OMICS Journals are welcoming Submissions

OMICS International welcomes submissions that are original and technically so as to serve both the developing world and developed countries in the best possible way.

OMICS Journals are poised in excellence by publishing high quality research. OMICS International follows an Editorial Manager® System peer review process and boasts of a strong and active editorial board.

Editors and reviewers are experts in their field and provide anonymous, unbiased and detailed reviews of all submissions.

The journal gives the options of multiple language translations for all the articles and all archived articles are available in HTML, XML, PDF and audio formats. Also, all the published articles are archived in repositories and indexing services like DOAJ, CAS, Google Scholar, Scientific Commons, Index Copernicus, EBSCO, HINARI and GALE.

For more details please visit our website:
http://omicsonline.org/Submitmanuscript.php

Journal of Molecular Biomarkers & Diagnosis

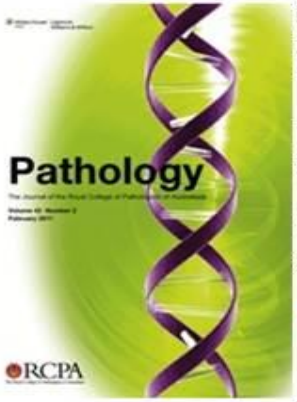
Open Access

ISSN-2155-9929

Pathology Focus

You are here: Home » Clinicopathological features including TFE3 expression in alveolar soft part sarcomas

Alveolar soft part sarcoma 'revisited': clinicopathological review of 47 cases from a tertiary cancer referral centre, including immunohistochemical expression of TFE3 in 22 cases and 21 other tumours



Rekhi *et al*
Pathology **44:1 January 2012**
ISSN: 0031-3025 • Frequency: 7/year • Subscribe Now • Journal Website

The authors reviewed 47 cases of alveolar soft part sarcoma that were either treated at Tata Memorial Hospital, Mumbai, India, or were referred in consultation from various parts of India. TFE3 immunohistochemical staining was performed on 22 alveolar soft part sarcomas and on 21 other tumours.

Read this article

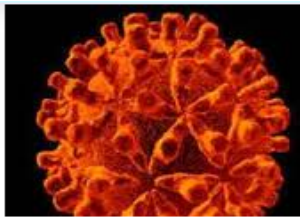
Don't miss out - further Free LWW Content is available for registered users!
Log into your account or register here to read these articles.

OMICS Publishing Group

ISSN-2155-9929

Journal of Molecular Biomarkers & Diagnosis

Open Access



Pathology (January 2012) 44(1), pp. 11–17

ANATOMICAL PATHOLOGY

Alveolar soft part sarcoma 'revisited': clinicopathological review of 47 cases from a tertiary cancer referral centre, including immunohistochemical expression of TFE3 in 22 cases and 21 other tumours

BHARAT REKHI*, ABHIJEET INGLE*, MANISH AGARWAL§, AJAY PURI†, SIDDHARTH LASKAR‡ AND NIRMALA A. JAMBHEKAR*

*Departments of *Pathology, †Surgical Oncology (Bone and Soft Tissues), and ‡Radiation Oncology, Tata Memorial Hospital, Parel, and §Department of Orthopaedics, P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, India*

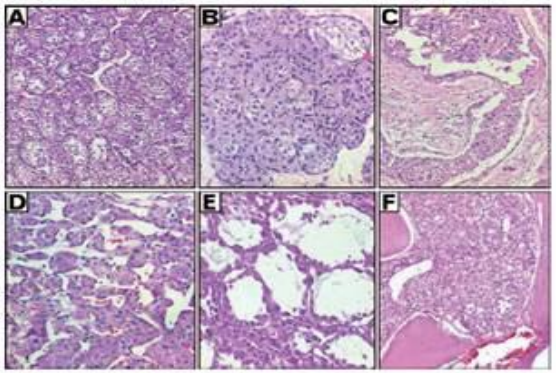


Fig. 1 H&E. (A) Classic pattern of alveolar soft part sarcoma comprising uniform organoid nests of tumour cells with intervening vasculature. (B) Small nests of tumour cells. (C) Intravascular tumour extension. (D) Haemangiopericytomatous vasculature. (E) Mucoid cysts within tumour. (F) Tumour infiltrating the bone.

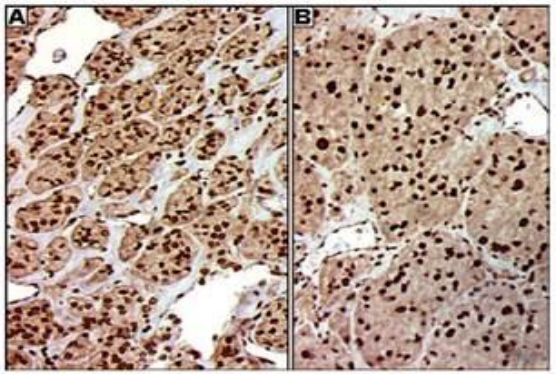
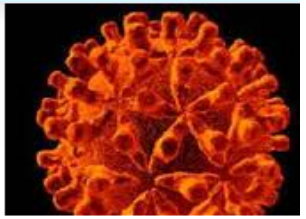


Fig. 3 (A) Intense intranuclear staining (3+) with TFE3 in a case of alveolar soft part sarcoma (DAB). (B) Higher magnification displaying intense intranuclear staining (3+) with TFE3 (DAB).

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929



Virchows Arch (2012) 461:687–697
DOI 10.1007/s00428-012-1335-7

ORIGINAL ARTICLE

Histopathological, immunohistochemical and molecular spectrum of myoepithelial tumours of soft tissues

Bharat Rekhi · Mukund Sable · Nirmala A. Jambhekar

Received: 7 July 2012 / Revised: 6 September 2012 / Accepted: 18 October 2012 / Published online: 25 October 2012

