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Pathology

NTRK- Rearranged Spindle Cell Neoplasm-A Rare Sinonasal MPNST Mimicker

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Abstract **Case Report**

NTRK- rearranged spindle cell neoplasms (NTRK- RSCNs) are rare soft tissue tumor molecularly characterized by NTRK gene rearrangement, which occur mostly in children and young adults, and rarely in adults. They predominantly occur in the extremities, head and trunk regions and may present as superficial or deep tumors. In this case, we report a malignant NTRK- RSCN that occurred in right nasal cavity of an adult. The patient was found to have a nasal obstruction with a clinical diagnosis of nasal polyposis. Pathological diagnosis was malignant spindle cell neoplasm. Immunohistochemistry of this patient showed positive S100, CD34 and p16 with negative SMA, SOX10, Beta catenin, STAT6.

Keywords: NTRK-rearranged spindle cell neoplasm, Soft tissue sarcoma, Nasal cavity, Immunohistochemistry, S100, CD34.

INTRODUCTION

Neurotrophic tyrosine kinase receptor kinase - rearranged spindle cell neoplasms (NTRK-RSCNs) are defined as an emerging entity of tumours according to the 5th edition of the World Health Organization (WHO) Classification of Soft Tissue and Bone Sarcomas [3]. NTRK fusions are pathogenetic alterations associated with various cancer types including papillary thyroid cancer, soft tissue sarcoma, colorectal cancer, glioma and spitz tumor [1,2]. Most NTRK-RSCNs entities are of low-grade, while a few cases display a higher-grade with markedly increased cellularity arranged in intersecting fascicles and a high mitotic count. Histologically, NTRK-RSCNs show a wide morphologic spectrum, usually with co-expression of CD34 and S100 and diffuse pan-TRK immunoreactivity [1, 4].

In this article, we report our diagnosis of an adult NTRK-RSCNs in nasal cavity by the clinical, imaging, histopathological, and immunohistochemistry characteristics, illustrating the role of integrated pathological diagnosis in rare and difficult tumors.

CASE REPORT

A 62- year- old female presented with complaints of right sided nasal obstruction for 3 months which was insidious in onset and gradually progressive with no aggravating and reliving factors. Her medical and family history was unremarkable.

On examination a smooth, pale, polypoidal globular mass is occupying the right nasal cavity and extending towards the posterior choana.

Investigation results were as follows:

CT PNS shows right nasal polyposis showing mass effect on the medial wall of right maxillary sinus and posterior nasal septum. (Fig.1)

During functional endoscopic sinus surgery, the lesion was firm and atypical for a nasal polyp and biopsy was performed.

Microscopically, tissue is lined by pseudo stratified ciliated columnar epithelium. Sub epithelium showed a spindle cell neoplasm arranged in fascicular, interlacing and focal storiform pattern. Tumor cells are

pleomorphic with vesicular to hyperchromatic wavy tapering nuclei, indistinct cytoplasm. Mitotic figures (o-2/ HPF), necrosis and hemorrhage were noted. Adjacent foci show fibro collagenous tissue, seromucious glands and chronic inflammatory cell infiltrate. (Fig.2)

Immunohistochemistry revealed S100, CD34 and p16 positivity. SMA, SOX10, Beta catenin, STAT6 negative. (Table.1) (Fig.3)

