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# Biphenotypic sinonasal sarcoma: A series of six cases with evaluation of role of β-catenin immunohistochemistry in differential diagnosis☆

Aanchal Kakkar[a], Madhu Rajeshwari[a], Pirabu Sakthivel[b], Mehar C. Sharma[a,*], Suresh C. Sharma[b]

[a] Department of Pathology, All India Institute of Medical Sciences, New Delhi 110029, India
[b] Department of Otolaryngology and Head and Neck Surgery, All India Institute of Medical Sciences, New Delhi 110029, India

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ABSTRACT

*Introduction:* Biphenotypic sinonasal sarcoma (BSNS) is a recently described mesenchymal tumor exclusive to the sinonasal region. It is a low grade sarcoma, displaying evidence of myogenic and neural differentiation. Role of β-catenin immunohistochemistry in distinguishing it from its morphological mimics is not well-established. We conducted this study to identify cases of BSNS from our archives, and to examine immunopositivity for β-catenin in them as well as in its close differential diagnosis.

*Methods:* All cases of nasal cavity and paranasal sinus mesenchymal neoplasms were identified. Histopathological features were reviewed. Cases showing smooth muscle actin (SMA) and S-100 immunopositivity, and typical morphology were reclassified as BSNS. β-catenin immunoexpression was assessed.

*Results:* Twenty-one mesenchymal tumors, including 12 sinonasal hemangiopericytoma (SNHPC), five solitary fibrous tumors (SFT), three BSNS, and one synovial sarcoma were identified. Three SNHPC cases were reclassified as BSNS. BSNS patients included one male and five females, with mean age of 51 years. Five BSNS cases (83.3%) showed nuclear β-catenin immunopositivity. SNHPC cases also were β-catenin positive (60%).

*Conclusion:* BSNS is a rare sinonasal neoplasm, frequently misdiagnosed as SNHPC and SFT. β-catenin immunopositivity is seen in majority of cases, indicating a role in pathogenesis. However, due to positivity in other tumors like SNHPC, it has limited role in differential diagnosis.

## 1. Introduction

Biphenotypic sinonasal sarcoma (BSNS) is a novel entity showing dual neural and myogenic differentiation that was recently added to the spectrum of mesenchymal neoplasms occurring in the nasal cavity and paranasal sinuses [1-4]. Its identification as a separate entity was supported by the presence of a distinctive genetic signature viz. t(2;4) resulting in fusion of PAX3 gene, which behaves as a regulator of neural crest and myogenic differentiation, with a variety of fusion partners [5,6]. Prior to this, these tumors were diagnosed as other benign or low grade mesenchymal tumors, including fibrosarcoma, malignant peripheral nerve sheath tumor (MPNST), myofibrosarcoma, and nerve sheath tumors, probably owing to immunopositivity of tumor cells with S-100 and smooth muscle markers [5,7]. Till date, approximately 36 cases of this tumor have been reported in literature [5,8-12]. However, there is no report of BSNS from the Indian subcontinent.

β-catenin is a protein encoded by the CTNNB1 gene, an integral part of the Wnt signalling pathway. Immunopositivity for β-catenin has been described in various mesenchymal neoplasms including fibromatosis, solitary fibrous tumor, and synovial sarcoma [13]. However, staining pattern for β-catenin has not been analyzed extensively in BSNS, with only one study till date [11]. We therefore conducted this study to identify cases of BSNS from our archives, and to perform β-catenin IHC in these tumors in order to assess its utility in differentiating from other sinonasal mesenchymal tumors.

## 2. Methods

All cases of nasal cavity and paranasal sinus mesenchymal neoplasms that were diagnosed over a period of 8 years (2009 to 2016) were identified from the archives of the Department of Pathology at our Institute. These included cases of BSNS, sinonasal hemangiopericytoma, solitary fibrous tumor, fibrosarcoma, MPNST and synovial sarcoma. HE stained slides were retrieved, along with formalin-fixed paraffin-embedded tissue blocks. Clinical information was obtained from the pathology requisition forms and retrospective chart review.

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* Corresponding author at: Department of Pathology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India.
*E-mail address:* sharmamehar@yahoo.co.in (M.C. Sharma).