Abstract Primary soft tissue myoepithelial tumours (METs) are rare. Recent studies have shown *EWSR1* rearrangement in certain METs. We present clinicopathological, immunohistochemical and molecular features of 14 primary soft tissue METs. Fourteen tumours, five benign and nine malignant, occurred in 12 men and two women, with an age range of 18–60 years (mean, 39.2); in upper extremities, four (29 %); chest wall, three (21 %); paraspinal region, three (21 %); pelvis, two (14 %) and lower extremities, two (14 %). Tumour size varied from 2 to 21.6 cm (mean, 8.7). Microscopically, most tumours were at least focally circumscribed. Morphological heterogeneity was noted, commonest patterns being cord-like and diffuse arrangement of polygonal cells in a myxoid stroma. By immunohistochemistry, tumours were positive for epithelial membrane antigen (EMA) (10/12, 83 %), cytokeratin (CK)/MNF116 (3/12, 25 %), p63 (7/10, 70 %), CD10 (4/6, 67 %), calponin (6/6, 100 %), S-100P (11/13, 85 %), glial fibrillary acidic protein (GFAP) (6/12, 50 %), smooth muscle actin (SMA) (3/9, 33 %), INI1/SMARCB1 (6/10, 60 %), brachyury (0/11), CD34 (0/5) and vimentin (4/4, 100 %), implying 93 % positivity for at least one epithelial marker. *EWSR1* gene rearrangement was detected in 3/6 (50 %) METs (one benign and two malignant) and in an eccrine porocarcinoma which was included for reasons of comparison. Outcome details were available for six patients all surgically treated; three tumours (two malignant and one benign) resected with unknown marginal status recurred; two patients died and a single patient with myoepithelial carcinoma, who underwent a wide excision, is disease-free. This study illustrates the wide morphological spectrum of soft tissue METs, including benign and malignant subtypes. EMA and S-100P are optimal markers that should be supplemented with broad spectrum keratins, such as AE1/AE3, along with p63, GFAP and calponin in case of need but the results must be correlated with morphological features. Brachyury is useful in separating parachordoma/myoepithelioma from chordoma. *EWSR1* rearrangement mostly occurs in METs that are deep-seated, irrespective of benign or malignant behaviour. Most malignant METs are INI1 negative.

Keywords Soft tissue myoepithelioma · Soft tissue myoepithelial carcinoma · *EWSR1* rearrangement · FISH · Parachordoma

Introduction

Myoepithelial tumours (METs), including myoepithelioma and myoepithelial carcinoma, are rare in the musculoskeletal system. According to the World Health Organisation (WHO) Classification of soft tissue tumours, myoepithelioma, mixed tumour and parachordoma constitute a common spectrum of tumours, in which mixed tumour is composed of epithelial and myoepithelial elements within a hyalinised or chondromyxoid stroma, myoepithelioma of myoepithelial cells which lack ductal differentiation and parachordoma displays clear cells [1]. Subsequent to the initial study of 19 mixed tumours and myoepitheliomas of soft tissues by Kilpatrick et al. [2], others have documented case reports and series, expanding upon the histomorphological spectrum and immunohistochemical profile of METs [3–8]. The literature on genetic altera-

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929

Pathological findings

Grossly, the MET were often well-defined with grey-white, glistening/myxoid, cystic to fleshy cut surfaces. Microscopically, most tumours were at least focally circumscribed in ten cases and infiltrating in four cases. Tumours were mostly multinodular. Various tumour cell arrangements were noted, including cord-like (7), sheet-like/diffuse (6), clusters (5), nests/lobules (3), trabeculae (3), pseudo-acinar/rosetting, without ductal formation (2), alveolar (1), rhythmic palisades (1) and predominantly reticular (1). The stroma was variable and mostly myxoid (5), followed by hyaline/sclerotic (3), myxohyaline (3), collagenous (2), myxochondroid (1) and osteochondroid (1). Calcification was observed in two tumours, including a single case that displayed mineralised bone formation. Varying proportions of diverse cell types were noted, mostly polygonal/epithelioid (12), followed by clear (5), spindle (5), plasmacytoid (1), rhabdoid (2) and small round (1) cell types.

Nine of the 14 (64 %) tumours fulfilled criteria of malignancy, justifying a diagnosis of myoepithelial carcinoma. Mitotic figures were absent in all five myoepitheliomas and varied from ten to 50/10 hpf in nine myoepithelial carcinomas, all accompanied with at least moderate (seven cases) to marked (two cases) nuclear atypia. Perineural invasion was identified in a single case. The skin adnexal tumour was a circumscribed dermal tumour, composed of infiltrating nests of basaloid tumour cells which exhibited focal squamous and clear cell differentiation with prominent duct formation and intervening sclerosis and focal cystic change. There were readily identifiable mitoses, moderate nuclear atypia and focal tumour necrosis, justifying a diagnosis of eccrine porocarcinoma.

Immunohistochemical findings

By immunohistochemistry, tumour cells were variably positive for epithelial membrane antigen (EMA) (10/

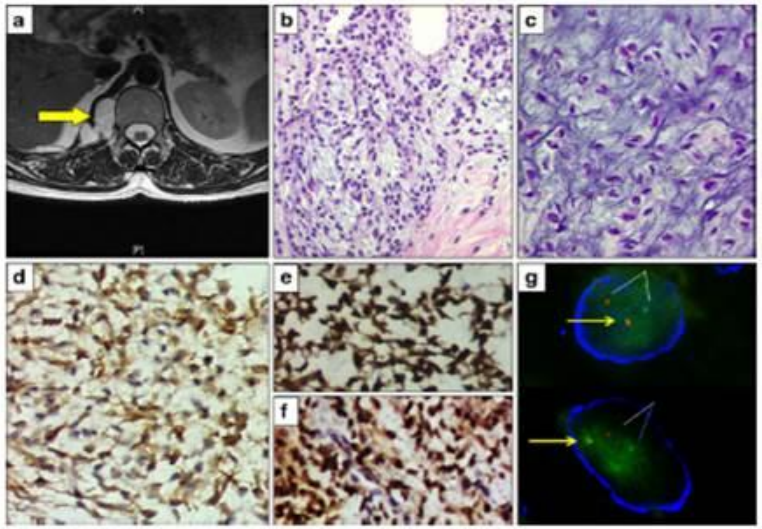


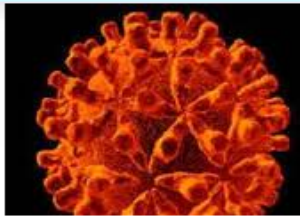
Fig. 2 Case 2. a Magnetic resonance imaging (MRI) findings. Axial T2-weighted image showing a lobulated, hyperintense mass in right paravertebral region involving the psoas muscle, expanding the neural foramen of D12 to L2 vertebrae. b Histopathological features. Polygonal to spindly cells in clusters and cords, embedded in a myxoid stroma. c Tumor cells on higher magnification. d EMA positivity. e Diffuse S-100P positivity. f Diffuse p63 positivity. g *EWSR1* rearrangement detected in the form of split signal (*double arrows*) in tumor cells, in contrast to single-fused signals (*pointed arrows*). b H&E ×200. c H&E ×400. d DAB ×400. e DAB ×400. f DAB ×400. g DAPI ×1,000

OMICS Publishing Group

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929



APMIS ACTA PATHOLOGICA, MICROBIOLOGICA ET IMMUNOLOGICA SCANDINAVICA

APMIS

DOI 10.1111/apm.12272

Histopathological, immunohistochemical and molecular cytogenetic analysis of 21 spindle cell/ sclerosing rhabdomyosarcomas

BHARAT REKHI and TANVI SINGHVI

Department of Pathology, Tata Memorial Hospital, Mumbai, India

Rekhi B, Singhvi T. Histopathological, immunohistochemical and molecular cytogenetic analysis of 21 spindle cell/sclerosing rhabdomyosarcomas. APMIS 2014.