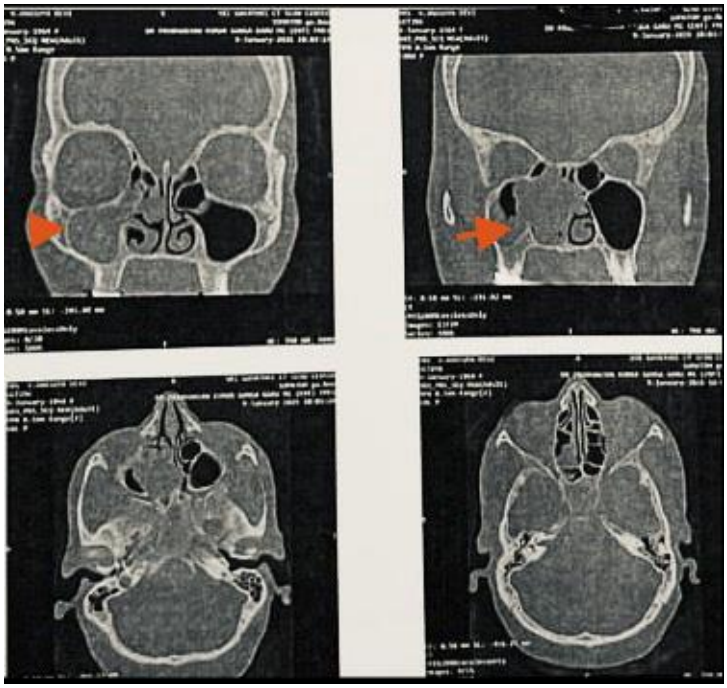

Fig. 1: CT PNS showing right nasal polyposis with mass effect on the medial wall of right maxillary sinus and posterior 1/3rd nasal septum

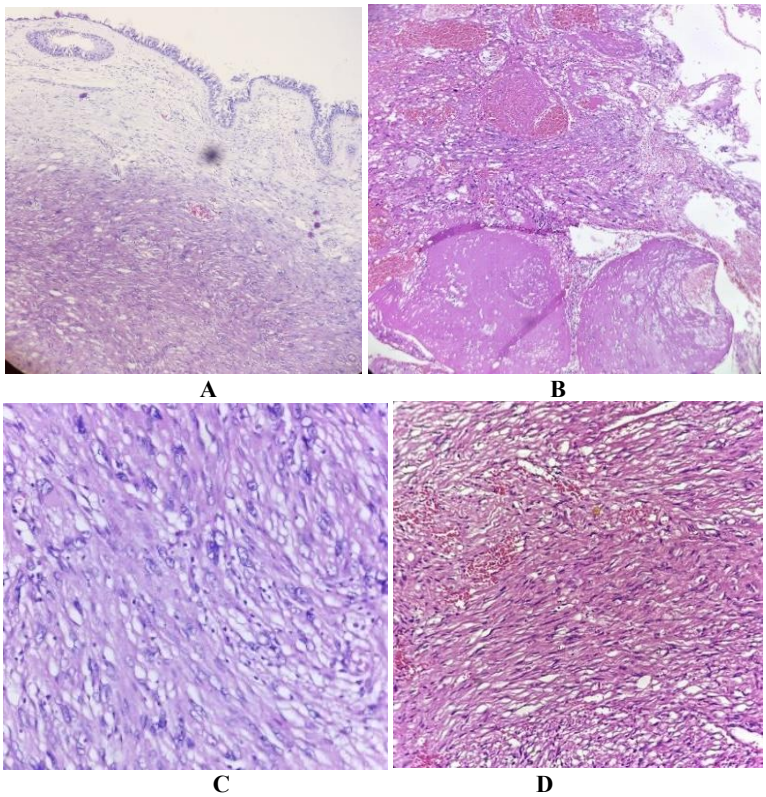

Fig. 2: Microscopy shows tissue sections lined by ciliated columnar epithelium(40X) (A) with underlying tumor having spindle shaped cells (40X) (B) with pleomorphic nuclei(1000X) (C) with areas of hemorrhage and necrosis(1000X) (D)

Table 1: Immunohistochemistry shows tumor cells positive for S100, CD34 and p16

MARKER	RESULT
S100	Positive
SMA	Negative
KI-67%	3%
CD34	Positive
P16	Positive
STAT6	Negative
TLE1	Negative

