E** and **2-F**) Sagittal and axial sections of postcontrast T1-weighted fat-suppressed MRI showing enhancement. MRI = magnetic resonance imaging.

neously enhancing extradural soft-tissue lesion with non-enhancing necrotic areas in the left anterolateral portion of the spinal canal from C3-C6 vertebral body levels with stripping of the posterior longitudinal ligament. The mass measured 4.4 × 3.0 × 2.4 cm and was heterogeneously hyperintense on T2-weighted and STIR images and hypointense on T1-weighted sequences. It was compressing the cord with resultant myelomalacic changes at C4 and C5 levels (Fig. 2). A positron emission tomography (PET-CT) scan suggested the primary site to be the cervical spine with no distant metastasis. A tumor board meeting consisting of the spine surgeon, radiologist, and pathologist suggested a differential diagnosis of chordoma, metastasis, plasmacytoma, and a myoepithelial tumor on the basis of radiological studies. Granulomatous infection-like tuberculosis was also included.

With an established neurological deficit, it was decided to decompress the cord. A C3-C6 decompression left hemilaminectomy with the removal of posterior spinal elements and lateral mass was performed with an attempted complete resection of the tumor. The spine was stabilized with C3-C6 lateral mass and C7 pedicle screw fixation. A fibular strut allograft was placed on the left side between C3 and C7 to further augment the stabilization and fixed with a screw. The intraoperative sample was sent for a full histopathological examination, which revealed a nonencapsulated tumor with multinodular pattern (Fig. 3). A frozen section examination was not performed because it was felt during the surgery that a complete removal of the tumor was not possible with a single approach, and hence, the patient anyways would require a second-stage surgery. Tumor morphology was heterogenous in the form of an admixture of epithelioid and spindle cells seen embedded within the dense chondromyxoid matrix. Lobular arrangement was conspicuous within areas containing epithelioid cells. Tumor cells were arranged in variegated patterns, including reticular, cord-like, trabecular, and

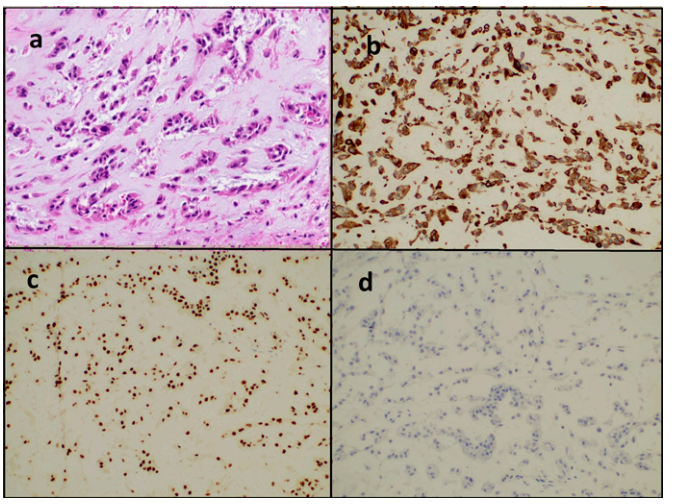

Fig. 3

Histopathological and immunohistochemistry findings of the tumor. (**Fig. 3-A**) Microphotograph of the myoepithelial carcinoma showing tumor cells arranged in nests and pseudoglandular pattern. Tumor cell nuclei show moderate atypia in the form of nuclear enlargement, hyperchromasia, and pleomorphism (20× magnification, hematoxylin and eosin stain). (**Fig. 3-B**) Positive staining for cytokeratin (IP, ×200), (**Fig. 3-C**) positive staining for SOX 10 (Immunoprecipitation, ×200), and (**Fig. 3-D**) negative staining for brachyury (IP, ×400).

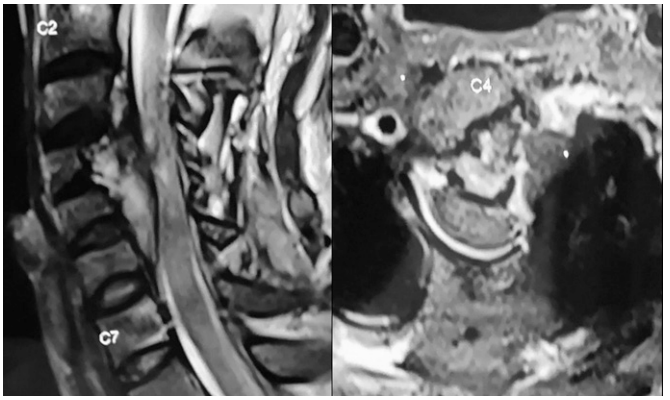

Fig. 4

T2-weighted sagittal and axial sections of the MRI showing remnant mass on the anterior cord aspect with left-sided hemilaminectomy and removal of left pedicle and lateral mass of the C4 vertebra. MRI = magnetic resonance imaging.