Recently, spindle cell/sclerosing rhabdomyosarcoma (RMS) has been recognized as another distinct variant of a RMS. We evaluated clinicopathological features of 21 cases of spindle cell and sclerosing RMS and performed fluorescent *in situ* hybridization (FISH) testing in 10 (47.6%) tumours. Twenty-one tumours occurred in 16 males and 5 females (mean age, 19.7 years); commonly in the head and neck region (8) (38%) and extremities (7) (33.3%), followed by paratesticular region (2) (9.5%), chest wall (1), abdomen (1), pelvis (1) and paraspinal region (1). Average tumour size was 7.9 cm. Histopathologically, tumours that were spindle cell type (8) (38%) mostly occurred in the head and neck region, while sclerosing type (10) (47.6%) mostly occurred in the extremities. Remaining three (14.2%) tumours were mixed (sclerosing with spindle cell type). Tumour areas resembling embryonal RMS (ERMS) and alveolar RMS (ARMS) were noted in eight and three tumours respectively. Immunohistochemically, tumour cells were positive for desmin (21/21) (100%), MyoD1 (19/19) (100%), myogenin (13/15) (86.6%), SMA (2/3) and MIC2 (1/8) (12.5%). On FISH testing, none of the 10 tumours exhibited RMS1 (PAX3-FOXO1) or RMS 2 (PAX7-FOXO1) fusion. Eighteen patients underwent surgical resection and were offered adjuvant chemotherapy (CT) (4 cases), adjuvant CT + radiotherapy (RT) (4 cases) and adjuvant RT (1 case). Two patients underwent CT and a single patient received CT + RT. On follow-up (16 cases) (2–36 months), six tumours recurred and nine metastasized. Spindle/sclerosing RMSs are aggressive tumours and occur commonly in the head and neck and extremity sites. These tumours are histopathologically interrelated. Their immunohistochemical and cytogenetic profile is closer to ERMS than ARMS.

Key words: Rhabdomyosarcoma; sclerosing rhabdomyosarcoma; spindle cell rhabdomyosarcoma; spindle cell/ sclerosing rhabdomyosarcoma; FISH testing in sarcomas.

Bharat Rekhi, Department of Pathology, Tata Memorial Hospital, Dr E.B. Road, Parel, Mumbai, India, 400012, e-mail: rekhi.bharat@gmail.com

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929

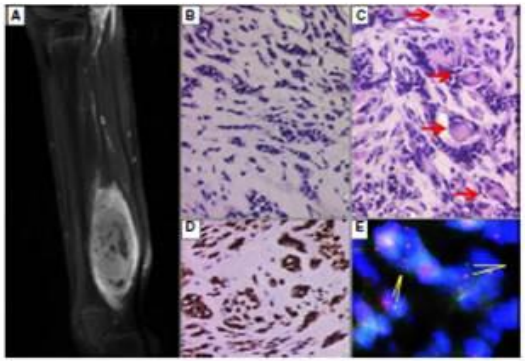


Fig. 3. Case 10. Sclerosing rhabdomyosarcoma. A. Magnetic resonance imaging (MRI) showing a large lobulated soft tissue mass measuring along the posterolateral aspect of the lower half of the left leg, appearing hypointense on T1W and heterogeneously hyperintense on T2 W and STIR sequences B. Tumour cells arranged in cords and microalveoli in a pseudochondroid matrix. H and E × 200. C. Distinct rhabdomyoblastic cells noted within other round tumour cells (arrows). H and E × 400. D. Diffuse MyoD1 positivity within tumour cells. DAB × 400. E. Lack of RMSI, SPEC t(2; 13) fusion. DAPI × 1000.

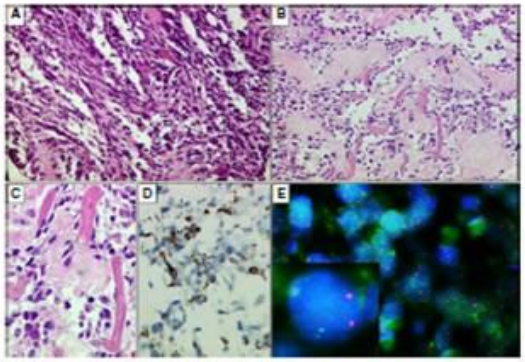


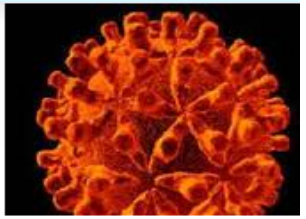
Fig. 4. Case 3. Sclerosing and spindle cell rhabdomyosarcoma. A. Spindly sarcomatous tumour with cells arranged in fascicular pattern. H and E × 100. B. Tumour areas resembling sclerosing rhabdomyosarcoma with interspersed rhabdomyoblasts. H and E × 200. C. Tumour rhabdomyoblasts amidst hyaline matrix/stroma. H and E × 400. D. Desmin positivity. DAB × 400. E. Lack of RMSI, SPEC t(2, 13) fusion. DAPI × 1000.

well as scattered round cells. We identified foci of round cells in three tumours (two of spindle cell type and one of mixed type) and pleomorphic cells in a single spindle cell RMS. Mentzel et al. (3) identified round/polygonal and spindle-shaped tumour cells. Subsequently, others (10, 14, 17)

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929



Pathol. Oncol. Res. (2014) 20:503–516
DOI 10.1007/s12253-013-9721-2

RESEARCH

Clinicopathological and Molecular Spectrum of Ewing Sarcomas/PNETs, Including Validation of EWSR1 Rearrangement by Conventional and Array FISH Technique in Certain Cases

Bharat Rekhi · Ulrich Vogel · Ranjan Basak · Sangeeta B. Desai · Nirmala A. Jambhekar

Received: 17 January 2013 / Accepted: 5 November 2013 / Published online: 30 November 2013