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**Table 1**
Clinicopathological details of six patients with biphenotypic sinonasal sarcoma.

| Patient no. | Age/sex | Presenting features | Location | Treatment received | Initial pathology diagnosis | Follow up |
|---|---|---|---|---|---|---|
| Patient 1 | 65 years/male | Nasal obstruction, epistaxis | Right nasal cavity | Right lateral rhinotomy and excision; no adjuvant therapy | SFT | n/a |
| Patient 2 | 70 years/female | Nasal obstruction, epistaxis | Left nasal cavity and maxillary sinus | Biopsy; lost to follow-up | SNHPC | n/a |
| Patient 3 | 32 years/female | Epistaxis, nasal obstruction, sinusitis | Left nasal cavity, maxillary, ethmoid sinus, minimal extradural intracranial extension | Left lateral rhinotomy and excision; no adjuvant therapy | SNHPC | NED at 56 months; died of unrelated cause |
| Patient 4 | 42 years/female | Nasal obstruction, epistaxis | Left nasal cavity, maxillary and ethmoid sinus | Biopsy; refused treatment | BSNS | AWD at 18 months |
| Patient 5 | 52 years/female | Nasal obstruction, epistaxis, sinusitis, nasal mass | Right nasal cavity, maxillary, ethmoid, sphenoid, frontal sinuses, intracranial extension | Biopsy; refused treatment | BSNS | AWD at 10 months |
| Patient 6 | 45 years/female | Nasal obstruction | Right nasal cavity, ethmoid sinus, nasopharynx | Biopsy followed by Right lateral rhinotomy and excision | BSNS | Post- operative period uneventful |

AWD: alive with disease; BSNS: biphenotypic sinonasal sarcoma; NED: no evidence of disease; SFT: solitary fibrous tumor; SNHPC: sinonasal hemangiopericytoma.

Histopathological features were reviewed by three pathologists (AK, MR, MCS). Approval was obtained from the Institute Ethics Committee to conduct this study on patient tumor samples.

Immunohistochemistry (IHC) was performed using primary antibodies against smooth muscle actin (SMA), S-100, CD34, CD99 and bcl-2 by the streptavidin biotin conjugate immunoperoxidase method, as described previously [14]. Cases showing dual SMA and S-100 positivity were recognized as BSNS. β-catenin IHC was performed in all cases identified as BSNS, as well as in an equal number of cases of SNHPC for comparison.

## 3. Results

Twenty-one mesenchymal tumors were diagnosed during the study period. They included 12 SNHPC, five SFT, three BSNS, and one SS. Following immunohistochemistry for SMA and S-100, three of the 18 non-BSNS cases showed dual SMA and S-100 positivity and were re-classified as BSNS. The six BSNS patients ranged in age from 32 to 70 years (mean: 51 years; median: 48.5 years), and included 1 male and 5 females (Table 1). Of the 6 cases, two had previously been diagnosed as SNHPC and one as SFT. All patients presented with complaints of nasal obstruction. All six cases were located in the nasal cavities (Fig. 1). In Case 3, the tumor extended to the ethmoid sinus and base of skull.

On morphological evaluation (Fig. 2a–c), all the six BSNS cases were unencapsulated, poorly circumscribed tumors composed of spindle shaped cells arranged in short intersecting fascicles, and focally in storiform pattern. Cellularity was moderate. Tumor cells had uniform-appearing, elongated vesicular nuclei. They displayed minimal pleomorphism and infrequent mitoses, ranging from to 0–3/10 high power fields. The tumor cells were embedded in a collagenous stroma. Sparse inflammatory cell infiltrate was seen interspersed between the tumor cells, comprising of lymphocytes and mast cells. Staghorn vasculature was seen in two cases. Necrosis was not identified. Prominent epithelial invaginations of columnar epithelium were seen within the spindle cell proliferation in four cases (66.7%), all of which showed focal squamous metaplasia, mimicking squamous cell carcinoma. In three cases (50%), tumor cells were infiltrating bone. Rhabdomyoblastic differentiation was not seen. Diffuse SMA staining (Fig. 2d) was present in three cases (50%), and it was seen focally in three cases (50%). S-100 staining ranged from focal to diffuse (Fig. 2e). On β-catenin immunostaining, five of six BSNS cases (83.3%) showed diffuse and strong nuclear positivity (Fig. 2f). Of five cases of SNHPC on which β-catenin IHC was performed, three (60%) showed nuclear positivity. However, none of the other tumors showed β-catenin immunostaining.

Follow-up was available for four patients: Patient 3 was disease free for a period of 56 months, following which she developed tubercular meningitis and died of this disease. Patient 4 was alive with disease at last follow-up at 18 months, while Patient 5 was alive with disease at last follow-up at 10 months. Patient 6 was operated recently, and post-operative period was uneventful.

## 4. Discussion

Biphenotypic sinonasal sarcoma is a recently described low grade malignant mesenchymal neoplasm seen exclusively in the upper sinonasal tract [1-3]. It is characterized by infiltrating spindle shaped cells with minimal pleomorphism that exhibit immunopositivity for both SMA and S-100. Due to this, BSNS was first described by Lewis et al. as a low grade sinonasal sarcoma with neural and myogenic differentiation [5]. In their series, a strong female predilection was described, and majority of tumors were located in the nasal cavity and ethmoid sinuses [5]. We present our experience with six cases of BSNS. Similar to previous series, our patients had a mean age of 51 years [4]. The tumors were located in the nasal cavity and ethmoid sinuses, with extension to skull base in one case. In literature, extension to the cribriform plate has