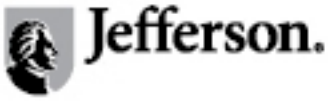

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Biphenotypic Sinonasal Sarcoma-Case Report and Review of Clinicopathological Features and Diagnostic Modalities.

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Title: Biphenotypic sinonasal sarcoma – Case report and review of clinicopathological features and diagnostic modalities

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Abstract

Background: Biphenotypic sinonasal sarcoma is a recently described malignancy showing dual differentiation with both myogenic and neural elements. Due to its histologic similarities to other sinonasal malignancies, it is a diagnostic challenge.

Objective: To report a case of Biphenotypic sinonasal sarcoma and to consolidate data and provide a comprehensive review regarding pathological differences between Biphenotypic sarcoma and other sinonasal malignancies and diagnostic modalities used for Biphenotypic sarcoma.

Material and methods: A systematic review of all cases of biphenotypic sinonasal sarcoma was performed using electronic databases (PubMed and Medline). Data collected included age, gender, symptoms, sub-site of origin, immunophenotyping, metastasis, recurrence, treatment, duration of follow up and survival outcomes.

Results: Ninety-five cases of biphenotypic sarcoma were found with mean age at diagnosis of 52.36 years (Range, 24-87 years). Female to male ratio was 2.27:1. Extra-sinonasal extension was present in 28%. Immunophenotyping revealed that S-100 and SMA were consistently positive while SOX-10 was consistently negative. PAX3-MAML3 fusion [t (2; 4) (q35; q31.1)] was the most common genetic rearrangement. Surgical excision with or without adjuvant radiotherapy was the most frequent treatment modality used. Recurrence was observed in 32% of cases with follow up. None of the cases reported metastasis. Three patients had died at the time of publication that included one case with intracranial extension.

Conclusion: Biphenotypic sarcoma is distinct sinonasal malignancy with unique clinicopathological features. Testing involving a battery of myogenic and neural immunomarkers is essential for diagnostic confirmation and is a clinically useful endeavor when clinical suspicion is high.

Introduction

Sinonasal malignancies are a diagnostic and therapeutic challenge due to the sheer histologic diversity and proximity to vital structures like the orbit, cranial nerves, and brain. Early diagnosis is often confounded by non-specific symptoms which can be mistaken for benign disease. In addition, there exists a considerable degree of histologic overlap among distinct sinonasal malignancies, making diagnosis on biopsy challenging. One of the most recent sinonasal malignancies described in the latest WHO edition of head and neck tumors is biphenotypic sinonasal sarcoma (BSNS).[1] The existence of this unique tumor was initially suspected based on earlier work,[2,3] followed by a few publications detailing clinicopathological features only recently reported.[4-10]

Perhaps, most characteristic of BSNS is the presence of both myogenic and neural differentiation. Pathologic descriptions of BSNS include a highly cellular spindle cell neoplasm with monomorphic picture on histology with S-100 and actin positivity on immunophenotyping. Additional pathological studies including immunophenotyping and fluorescent in situ hybridization (FISH) studies confirm the diagnosis. Clinically, the tumor is slowly progressive with a predilection for upper aero digestive tract. However, locally aggressive spread may occur in up to half of the affected patients.[4]

Most of the reported cases of BSNS have been isolated cases or small case series. Efforts are ongoing to consolidate all relevant data regarding BSNS with special emphasis on diagnostic modalities. Here we present a case of a patient treated for BSNS and review the current literature concerning this newly identified tumor, with emphasis on clinicopathologic features and diagnostic modalities.

Materials and methods:

An exhaustive literature review was performed using electronic databases (PubMed and Medline) and all relevant publications in English that included cases of BSNS were included. An additional manual search was performed by cross-referencing the retrieved cases. The following search terms were used:

"sinonasal", "sinus" "nasal", "biphenotypic" and "sarcoma". The first case of BSNS was described in 2012. Therefore, studies published before 2012 were excluded. Diagnosis of BSNS requires both pathological analysis and immunophenotyping of the sample. Cases with incomplete, insufficient, inconsistent diagnostic information and doubtful diagnosis were excluded. The following data were collected from all cases: age, gender, symptoms, sub site of origin, immunotyping, metastasis, recurrence, treatment, duration of follow up and survival outcomes at the time of publication of the respective case.