Abstract Over the years, a wide clinicopathological spectrum has been identified within Ewing family of tumors (EFTs). As these tumors are chemosensitive, their correct and timely identification is necessary. The aims of this study were (1) to present the diverse clinicopathological and molecular profile of EFTs in our settings, (2) to identify a pragmatic approach for diagnosing EFTs, especially for application of ancillary techniques, namely RT-PCR for specific transcripts (EWS-FLI1, EWS-ERG) and FISH for *EWSR1* gene rearrangement, in certain cases and (3) to show the utility of tissue microarray in establishing a new FISH test. Fifty-eight EFTs were identified in 38 males and 20 females within an age-range of 1–65 years (median, 16), mostly in lower extremities (14) (24.1 %). Therapeutically, most patients underwent neoadjuvant chemotherapy with subsequent surgery. Histopathologically, diagnosis of EFTs was initially offered in 41/58 (70.6 %) tumors. On review, 59 % tumors showed diffuse pattern, while 41 % displayed rosettes. Immunohistochemically, tumor cells were mostly diffusely positive for CD99 (48/52) (92.3 %); FLI-1 (17/18) (94.4 %); variably for BCL2 (16/18) (88.8 %), synaptophysin (6/20) (35 %), S100-P (2/7) (28.5 %), CD56 (2/5) (40 %), NSE (2/5) (40 %), calponin (3/4) (75 %), EMA (5/24) (20.8 %) and CK (3/24) (12.5 %), the latter two mostly focally. Fifty five tumors were *EWS-FLI1* positive, while a single tumor was *EWS-ERG* positive. Sensitivity for PCR was 61 %. *EWSR1* rearrangement was detected by FISH in 12/13 Ewing sarcomas/PNETs. Sensitivity for *EWSR1* test was 92.3 % and specificity was 100 %. Thirty-eight tumors, including 14 molecular confirmed EFTs and 21 other tumors were tested for *EWSR1* rearrangement. Among 21 unrelated tumors, *EWSR1* rearrangement was detected in few myoepithelial tumors, occasional desmoplastic small round cell tumor and an extraskeletal myxoid chondrosarcoma. Further, a tissue microarray with a separate set of 8 EFTs, confirmed at another laboratory was analysed for validation of *EWSR1* rearrangement test. 23/28 (82.1 %) tissue cores of the tissue microarray, stained by FISH were interpretable, including *EWSR1* rearrangement, detected in 20/28 tissue cores; not detected in 3 liver cores and uninterpretable in 5 (17.8 %) cores. Classical EFTs can be diagnosed with diffuse, membranous CD99 positivity, intranuclear FLI1 positivity and LCA negativity in malignant round cells. In unconventional cases, it is indispensable to reveal the concomitant fusion m-RNA by RT-PCR. In case of negative molecular results, it is necessary to prove *EWSR1* rearrangement by FISH. These tests should be interpreted with clinicopathological correlation. Tissue microarrays for FISH are useful during validation of a new test, especially when sarcomas like EFTs show less genetic heterogeneity within tumor cells.

Keywords Ewing sarcoma · PNET · *EWS-FLI1* · *EWSR1* rearrangement · FISH in soft tissue tumors · Molecular pathology of soft tissue sarcomas · Array FISH

B. Rekhi (✉) · R. Basak · S. B. Desai · N. A. Jambhekar
Department of Pathology, Tata Memorial Hospital,
Parel, Mumbai, India
e-mail: rekhi.bharat@gmail.com

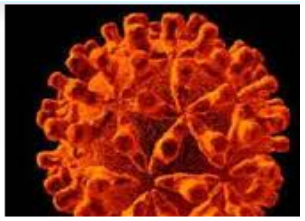
U. Vogel

OMICS Publishing Group

ISSN-2155-9929

Journal of Molecular Biomarkers & Diagnosis

Open Access



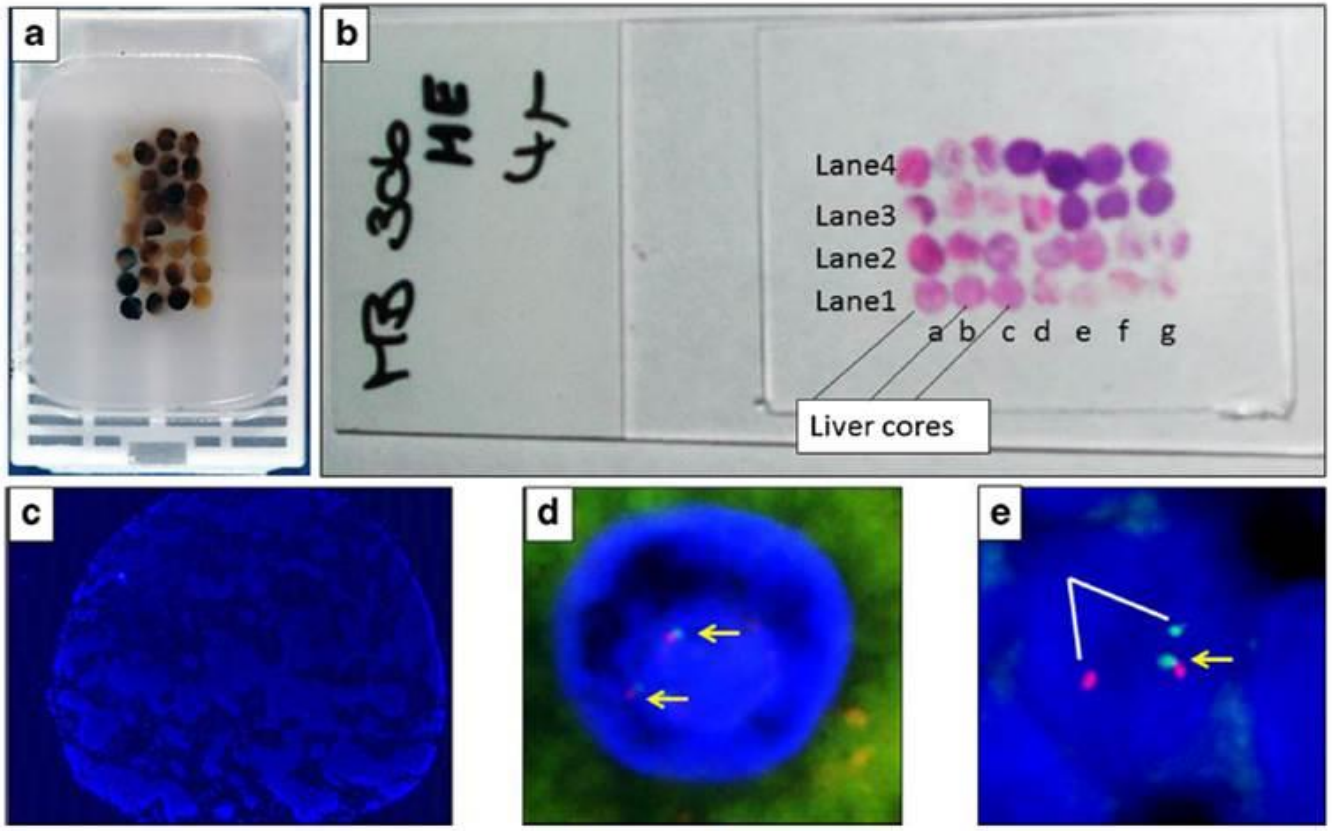


Fig. 6 Microarray FISH. **a**. Array block. **b**. Array slide marked with *lanes* and *rows*, including liver tissue cores (control and for identification). H & E. **c** single core in slide stained for FISH for *EWSR1* rearrangement. DAPI×100. **d** *Lane 1c*. Liver cells displaying intact alleles represented by fused signals. DAPI×1,000. **e** *Lane 3f*. Nuclei from one of the tumor cores displaying *EWSR1* rearrangement. DAPI×1,000