pseudoglandular patterns. Cytoplasmic clearing was present in a few cells which resembled "physaliperous" cells. Nucleoli were evident in a few cells. Nuclear atypia was evident in the tumor cell nuclei in both cell types. Nuclei were enlarged, hyperchromatic, and pleomorphic. Mitotic activity was not conspicuous (2/10 high-power fields). Necrosis was seen in small parts of the tumor. The immunohistochemistry (IHC) profile revealed co-expression of epithelial marker (AE1/AE3 and cytokeratin), SOX 10, and S100. IHC was negative for Epithelial Membrane Antigen (EMA) and p63. Nuclear expression of Integrase Interactor (INI)-1 was retained in tumor cells. Immunostaining for brachyury (expected to be positive in chordoma) and CD34 was negative. Characteristic tumor morphology along with the IHC profile helped establish the diagnosis of myoepithelial tumor of soft tissues. Further categorization into myoepithelial carcinoma was based on the presence of nuclear atypia according to current diagnostic criteria[6] (Fig. 3). Considering the rarity of this diagnostic entity, the histopathological diagnosis was also verified by an independent onco-histopathologist. Postoperatively, the motor power improved by 2 Medical Research Council grades in the C4 and C5 myotomes.

A postoperative MRI was performed, which confirmed a mass consistent with the residual tumor (Fig. 4). As a result, a decision to decompress anteriorly with the removal of the remaining tumor was taken and the patient was operated again 3 weeks after the index surgery. A C4 and C5 corpectomy was performed, and the mass was removed. During removal from the C4 foramen transversarium, the left vertebral artery was injured and ligated with metallic clips. The anterior column was reconstructed with C3-C6 interbody fusion with a mesh cage and an anterior cervical plate (Fig. 5). The postoperative MRI showed complete removal of all the visible mass, and a CT angiogram showed flow in both the cranial and caudal segments of the ligated vertebral artery.

The postoperative course of the patient was uneventful, and the patient was mobilized on day 1 postsurgery without any brace; the wound healed satisfactorily. The tumor board advised a course of radiotherapy 6 weeks after the final surgery, and the patient received 60 Gy of radiation in 30 fractions by volumetric modulated arc therapy. At the 1-year follow-up, the patient had no recurrence or further deterioration or appearance of any new symptoms.

Discussion

Myoepithelial tumors occurring in the skin and soft tissues are rare. Myoepithelial tumors arising within soft tissues are of uncertain histogenesis, although they replicate the morphologic spectrum of those arising within salivary glands. They are most frequently seen between third and fifth decades of life with no sex predilection[3]. Bones are rarely affected by myoepithelial tumors; the maxilla is the most common intraosseous site. There have been only a few reports of other sites, such as ilium, femur, tibia, sacrum, and spine[1,3].

Myoepithelial tumors of skin and soft tissues are currently classified as mixed tumors/chondroid syringomas, myoepitheliomas, and myoepithelial carcinomas/malignant myoepitheliomas. Mixed tumors/chondroid syringomas are analogous to those occurring in salivary glands, and they show a predominantly tubular or ductal differentiation associated with variable but distinct presence of the chondromyxoid matrix. Myoepitheliomas on the other hand show a much wider

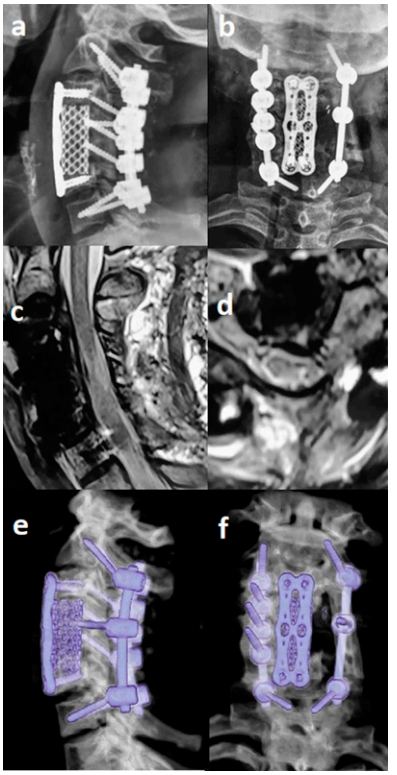

Fig. 5

Postoperative radiographs (**Figs. 5-A** and **5-B**), T2-weighted MRI images (**Figs. 5-C** and **5-D**), and 3D CT images (**Figs. 5-E** and **5-F**) showing the extent of decompression after the final surgery and instrumentation with the fibula strut.