Case Report:

We report an otherwise healthy 53 year old gentleman who presented for evaluation of progressive unilateral nasal obstruction and anosmia for several months. Examination revealed a large left sided soft tissue mass. Imaging showed complete opacification of the left frontal sinus with bony erosion of the medial orbit and skull base. Office biopsy was most consistent with a low-grade spindle cell carcinoma, with immunohistochemistry stains positive for S100 and negative for actin, desmin, and neurofilament. Though initially, a peripheral nerve sheath tumor was one of the differential diagnosis, as the patient had no clinical features of Neurofibromatosis-1, it was unlikely. He was taken to the operating room for an endoscopic endonasal approach for resection of the tumor. Intraoperatively, the tumor was found to be highly vascular and locally invasive, with destruction of superior portions of the lamina papyracea and exposure of periorbita within the nasal cavity on the left side. Tumor was adherent to the periorbita and, given the presumed benign nature of the tumor, a small amount of residual tumor was left attached to the periorbita. There was further destruction of the superior septum and portions of the cribriform plate, with gross tumor within the right ethmoid cavity and abutting the right orbit. Frozen pathology specimens remained consistent with a spindle cell tumor. His postoperative course was uneventful.

Final pathology returned as Biphenotypic sinonasal sarcoma with focal rhabdomyoblastic differentiation. This BSNS was characterized by a moderate to highly cellular proliferation of spindle cells arranged in interwoven fascicles (Figure 1). Occasional staghorn vessels and focal bone infiltration by the tumor

(features not shown) were also present. The histologic appearance of the tumor was compatible with a low to, at most, intermediate grade lesion, reflecting the lack of mitotic activity or tumor necrosis, and the absence of significant cellular or nuclear pleomorphism. Based upon this histomorphology, the pathologic differential diagnosis included BSNS, schwannoma, solitary fibrous tumor and synovial sarcoma. In contrast to schwannomas, which classically display strong, diffuse S-100 staining, our tumor showed focal, patchy S100 positivity, a pattern commonly reported in BSNSs. Lack of cytokeratin (CAM5.2, cytokeratins 7 and 8) and CD34 staining in our tumor helped to rule out synovial sarcoma and solitary fibrous tumor, respectively. Additional immunohistochemical stains were positive for vimentin, and were negative for MELAN-A, HMB-45, and Calretinin. Lastly, the tumor displayed strong, widespread positive nuclear staining for MyoD1, which further supported the diagnosis of biphenotypic sinonasal sarcoma with rhabdomyoblastic differentiation. Furthermore, FISH analysis was performed which showed presence of PAX3-MAML3 fusion protein.

He was referred to both Radiation Oncology and Medical Oncology and underwent a PET-CT, showing no distant disease. He was again taken to the operating room for complete oncologic resection of the residual tumor which had intentionally been left attached to the left periorbita. The periorbita was resected via a transconjunctival orbitotomy, but the orbit, including the extraocular muscles, was spared. Margins were negative for tumor at the conclusion of the case. Again, recovery was uneventful. Multidisciplinary discussion was held, and the decision was made for adjuvant external beam radiotherapy (60 Gy in 30 fractions). Adjuvant chemotherapy was deemed unnecessary. He is doing well and free of disease at follow up.

Results:

Ninety-five cases of BSNS were documented in seven published reports.[4-10] Mean age at diagnosis was 52.36 years (range, 24-87 years). Female preponderance was noted (69%) with a female to male ratio of 2.27:1. On comparing the age distribution of patients, it was noticed that majority (27%) belonged to 5th decade (Table1). The most common symptoms observed were mainly related to mass effect of tumor

(Table 2). Out of twenty-eight cases in whom past history was recorded, four had a history of sinonasal surgery for presumed benign disease. In more than one-third of cases (37%), the site of origin was not clearly stated (Table 3). Of the rest, paranasal sinuses (PNS) were the most common site (30%), and ethmoid sinus was involved most frequently involved PNS, either alone or in combination with other PNS. Approximately almost one third of patients (28%) showed extra-sinonasal extension (Table 3). Mean size of the lesion was 3.95 cm. Radiological studies (reported in seven cases) revealed heterogeneous enhancing mass, hyperostotic bone formation (osteitis), and local destruction of lamina papyracea and skull base including cribriform plate. PET scans showed a low uptake (SUV max of 2.9).[5]