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929

Pathology – Research and Practice 209 (2013) 758–766

Contents lists available at ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp

Original article

Immunohistochemical validation of INI1/SMARCB1 in a spectrum of musculoskeletal tumors: An experience at a Tertiary Cancer Referral Centre

Bharat Rekhi *, Nirmala A. Jambhekar

Department of Pathology, Tata Memorial Hospital, Mumbai 400012, Maharashtra, India

ARTICLE INFO

Article history:
Received 22 June 2013
Received in revised form 16 July 2013
Accepted 7 August 2013

Keywords:
INI1/SMARCB1/hSNF5/BAF47
Epithelioid sarcoma
Extrarenal rhabdoid tumor
Synovial sarcoma
Immunohistochemistry of sarcomas

ABSTRACT

The purpose of this study was to evaluate and validate immunohistochemical (IHC) expression of INI1/SMARCB1 in various musculoskeletal tumors in the light of the established literature.

Twenty-seven cases of epithelioid sarcoma (ES); 4 of extrarenal rhabdoid tumor (ERRT) of soft tissue and 97 other tumors, including 16 cases of synovial sarcoma (SS), were evaluated for IHC expression of INI1 on formalin-fixed, paraffin-embedded tissue sections of various biopsies.

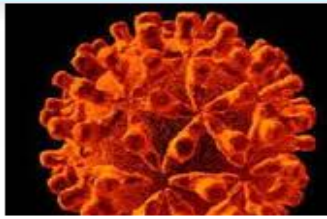
Out of 128 tumors, INI1/SMARCB1 staining was completely lacking in cases of ES (23/27) (85.1%), ERRTs (4/4) (100%), myoepithelial tumors (4/14) (28.5%) and in (1/16) (6.2%) cases of SS. Fourteen out of 15 SSs displayed a reduced staining pattern. Other 67 studied tumors were INI1-positive. Sensitivity for complete INI1 negativity in ES was 85.1%, and specificity with respect to its differentials, excluding ERRTs, was 94.8%.

Complete lack of INI1 immunostaining in most ESs indicates its value as a diagnostic marker for ESs, including those occurring at rare sites; in ERRTs and in some myoepithelial tumors, within an appropriate clinicopathological context, in all kinds of biopsies. ES, at least in some cases, is immunohistochemically the most closely related tumor to an ERRT. A unique pattern of reduced INI1 expression in a SS is useful during triage of some cases for molecular testing. Its expression should be interpreted in the tumor cells, rather than intermixed stromal cells and or inflammatory cells that retain INI1 expression.

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929



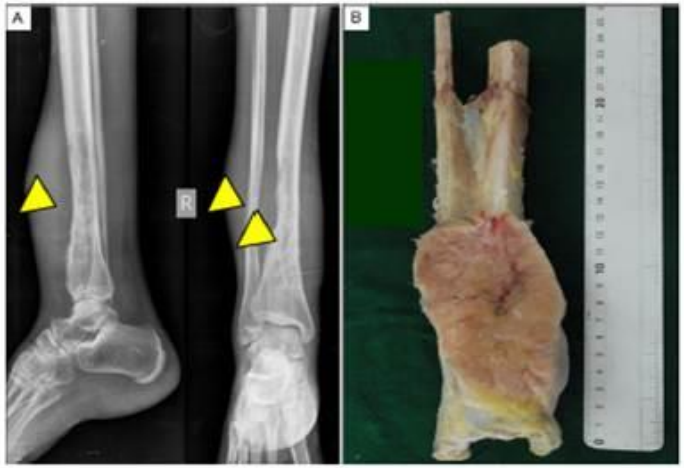


Fig. 5. (A) Plain radiograph displaying a diaphyseal sclerotic tumor in the leg with soft tissue shadow (arrow heads). (B) Gross specimen showing fleshy tumor involving soft tissues and both bones of lower limb.

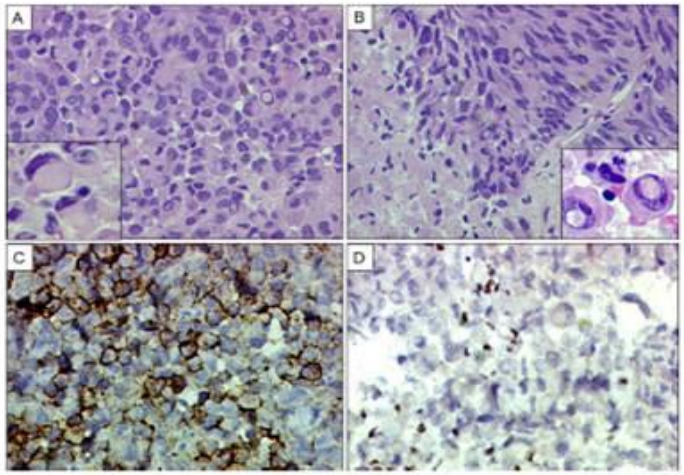


Fig. 6. Microscopic findings of tumor in Fig. 5. (A) Sheet-like arrangement of tumor cells with conspicuous "rhabdoid-like" morphology. Inset: Intracytoplasmic inclusions. H & E × 400. (B) Spindly and polygonal cells with areas of necrosis. Inset: prominent intranuclear pseudoinclusions. H & E × 400. (C) Tumor cells displaying Pan CK positivity. DAB × 400. (D) INI1/SMARCB1 negative tumor cells. DAB × 400.