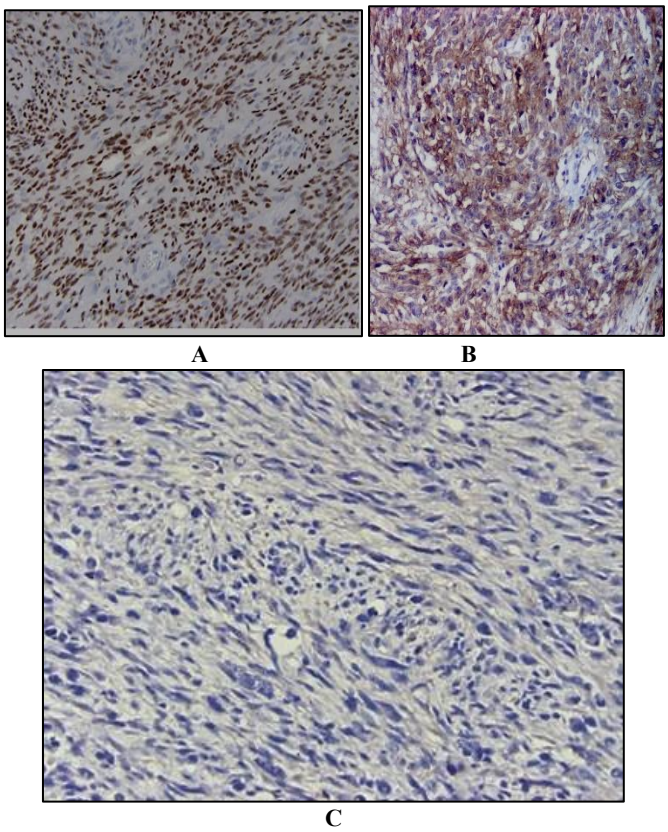

Fig. 3: Immunohistochemistry for s100-positive (a), CD34- positive (b), SMA- negative (c)

DISCUSSION

In the 2020 WHO classification of soft tissue tumors, NTRK -RSCNs was described as the new soft tissue sarcoma with multiple morphologic, histologic gradations and extensive clinical aggressiveness, with NTRK fusions as an important molecular characteristic feature [3]. However inflammatory myofibroblast tumors (IMT) [5], infantile fibrosarcoma's (IFS)[6], gastrointestinal stromal tumors (GIST) [7] reported with NTRK fusions poses a challenge to the differential diagnosis of NTRK -RSCNs, especially in the absence of adequate morphological, immunohistochemical characterization.

Histologically NTRK -RSCNs consists of spindle shaped cells which are highly infiltrative with monomorphic spindle cell population with haphazard arrangement [8], few cases show zoned appearance [11].

Immunohistochemically, NTRK -RSCNs shows co- expression of S100 protein and CD34 frequently [3]. In this case tumor cells are positive for CD34, p16 and focally positive for S100. Qiurui Cao et.al [9] reported adult NTRK -RSCN in the pelvis. Overfield CJ et. al [10] reported NTRK-rearranged spindle cell neoplasm of the lower extremity. NTRK -RSCNs in sinonasal cavity is extremely rare and challenging for diagnosis.

The close differential diagnosis of NTRK -RSCN are malignant peripheral nerve sheath tumour which shows marbled appearance with Uniform spindle cells with hyperchromatic, thin, wavy nuclei arranged in fibrosarcoma like growth pattern with foci of myxoid stroma, hyalinization and necrosis in high grade tumours. Immunohistochemically MPNST shows patchy positivity for S100 and SOX10 and negative for CD34. whereas NTRK -RSCN shows positive for S100, CD34 and negative for SOX10. Sometimes immunohistochemically they are difficult to

differentiate, on molecular studies NTRK gene fusions can be detected in NTRK -RSCN

Other differential diagnosis includes Spindle cell sarcoma, not otherwise specified which is seen most commonly in older individuals (> 50 years) and immunohistochemically negative for CD34, S100.

Tumour behaviour is related to the histologic grade and tumours with aberrant expression of tyrosine kinase receptors are therapeutically targetable resulting in improve patient outcomes.

CONCLUSION

NTRK- rearranged spindle cell neoplasm is a rare sinonasal tumor that can mimic MPNST. Correlation of morphology and immunohistochemistry is important for accurate diagnosis.

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