Pathologically, both neural and muscle immunomarkers were utilized to establish the diagnosis (Table 4). FISH studies were performed in 66% cases (Table 5). On analyzing the clinical differences between the classical and novel gene rearrangements, it was observed that novel mutations involving PAX 3 were more likely to occur in younger patients (median age 35 years), while double negative fusions were more common in older patients (median age 60 years), in comparison to classical genetic rearrangements (median age 47 years).[8] Additionally, the classical PAX3-MAML3 genetic rearrangement were more common in female as compared to male patients.[8] It is worth noting that 2 cases of PAX-NCOA1 fusion protein and one case of PAX-FOXO1 fusion protein showed a distinctive rhabdomyoblastic differentiation[6,7] while cytogenetic analysis of the 3 remaining cases of rhabdomyoblastic differentiation and one case of fibroblastic differentiation was not performed.[4,5] Cytogenetic analysis were performed in 2 other cases which reveled t(2,4) translocation.[4] Reverse transcriptase-polymerase chain reaction (RT-PCR) for synovial sarcoma fusion transcripts (SYT-SSX1 AND SYT-SSX2) was negative in all cases tested (21 cases).[4,10]

Among cases with reported treatment (8%, 8 cases), surgical excision with or without post-operative radiotherapy was the most common modality used (Table 6). After completion of the treatment, 36% (34/95) were followed for a mean duration of 4.61 years (range, 3 months - 28 years). Recurrence was

observed in 32% (11/34) for whom follow up data was available, out of which 82% were females with a mean age of 49 years (Range, 24-69 years). Though primary disease was more common in PNS (Table 3), 64% of cases who showed recurrence had primary disease of nasal cavity, either alone or with PNS involvement (Table 7). None of the cases reported metastasis. The average duration until appearance of recurrence was 2.4 years. An additional patient showed evidence of disease on imaging at one year follow-up which was suspected to be residual disease.[8]

On follow up, it was noticed that three patients had succumbed to disease, and all three were reported to have developed recurrence. One of these cases had evidence of recurrence twice during the duration of follow up, once at 2 years and the next at 4 years after completion of primary treatment.[9] Intracranial involvement was present during the second recurrence and patient expired 8 months after diagnosis of the same. Non-tumor-related causes were reported for the other two cases.[4]

Discussion:

The most distinctive feature of BSNS is the presence of dual differentiation with both myogenic and neural elements. Owing to low mitotic rate of the spindle cells present, it is also known as low-grade sarcoma or spindle cell sarcoma.[11] In some cases, as with our patient, rhabdomyoblastic differentiation (11%) has also been reported.[6,7,12] In one of the cases of BSNS, fibroblastic differentiation has been observed[5] and it is currently unknown whether fibroblastic differentiation is a precursor to myogenic differentiation or whether it represents a distinct subset of patients with BSNS with unique local cellular factors leading to fibroblastic differentiation.

Another distinctive pathological feature is the entrapment of hyperplastic respiratory epithelium leading to gland or cyst formation (so-called “pseudo-gland formation”) seen in 70% cases. In addition, hyper-cellularity, bone invasion (20%), hemangiopericytoma-like staghorn vessels, overlapping cells,

herringbone patterns have been documented.[13] Although, some of these pathological characteristics of BSNS are distinct, none are exclusive to BSNS.

A variety of sinonasal malignancies, including cellular schwannoma (CS), low grade malignant peripheral nerve sheath tumor (LG-MPNST), leiomyosarcoma (LMS), fibrosarcoma (FS), synovial sarcoma (SS), glomangiopericytoma (GPC), solitary fibrous tumor (SFT), inverted papilloma (IP), fibromatosis and malignant melanoma, may pathologically mimic BSNS. The differentiating pathological characteristics of BSNS in comparison to other common sinonasal malignancies has been depicted below (Table 9).[4,14,15] However, diagnosis of BSNS based on pathological features alone is not possible due to the potential for pathological overlap. Therefore, immunophenotyping is a pre-requisite for diagnosis.