OMICS Publishing Group

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929

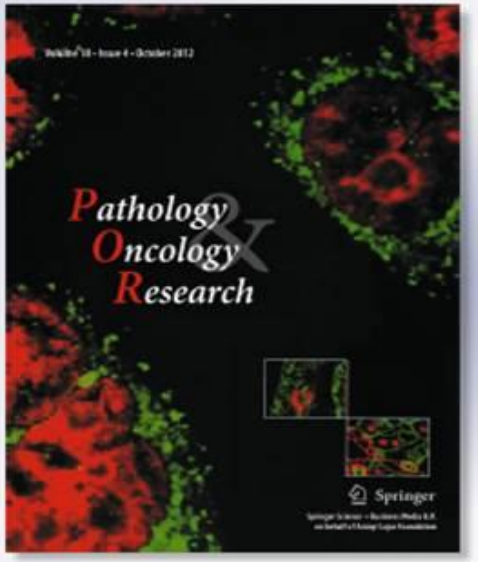
Desmoplastic Small Round Cell Tumor-Clinicopathological Spectrum, Including Unusual Features and Immunohistochemical Analysis of 45 Tumors Diagnosed at a Tertiary Cancer Referral Centre, with Molecular Results t(11; 22) (p13; q12) (EWS-WT1) in Select Cases

Bharat Rekhi, Sharique Ahmed, Ranjan

Pathology & Oncology Research
Official Journal of the Arányi Lajos Foundation

ISSN 1219-4956
Volume 18
Number 4

Pathol. Oncol. Res. (2012) 18:917-927
DOI 10.1007/s12253-012-9522-z



Springer

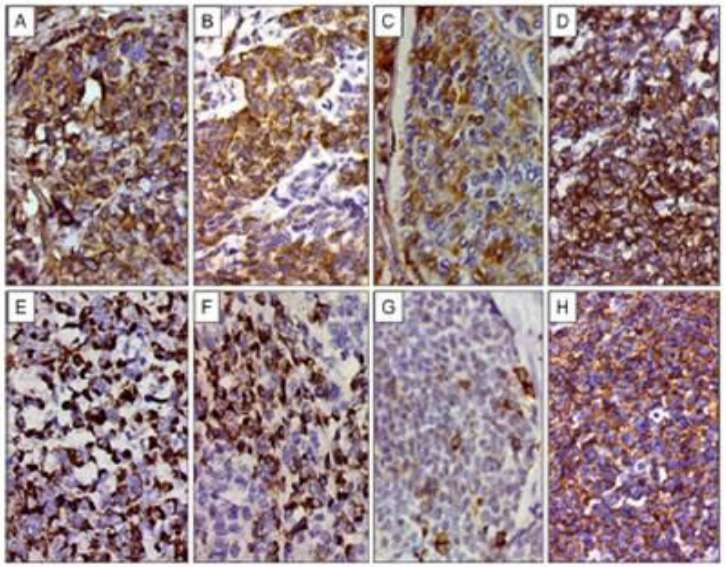


Fig. 4 Immunohistochemical staining in various DSRCTs. a Diffuse cytoplasmic vimentin positivity. High power. b Focal cytoplasmic and membranous CK positivity within tumor cells. High power. c Focal cytoplasmic EMA positivity. High power. d Diffuse cytoplasmic membrane positivity with CD56. High power. e Discrete nuclear and paranuclear WT1 positivity. High power. f Focal intracytoplasmic 'dot-like' desmin positivity. High power. g Focal synaptophysin positivity. High power. h Unusual membranous MIC2 positivity (Case 23). High power

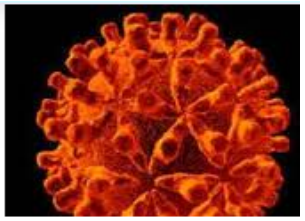
(100 %), MIC2/CD99 (51.3 %), NSE (75 %), synaptophysin (36.8 %) and chromogranin (11.1 %) and WT1 (81.4 %). These results were mostly comparable with earlier studies, except a lower CK positivity in our series [5, 11, 13, 14]. This was in view of availability of MNF116 in our laboratory at the time of these cases, rather than AE1/AE3, a relatively broad spectrum CK that was utilized in previous studies [5, 8, 11, 13]. We observed EMA as a useful marker in confirmation of epithelial differentiation. In contrast to previous studies [5, 11, 13], we observed a relatively higher positivity for MIC2/CD99 that mostly showed cytoplasmic positivity. However, five tumors displayed focal to diffuse membranous MIC2 positivity, wherein Ewing sarcoma/PNET was the closest differential. Three of these tumors were confirmed as DSRCTs by molecular analysis. The other two tumors revealed 'classic' morphology and polyphenotypic expression of a DSRCT. Membranous MIC2 positivity in a DSRCT was also noted in an earlier published case report [16]. PNET and neuroblastoma were objectively ruled out in view of polyphenotypic expression of epithelial, mesenchymal, including myogenic and neural markers in other DSRCTs, although overlapping expression of epithelial markers is uncommonly noted in Ewing sarcoma/PNET [17]. Conversely, rarely, polyphenotypic expression might not be seen in DSRCT, that otherwise displays the characteristic transcript EWS-WT1, on molecular analysis [16]. WT1 was observed to be a useful marker, as noted in earlier 2 studies [5, 6]. However, in contrast to Gerald et al. [5], we, like Lae et al. [13], observed discrete paranuclear to nuclear WT1 positivity. This was in view of WT1 protein utilized in the present study corresponding to the amino, rather than carboxyl terminal. MyoD1 and myogenin negativity in all

OMICS Publishing Group

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929



Indian J Med Res 136, November 2012, pp 170-179

Immunohistochemical validation of *TLE1*, a novel marker, for synovial sarcomas

Bharat Rekhi*, Ranjan Basak**, Sangeeta B. Desai*,** & Nirmala A. Jambhekar*

*Department of Pathology, Tata Memorial Hospital, Mumbai & **Department of Molecular Pathology, Advanced Centre for Treatment, Research & Education in Cancer (ACTREC), Navi Mumbai, India

Received July 26, 2011

Background & objectives: Logistic and financial constraints limit application of several available immunohistochemical (IHC) markers and molecular analysis in every case of synovial sarcoma, diagnosed in our settings. Recently, *TLE1* has been recognized as a robust IHC marker for diagnosing a synovial sarcoma. Here, we present IHC features of synovial sarcomas, including *TLE1* expression in these cases and in some other tumours.

Methods: Conventional sections from 42 synovial sarcomas (30 retrospective & 12 prospectively diagnosed) were subjected to TLE1 IHC staining, including 21 tumours confirmed with molecular testing. TLE1 immunostaining was graded from 0, 1+, 2+, 3+, with 2+ or 3+ grades interpreted as positive staining.

Results: Of the 42 tumours, 26 (61.9%) were of monophasic spindle cell type, 13 biphasic type (30.9%), two (4.7%) calcifying type and remaining one (2.3%) was a poorly differentiated synovial sarcoma. On immunohistochemistry (IHC), tumours were positive for epithelial membrane antigen (EMA) (26/34, 76.4%), cytokeratin (CK)7 (6/10, 60%), CKΔMNF116 (6/21, 28.6%), B cell lymphoma 2 (BCL2) (36/37, 97.3%), cluster of differentiation molecule 99 (MIC)2 (23/31, 74.1%) and transducin-like enhancer of split 1 (TLE1) (40/42, 95.2%), while negative for CD34 in all 21 tumours, wherever performed. TLE1 was also positive in tumour controls, including schwannomas (5/5, 100%), neurofibromas (2/2, 100%), malignant peripheral nerve sheath tumors (2/12, 17%) and Ewing sarcomas (4/10, 40%). TLE1 sensitivity for diagnosis of synovial sarcomas was 95.2 per cent. Its overall specificity was 63.7 per cent, whereas with regards to tumors forming its closest differential diagnoses, its specificity was 72 per cent.