TABLE I Review of Literature of Primary Epitheliomas Related to the Spine*

S. No.	Reference	Patient		Lesion			Recurrence/Outcome
		Age	Sex	Site	Malignant Potential	Immunohistochemistry Profile	
1.	Kurzawa et al.[2]	27	F	Sacrum	N/A	S100 + /EMA + /vimentin + /SMA −	N/A
		45	F	L1 vertebra	Benign	S100 + /EMA − /vimentin + /SMA −	No recurrence at 35 months
2.	Savardekar et al.[4]	50	M	T10 vertebra	Malignant	S100 + /EMA − /vimentin + /SMA +; Ki-67 index— 40%	Multiple recurrences at 60 months
3.	Ghermandi et al.[1]	62	M	T11 vertebra	Benign	S100 − /EMA + /vimentin/SMA −; Ki-67 index—12%	None at 12 months
4.	Moussaly et al.[5]	33	F	Posterior neck with spinal extension	Malignant	S100+/EMA+/vimentin +/CD99+	Died at 1 month
5.	Antonescu et al.[3]	45	F	L1 vertebra	Benign	S100 + /EMA /CK +	N/A
6.	This study	36	M	C3-C6 vertebrae	Malignant	S100+/EMA/brachyury/p63/ SOX 10+/CK+	None at 6 months

*CK = cytokeratin; EMA = epithelial membrane antigen; N/A = not available; SMA = smooth muscle actin.

morphologic spectrum consisting not only of an admixture of various cell types but also displaying variegated morphologic patterns. Both mixed tumors and myoepitheliomas are benign tumors, which have a propensity to recur locally but with no metastatic potential[6]. An infiltrative growth pattern is seen in both benign and malignant myoepithelial tumors so that the pattern is not indicative of malignancy. Myoepithelial carcinomas in the skin, soft tissue, and bones differ from those occurring in salivary glands, wherein the invasive growth pattern is considered to be the criterion of malignancy. Instead, diagnosis of malignancy in myoepithelial tumors of the skin and soft tissue is based on the presence of moderate-to-severe nuclear atypia[6]. Necrosis and mitoses are also commonly associated with myoepithelial carcinomas.

Our case in discussion was diagnosed as myoepithelial carcinoma based on the morphology and the combination of epithelial and neural markers on IHC[6,7]. Myoepithelial tumors express epithelial markers, such as EMA, AE/AE3, and cytokeratin[6,7]. Myogenic markers are of limited diagnostic value. Loss of expression of INI1 on IHC is a useful diagnostic adjunct. However, INI1 expression was retained in the tumor cell nuclei in our case[6]. Because of the occurrence at the cervical spine and the presence of physaliferous cells on histopathology examination, a differential diagnosis of chordoma was also considered, which was ruled out based on the negative immunohistochemical staining for brachyury. An analysis of the genetic makeup revealed that more than half of the tumors outside salivary glands carried an EWSR1 gene rearrangement[3,4,8]. We did not investigate our case for EWSR1 gene rearrangement.

Kurzawa et al. described 8 cases of skeletal myoepithelial carcinoma of which 1 was in the L1 vertebra, 1 in the sacrum, and the rest in nonspine locations[2]. Savardekar et al. described a primary myoepithelioma of D10 with 2 recurrences in 5 years and eventual malignant transformation[4]. Ghermandi et al. described a myoepithelioma of D11 which had 1 recurrence within the first 12 months of the surgery[1]. All these 3 studies reported benign primary tumor at presentation. Moussaly et al. reported a soft-tissue posterior neck myoepithelial mass with spinal extension leading ultimately to mortality after metastasis. However, the primary tumor was located outside the spine[3] (Table I). We could not find a single previously published report of malignant primary myoepithelial tumor in the spine.

A definitive management protocol for myoepithelial tumors is not yet established. A wide surgical resection of the tumor remains the most preferred management, although this is not always possible because of the local site limitations as was the case in our patient as well. The role of radiotherapy and chemotherapy in the management is ill-defined. Radiotherapy was used postoperatively by Savardekar et al., Ghermandi et al., and Rekhi et al., although the details of the same were not available[1,4,9]. There have been reports obtaining varying response after chemotherapy in myoepithelial tumors[10,11]. Nieder et al. used both radiotherapy and chemotherapy but were not able to observe any response to either of the two[12]. Giridhar et al. found that radiotherapy decreases locoregional recurrence, but chemotherapy did not have a similar effect[11].

Myoepithelial tumors, both benign and malignant, have a potential for recurrences. The incidence of local recurrence in myoepitheliomas is up to 18%[6]. Myoepithelial carcinomas have higher chances of local recurrence of up to 42% along with potential for distant metastasis of up to 52%[6]. Histopathology along with IHC is essential for accurate diagnosis. A locally

aggressive behavior should alert the clinician to the possibility of this diagnosis. A PET-CT scan can help rule out distant spread or a different primary. Because of the rarity of this disease entity, definitive guidelines for management do not exist. A team approach consisting of the surgeon, radiologist, oncologist, pathologist, and radiotherapist with a close follow-up of the patient is needed for a long-term fruitful outcome. ■

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