Immunophenotypical analysis reveals that S-100 (neural marker) and SMA (myogenic marker) are consistently positive in BSNS while, SOX-10 (neural crest differentiation marker) is consistently negative.[6] Comparison of immunomarkers of BSNS with other sinonasal tumors (Table 8) reveals the differences in distribution of these markers.[16-24] Due to patchy distribution of some of these markers, one of the major pitfalls of immunophenotyping is a missed diagnosis of BSNS owing to small sample size or sampling errors. However, analyzing the overall morphological picture helps to narrow down the differential diagnoses. For instance, in our case, triton tumor (variant of MPNST) was one of the closest differentials. Though these tumors exhibit common immunomarker positivity, histologically MPNST exhibits a high mitotic rate and often tumor necrosis. BSNS on the other hand, displays a low to, at most, intermediate grade histology with a low (in this case 0%) mitotic rate and an absence of tumor necrosis. Additionally, the patient had no features of Neurofibromatosis-1 on clinical exam.

Molecular studies, mainly the FISH analysis, are a new addition to the list of diagnostic modalities used for BSNS. In some cases, determination of a particular genetic aberration can confirm the diagnosis of BSNS. PAX3-MAML3 fusion [t (2; 4) (q35; q31.1)] is a classical fusion protein found in 79-96% of

cases.[11,13] In fact, our case is the first case of PAX3-MAML3 fusion protein positive BSNS with rhabdomyoblastic differentiation. PAX 3 rearrangement is a characteristic finding, as it has not been seen in any other sinonasal malignancy. It is the most frequent genetic rearrangement described in BSNS. PAX-3 is a transcription factor, which stimulates commitment along both neural crest and skeletal muscle cell lines, and blocks terminal differentiation.[2,25-28] It also has a significant role in nasal development. In difficult cases, in order to determine the histopathological diagnosis, the absence of a genetic aberration can also help in the diagnosis of BSNS. For instance, monophasic synovial sarcoma (SS) cannot be differentiated conclusively from BSNS on pathological or immunophenotypic analysis. In such cases, absence of a SS18 translocation on molecular studies confirms the diagnosis of BSNS as this translocation is required for SS.[4,11]

However, molecular studies too, are not without pitfalls. Though a large number of BSNS exhibit the classical PAX3-MAML3 rearrangement, a subset of biphenotypic sinonasal sarcomas show no PAX3 or MAML3 involvement (Table 5). Therefore, reports of FISH analysis need to be read with caution. In fact, several novel genetic rearrangements seen in BSNS have been recently defined (Table 5).[11] Therefore, owing to the absence of immunophenotyping and lack of appropriate molecular studies in the past, there is a possibility that a majority of the cases of BSNS have been incorrectly labelled as other sinonasal tumors. Therefore, it would not be surprising if the prevalence of genuine BSNS is larger than reported.

When compared to other head and neck sarcomas , BSNS is seen to be clinicopathologically distinct.[5,12,29-33] Interestingly, alveolar rhabdomyosarcoma, which is often characterized by a high metastatic potential and worse prognosis, shares a similar genetic aberration (involving PAX 3 gene) as compared to BSNS.[8,34] Difference in the cell of origin and its microenvironment could be the reason for the stark clinicopathological dissimilarities between the two malignancies.[8,35] In this context, it is essential to determine if BSNS truly represents a sarcoma or is a sarcomatous variant of a fibrous tumor. In addition,

further studies are required to investigate the molecular basis and cellular factors leading to the formation of this tumor.

Clinically, BSNS is generally considered to behave less aggressively than other more common sinonasal malignancies such as sinonasal undifferentiated carcinoma or poorly differentiated squamous cell carcinoma. As with the case presented here, treatment regimens may be consequently de-escalated (e.g. treated with adjuvant radiation alone, rather than with adjuvant chemoradiotherapy) in appropriate cases. However, given the paucity of information on treatment among published cases, very little can be conclusively suggested regarding optimal treatment modality. Therefore, it is suggested that future case reports on BSNS should include complete treatment details for meaningful comparison between different treatment strategies.

Conclusion:

BSNS is distinct sinonasal malignancy with dual differentiation. Its clinical behavior, pathological features, immunophenotypic presentation, standard of care and prognostic outcomes are entirely different not only from other non-sarcomatous sinonasal malignancies, but also from other head and neck sarcomas.