Interpretation & conclusions: Although molecular confirmation is the diagnostic gold standard for synovial sarcoma, TLE1, in view of its high sensitivity may be a useful marker within the optimal IHC panel comprising EMA, BCL2, MIC2, CD34 and CK7, especially on small biopsy samples, for substantiating a diagnosis of synovial sarcoma. Awareness of TLE1 expression in other tumours and its correct interpretation are necessary.

Key words Immunohistochemistry of synovial sarcoma - molecular analysis of synovial sarcomas - synovial sarcoma - *TLE1* - t(X; 18) (SYT-SSX)

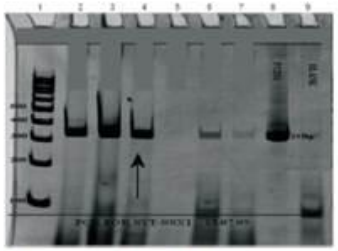


Fig. 4. Polymerase chain reaction (PCR) analysis of SYT-SSX translocation using SYT and SSX1 primers. Reactions were subjected to electrophoresis on 10% polyacrylamide gel. Lane 1: the DNA size markers in base pairs (bp); Lanes 2 and 3: PCR run performed with cDNA from an already reported positive cases (331 bp) acting as positive control; Lane 4: PCR run performed with cDNA from test sample (arrow) showing positive band (331 bp); Lane 5: PCR run performed with cDNA from an already reported negative case acting as negative control; Lane 6: PCR run performed with cDNA from an earlier case, revealing weak band, interpreted as "inconclusive"; Lane 7: PCR run performed with cDNA from an unrelated tumour acting as negative control; Lane 8: Positive control DNA (pTZ57R/T-SYT-SSX1-331bp); Lane 9: PCR amplification without DNA template (Blank) to rule out contamination.

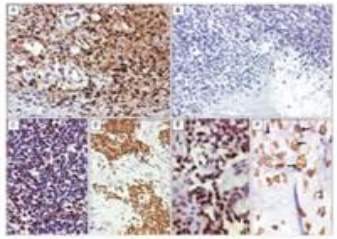


Fig. 5. A. Diffuse TLE1 positivity in a neurilemoma/schwannoma. TLE1 positivity also noted within endothelial cells of vessels. DAB x 200. B. TLE1 negativity in MPNST (high-grade) DABx 200C. C. TLE1 positivity (2+) in a case of Ewing sarcoma/PNET. DAB x 200. D. TLE1 positivity (3+) in a desmoplastic small round cell tumour (DSRCT). DAB x 200. E. TLE1 positivity (2+) noted in a case of adamantinoma. DAB x 400. F. Negative nuclear staining, but positive cytoplasmic staining for TLE1 in chordoma. DAB x 400.

An isolated case of an undifferentiated sarcoma, composed of round to spindle cells, arising in the broad ligament that showed IHC features suggestive for a synovial sarcoma, but showed negative translocation results for synovial sarcoma, Ewing sarcoma and desmoplastic small round cell tumour, displayed positive TLE1 staining (Tables III, IV).

Overall sensitivity of TLE1 staining in synovial sarcomas was 95.2 per cent and in cases that were confirmed with molecular results, the same was 90.4 per cent. Its overall specificity was 63.7 per cent, and specificity for synovial sarcomas with regards select differential diagnoses, despite IHC, was 72 per cent. Besides various tumours, we also observed TLE1 positivity was also observed in endothelial cells, basal keratinocytes and adipocytes.

it is amenable to treatment modalities, including chemotherapy. Hence, its correct identification is vital. Several IHC markers are employed for its objective diagnosis and in differentiating it from it's diagnostic mimics. The diagnostic challenge is further amplified with limited biopsy material, wherein focal expression, especially of epithelial markers, might be lacking, thereby creating a challenge in exact recognition, especially of monophasic spindle cell and poorly differentiated subtypes of synovial sarcoma.

Although an extensive panel of IHC markers is available for diagnosing a synovial sarcoma, there has been no single, fairly specific and sensitive marker for the same. In the present study, markers displaying high sensitivity and reasonable specificity comprised EMA, BCL2, and MIC2. Noteworthy, expression of MIC2 in synovial sarcomas is cytoplasmic, rather than diffuse cytoplasmic membranous positivity, as noted in Ewing sarcoma/primitive neuroectodermal tumor (PNET). Vimentin and calponin display high sensitivity, but low specificity. CK expression in the present study was low as we have MNF116, rather than AE1/AE3 that

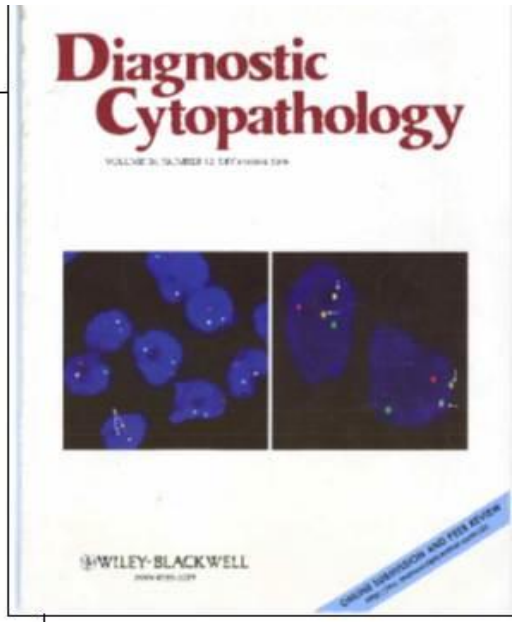
OMICS Publishing Group

Journal of Molecular Biomarkers & Diagnosis

ISSN-2155-9929

Open Access

Image appeared on Journal cover page



Spectrum of Cytomorphological Features, Including Literature Review, of an Extraskeletal Myxoid Chondrosarcoma With t(9;22)(q22;q12) (TEC/EWS) Results in One Case

Rajiv Kumar, M.D.,[1] Bharat Rekhi, M.D., D.N.B., M.I.A.C., M.A.S.C.P.,[1*] Nadia Shirazi, M.D.,[2] Anurita Pais, M.Sc., Ph.D.,[3] Pratibha Amare, M.Sc., Ph.D.,[3] Deepali Gawde, M.Sc.,[3] and Nirmala Jambhekar, M.D., D.P.B.[1]

Extraskeletal myxoid chondrosarcoma (EMC) is an uncommon soft tissue sarcoma with evolving literature on its cytomorphological features and limited documentation of its molecular analysis. Herein, we present cytological features, including review, of four cases of an EMC. Smears were predominantly hypercellular, comprising tumor cells arranged in clusters, trabeculae, and cords against a variable chondromyxoid background. Cells were mainly polygonal shaped with round to indented nuclei, uniform chromatin, displaying intranuclear inclusions, grooves, and eosinophilic to finely vacuolated cytoplasm. Three cases revealed presence of "rhabdoid" cells. All cases had histopathologic confirmation. One case displayed t(9;22)(q22;q12) translocation by fluorescent in situ hybridization (FISH), on smears.
Diagn. Cytopathol. 2008;36:868–875.