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Figures:

Figure 1: Histological features of Biphenotypic sinonasal sarcoma (BPSS). (A) The tumor exhibits a proliferation of uniform spindle cells in fascicles arranged in a herringbone pattern (hematoxylin-eosin stain, original magnification x400). (B) The tumor cells show focal patchy S100 expression, which supports a diagnosis of BPSS (anti-S100, original magnification x400). This immunophenotype differs from the diffusely positive S100 expression that would be expected in a Schwannoma. (C) The tumor displayed rhabdomyosarcomatous differentiation, as evidenced by the strong, focal, nuclear MyoD1 expression (anti-MyoD1, original magnification x400; insert x1000).

Tables:

Table 1: Details of age distribution

Age at diagnosis	**N (%)**
Less than 20 years	00 (00.00)
21-30 years	03 (03.15)
31-40 years	11 (11.57)
41-50 years	26 (27.36)
51-60 years	11 (11.57)
61-70 years	11 (11.57)
71-80 years	05 (05.26)
81-90 years	03 (03.15)
Unknown	25 (26.31)
Total	95 (100.0)

Table 2: Details of frequently reported clinical symptoms

Nasal complaints	Nasal obstruction, rhinorrhea (may be purulent), Anosmia, Nasal congestion, Recurrent epistaxis
Sinus complaints	Frequent sinus infections refractory to antibiotics, facial pain, facial discomfort/pressure, supra orbital swelling
Ophthalmological complaints	Diplopia, proptosis, Blurred vision, periorbital pressure, epiphora
Oral complaints	Dysgeusia

Table 3: Details of site of origin of tumor in the sinonasal area and extra-sinonasal extension

Site	**Sub site**	**N (%)**
Nasal Cavity (NC)	Septum	02
	Lateral wall	02
	Unknown	14
	Total	**18 (18.94%)**
Paranasal sinuses (PNS)	Ethmoid	15
	Frontal	04
	Sphenoid	01
	Maxillary	00
	Ethmoid + Frontal	05
	Ethmoid + Sphenoid	01
	Unknown	03
	Total	**29 (30.52%)**
Nasal cavity and paranasal sinuses	NC + Ethmoid	09
	NC + Frontal + Ethmoid	03
	NC + Sphenoid	01
	Total	**13 (13.68%)**
Unknown	**Unknown**	**35 (36.84%)**
Site of extra-sinonasal extension (ESE)		
Orbit	12 (44.44%)	
Cribriform plate / Skull base	10 (37.03%)	
Intracranial	04 (14.81%)	
Oropharynx	01 (03.70 %)	
Total*	**27 (100.0%)**	

* The total number of cases with extra-sinonasal extension (ESE) could be lower than this number as occasionally the same patient has ESE in different sub-sites. For instance, one of the patients[10] had ESE to 3 different sub sites- orbit, skull base and intra cranial area.

Table 4: Details of Immunophenotyping studies

Markers/Ref.	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**	**%**
S-100	28/28	1/1	7/7	1/1	42/43	11/11	3/3	93/94	98.93
SMA	23/25	0/1	5/5	1/1	39/42	11/11	3/3	82/88	93.18
MSA	14/16	0/1	4/4				0/1	18/21	85.71
Beta catenin		1/1				10/11		11/12	91.66
EMA	3/19	0/1		0/1			0/1	3/22	13.63
Myo-D1			3/7		11/33			14/40	35.00
Myogenin / Myf4		0/1	1/7	1/1	2/23	3/10	0/1	7/43	16.27
Desmin	4/20	0/1	4/7	1/1	16/36	4/11	2/3	31/79	39.24
Keratin	2/22	0/1	2/5				0/2	4/30	13.33
CD34	5/21		1/5				0/2	6/28	21.42
SOX10			0/7			0/11	0/1	0/18	00.00
Vimentin		1/1						1/1	100.0
h-Caldesmon		1/1						1/1	100.0
Factor XIIIa						8/10		8/10	80.00
Calponin			1/1					1/1	100.0
TLE1				1/1				1/1	100.0
ER/PR		0/1						0/1	00.00

*Each box denotes the proportion of positive cases for that particular immunomarker. The numerator denotes the number of positive cases while the denominator denotes the number of cases tested.

Table 5: Details of FISH analysis

Sl. No	**Types of rearrangements / References**		**6**	**7**	**8**	**9**	**N (%)**
1	*Classical rearrangement* (PAX3-MAML3)		4		24	5	33 (52.38%)
2	*Novel rearrangements* (Either PAX3 or MAML3)	PAX3-FOXO1		1	3		04
		PAX3-NCOA1	2		1	1	04
		PAX3-X	1		11	2	14
		MAML3- X			1		01
	Total						23 (36.5%)
3	*Double negative* (Both PAX3 and MAML3 absent)				4		04 (6.34%)
4	*Failed testing / Tissue not available*					3	03 (4.76%)
Total			7	1	44	11	63 (100%)

Table 6: Details of treatment modalities utilized

Treatment of primary disease			
1	Open approach	Cranial (Anterior) skull base resection[10]	01
2	Endoscopic anterior skull base resection	with cerebrospinal fluid (CSF) leak repair and frozen section of dural margins[5]	01
		With adjuvant chemoradiotherapy[7]	01
		with lamina papyracea excision[10]	01
3	Surgical treatment	With adjuvant chemoradiotherapy[6]	01
		No additional details available[8]	01
4	Orbital exenteration[9]		02
5	Treatment pending[10*]		01
6	Details not known[4,6,8,9]		86
Treatment of recurrence			
1	Open approach (Extended Craniofacial resection)	Without adjuvant radiotherpay[4]	02
		With orbital exenteration and adjuvant radiotherapy[4]	01
2	Endoscopic anterior skull base resection	With dura resection and frozen section of dural margins with CSF leak repair [10]	01
3	Details not known[4,6,9]		07

*As patient had severe aortic stenosis, treatment was pending at the time of publication as patient had undergone valve replacement surgery.

Table 7: Details of cases which developed recurrence

Sl. No	Reference	Age (Years)	Gender	Site of primary	Time of recurrence	Outcome
1	4	52	F	PNS (F / E)	NK	I
2	4	69	F	NC	NK	D
3	4	69	M	NC / PNS (E)	NK	D
4	4	38	F	NC / SB	NK	F
5	4	47	F	PNS (E) / SB	NK	I
6	4	24	F	PNS (E / S)	NK	I
7	4	45	F	NC / SB	NK	F
8	6	46	F	NC (Septum)	36 months	F
9*	9	39	F	PNS (F)	24 and 48 months	D
10	9	46	F	NC (Septum)	36 months	F
11	10	67	F	NC / PNS (F / E)	17 months	F

* Recurrence was seen twice.

I =Inadequate follow up after treatment of recurrent disease; F: Free of disease at last follow up after treatment of recurrence; D: Dead at the time of last follow up; NC: Nasal cavity; PNS: Paranasal sinuses; E: Ethmoid sinus; F: Frontal sinus; S: Sphenoid sinus; SB: Skull base.

Table 8: Comparison of distribution of immunomarkers between BSNS and other sinonasal malignancies

	BSNS	CS	LG-MPNST	LMS	FS	SS	GPC	SFT
SOX -10	-	+/-	+					
Beta catenin	**+(F,W)**	-	-	-	-	+(F)/-	+(D,S)	
S100	**+(D/F)**	+(D)	+(F)	-	-	+/-	-	-
Myogenin	+	-	-(+)*	+(D)		+/-	-	
Factor XIIIa	+					-		
Desmin	**+/-(MF/P)**	-	-(+)*	+(D)			-	
SMA	**+(MF/P)**	-	-(+)*	+(D)	-	+/-		-
CK (AE1/AE3)	**+/-(F)**					+(F)		
TLE 1						+		
EMA	**+/-(F)**					+(F)/-		
CD34	**+(F)**							+(D,S)
STAT6								+
h-Caldesmon	**+(D)**	-						
MSA	**+(MF/P)**							
SS18-SSX fusion	-					+		

CS: Cellular Schwannoma; LG-MPNST: Low grade malignant peripheral nerve sheath tumor; LMS: Leiomyosarcoma; FS: Fibrosarcoma; SS: Synovial sarcoma GPC: Glomangiopericytoma; SFT: Solitary fibrous tumor; W: Weakly positive; S: Strongly positive; MF: Multifocal; D: Diffuse; P: Patchy; S: F: Focal; +: Positive; -: Negative; + / _: Positive or negative;

*Positive if rhabdomyoblastic differentiation present (Triton tumor)

Table 9: Comparison of pathological characteristics of BSNS with other similar sinonasal malignancies