Key Words: FNAC soft tissue tumors; extraskeletal myxoid chodrosarcoma; uncommon soft tissue sarcomas; FISH analysis

Extraskeletal myxoid chondrosarcoma (EMC) is a rare malignant soft tissue tumor, first described by Stout and Verner[1] and subsequently, identified as a tumor that exhibits morphologic and histochemical evidence of chondroid differentiation, by Enzinger and Shiraki.[2] It is primarily noted in the deep soft tissues of the proximal extremities and in the limb girdles of middle-aged males.[3,4] In contrast to a skeletal myxoid chondrosarcoma that is a high-grade sarcoma, an EMC is a low to intermediate grade sarcoma, with a relatively protracted clinical course.[5] Nonetheless, late recurrences and lung metastasis have been recorded.[3–5] Lately, molecular analysis have unraveled specific translocations in an EMC like t(9;22)(q22;q12), resulting in EWS-CHN(TEC) fusion gene product.[6]

Although the cytological features of various myxoid sarcomas have been fairly described, there is limited literature on a spectrum of cytomorphological features of an EMC.[7–9] Still rare is an objective confirmation with translocation results, especially on smears.[10,11]

Herein, we describe spectral cytomorphological features of an EMC, including its molecular analysis.

Case Reports

All four cases were referred to us for a primary diagnosis.

Journal of Molecular Biomarkers & Diagnosis

Open Access

ISSN-2155-9929

Contents lists available at SciVerse ScienceDirect

Annals of Diagnostic Pathology

Original Contributions

Spectrum of neuroendocrine carcinomas of the uterine cervix, including histopathologic features, terminology, immunohistochemical profile, and clinical outcomes in a series of 50 cases from a single institution in India

Bharat Rekhi MD, DNB, MIAC [a,*], Bharti Patil MD [a], Kedar K. Deodhar MD, FRC-Path [a], Amita Maheshwari MD [b], Rajendra A. Kerkar MS, FRCS [b], Sudeep Gupta MD, DM [c], Hemant B. Tongaonkar MS [d], Shyam Kishore Shrivastava MD, DNB [e]

[a] Department of Pathology, Tata Memorial Hospital, Parel, Mumbai, 400012, India
[b] Department of Surgical Oncology (Gynaecology), Tata Memorial Hospital, Parel, Mumbai, 400012, India
[c] Department of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai, 400012, India
[d] Department of Surgical Oncology (Uro-gynaecology), Tata Memorial Hospital, Parel, Mumbai, 400012, India
[e] Department of Radiation Oncology, Tata Memorial Hospital, Parel, Mumbai, 400012, India

ARTICLE INFO

Keywords:
Neuroendocrine carcinoma cervix
Small cell carcinoma cervix
Large cell neuroendocrine carcinoma cervix
Immunohistochemistry in cervix carcinomas
Cervix cancer

ABSTRACT

Neuroendocrine carcinomas of the cervix are uncommon, characterized by a histomorphological spectrum and, mostly, an aggressive clinical course. There are only few substantial studies on such cases documented from our country, where cervical cancer is the second most common cancer affecting women. Herein, we present a spectrum of 50 cervical neuroendocrine carcinomas, including histopathologic features, terminology, immunohistochemical (IHC) profile, and clinical outcomes, wherever available. Fifty tumors occurred in women, with their age ranging from 23 to 69 years (mean, 48.6 years; median, 46.5 years). Stagewise, among 25 cases, most cases (6, or 24%) presented with stage IIB. Average tumor size was 4.7 cm. On histopathologic review, 26 tumors (52%) were classified as small cell carcinoma (SMCA); 14 (28%), as large cell neuroendocrine carcinomas (LCNECs); 4 (8%), as SMCA + LCNECs; and 6, as mixed carcinomas, including 3 tumors (6%) with SMCA and squamous cell carcinoma (SCC), 2 tumors (4%) with LCNEC and adenocarcinoma, and a single tumor (2%) with LCNEC and squamous cell carcinoma. On IHC performed in 41 tumors (82%), 36 tumors (87.8%) were positive for at least a single neuroendocrine marker, and 22 (53.6%) expressed 2 neuroendocrine markers. Synaptophysin was positive in 22 (59.4%) of 37 tumors; chromogranin, in 27 (72.9%) of 37; CD56, in 8 (100%) of 8; and neuron-specific enolase in 7 (87.5%) of 8 tumors. Treatment wise, among 30 patients (60%), 6 (20%) underwent surgery, including Wertheim hysterectomy (5) and simple hysterectomy (1); 8 (26.6%) underwent surgery with adjuvant treatment, and 10 patients (33.3%) were offered chemotherapy and/or radiotherapy. On follow-up (27 patients, or 54%) over 1 to 144 months, 16 patients (59.2%) were alive with disease over median duration of 9 months, and 7 (25.9%) were free of disease over median duration of 26.5 months. There were 5 recorded deaths. Thirteen tumors (48.1%) metastasized, most commonly to liver. In cases with early stage disease and adjuvant treatment, including radiotherapy, LCNEC histology fared well. This study forms the largest documented series on cervical neuroendocrine carcinomas from our country, testifying the current histopathologic classification system. Although SMCAs can be recognized on morphology, LCNECs need to be correctly identified because these can be misdiagnosed in the absence of neuroendocrine markers. Synaptophysin, chromogranin, and CD56 are optimal IHC markers. Small cell carcinomas, pure or mixed, are relatively more aggressive. All these tumors are best treated with multimodal therapy. Early stage disease treated with radical surgery and adjuvant treatment seems to increase survival. Despite aggressive treatment, prognosis is dismal.

Molecular Biomarkers & Diagnosis Related Journals

- Advancements in Genetic Engineering
- Journal of Molecular and Genetic Medicine

For Upcoming Conferences

- http://www.conferenceseries.com/

OMICS Group **Open Access Membership**

OMICS publishing Group Open Access Membership enables academic and research institutions, funders and corporations to actively encourage open access in scholarly communication and the dissemination of research published by their authors.

For more details and benefits, click on the link below:

http://omicsonline.org/membership.php