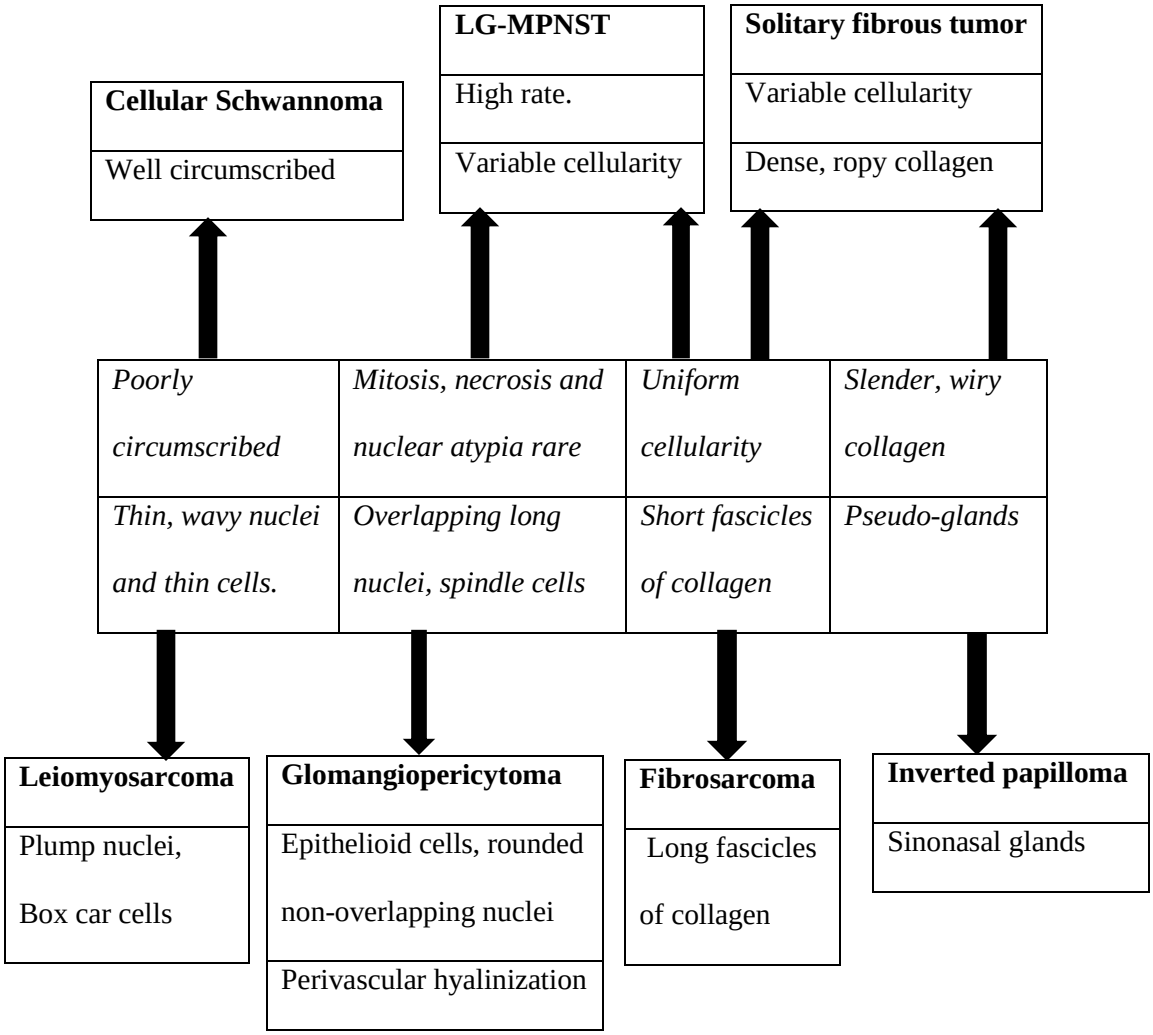

Table 9: It depicts comparison of pathological features between BSNS and its differential diagnosis. The inner central table denotes BSNS and the outer tables on both sides denote other sinonasal malignancies. Each characteristic in the central table highlight the starkly dissimilar features in BSNS in comparison to other malignancies. LG-MPNST: Low-grade malignant peripheral nerve sheath tumor