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Sarcomatous Transformation In A Recurrent Radiation-Naive Nasopharyngeal Angiofibroma: A Rare Entity

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Abstract

Nasopharyngeal angiofibroma (NA) is a histologically benign but locally aggressive, highly vascular neoplasm predominantly occurring in adolescent males. NA accounts for 0.05% of all head and neck tumors and may extend into surrounding structures. Treatment modalities include surgery, radiotherapy, and hormonal therapy. Occasional cases of sarcomas developing in patients receiving radiotherapy have been reported; however, sarcomatous transformation of radiation naive NA is extremely rare. We report a case of recurrent nasopharyngeal angiofibroma following surgery. Histopathological examination revealed sarcomatous transformation in a radiation-naive nasopharyngeal angiofibroma.

A 46-year-old male presented with complaints of on-and-off bilateral nasal block, an unprovoked nose bleed, and a change in voice over the past year. On elaborating on past history, the patient had undergone surgery for a nasopharyngeal tumor in 2015. A review of the previous slides in our institute confirmed the diagnosis of nasopharyngeal angiofibroma and ruled out any concomitant malignancy. The patient had no history of radiation exposure in the past. On further evaluation, rhinoscopy and Contrast enhanced-MRI (CE-MRI) showed a right nasopharyngeal mass lesion. Based on the histomorphology and immunohistochemistry, a diagnosis of Embryonal Rhabdomyosarcoma in a background of Nasopharyngeal Angiofibroma was favored

Sarcomatous transformation in angiofibroma is a rare finding. In radiation-naive patients, this entity is even rarer. The detection of malignant transformation in relatively benign neoplasms requires extensive sampling. Given the rarity of sarcomatous transformation in radiation naive NA, awareness of this entity is needed to aid in diagnosis.

Keywords: Nasopharyngeal Angiofibroma; Sarcoma ; Radiation ; Recurrent

Introduction

Nasopharyngeal angiofibroma (NA), also known as angiofibromatous hamartoma, or juvenile nasal angiofibroma, is a histologically benign but locally aggressive, highly vascular neoplasm predominantly affecting adolescent males.[1] The site of origin for this locally aggressive neoplasm is highly debatable,

as some claim it originates from the posterior nasal cavity and sphenopalatine foramen, whereas others claims its origin is in the nasopharyngeal and choanal regions. [2] NA accounts for 0.05% of all head and neck tumors and may extend into the surrounding structures; evidence of bony erosion in NA is also widely reported in medical literature.[3] Pre-operative embolization is done for all cases of NA except for very small lesions, followed by various other treatment modalities ranging from surgery, radiotherapy and hormonal therapy. [4] Occasional cases of sarcomas developing in patients receiving radiotherapy are reported; however, sarcomatous transformation of radiation-naive NA is extremely rare.[5,6] In our case, we report sarcomatous transformation in an elderly male who was previously treated by surgery alone but developed recurrence and was again treated surgically. Histopathology revealed transformation from an angiofibromatous area to an area with a high mitotic count and small round blue cells. Immunohistochemistry confirmed a sarcomatous transformation in NA.

Case Report:

A 46 year old male presented to the OPD with complaints of insidious onset bilateral nose block and unprovoked nose bleed for a duration of 1 year. There were no complaints of visual disturbance or headache; however, the patient complained of a change in voice, which was also insidious in onset and gradually progressive in nature. On elaborating the past history, the patient had undergone surgery for a nasopharyngeal tumor in 2015, which was reported as a nasopharyngeal angiofibroma. Review of the previous slides also confirmed the diagnosis of nasopharyngeal angiofibroma and ruled out any concomitant malignancy. The patient had no history of radiation exposure in the past. Rhinoscopy revealed an irregular, fleshy, polypoidal, reddish-brown mass obstructing the nasal cavity. Based on the present complaints and recurrence, contrast-enhanced magnetic resonance imaging (CE-MRI) of the nose and para-nasal sinuses (PNS) was advised. CE-MRI showed a large heterogeneous right nasopharyngeal mass lesion measuring 5.1x3.8x3.2 cm in its main cranio-caudal (CC) and axial diameters, respectively. The lesion showed heterogeneously hypointense T1 and hyperintense T2 signals with intense heterogeneous post-contrast enhancement and encroached upon the right para-pharyngeal fat planes and displaced them posterolaterally (Figs. 1a,b). Endoscopic excision of the tumor was performed. A specimen labeled "nasopharyngeal mass" was received by the histopathology department. Gross examination revealed multiple grey-white to reddish irregular soft tissue bits measuring approximately 4.3 x 3.5 x 2.4 cm. Multiple sections of the tumor revealed tissue bits lined by pseudo-stratified columnar respiratory epithelium. Underlying sub epithelium showed multiple infiltrative tumor foci with tumor cells arranged predominantly in nests with pleomorphic tumor cells, which are round-oval in shape with scant cytoplasm, coarse chromatin, and inconspicuous eosinophilic nucleoli (Fig 2 a,b). The tumor foci also revealed multiple atypical mitoses (7/10 hpf). Also noted were areas that showed blood vessels of various calibers admixed with spindle cells with ovoid-elongated nuclei and a moderate amount of eosinophilic cytoplasm reminiscent of angiofibromatous origin (Figs. 3 a,b). Based on light microscopy findings, a diagnosis of malignancy arising in a previously diagnosed and treated case of angiofibroma was considered. However, a battery of immunohistochemistry (IHC) markers was utilized to further categorize the neoplasm. The tumor cells were positive for desmin, myogenin (Fig. 4a), and MyoD1 (Fig. 4b). Vimentin and SMA were positive in angiofibromatous areas. Pan CK, LCA, Synaptophysin, S100, CD99, FLI 1, BCL2, EMA, Melan A, and HMB45 were negative, which helped us rule out a long list of differentials.

Based on the clinical history, radiology findings, histomorphology, and immunohistochemistry, a diagnosis of Embryonal Rhabdomyosarcoma with a background of Nasopharyngeal Angiofibroma was preferred. The patient was advised surgical removal of any residual tumor as well as a multi-drug chemotherapy and radiotherapy regimen; however, the patient refused treatment and was lost to follow up.

Discussion :

Nasopharyngeal angiofibromas are histologically benign, locally aggressive, highly vascular, and variably cellular soft tissue neoplasms found in young adolescent and prepubescent males; however, isolated case reports in middle-aged and even elderly males are prevalent in the medical literature.[7] NA

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as a disease is almost entirely a disease of males; however, in a female presenting with NA, a thorough evaluation of testicular feminization is a must.[8] In view of the sex and age distribution, NA is considered to be a hormone-dependent neoplasm, and the frequent expression of androgen receptors in the neoplastic cells also substantiates this fact.[9] NA are notoriously recurrent neoplasms; *Reyes et al.* in their meta-analysis encompassing nine studies where NA was treated by endoscopic or open surgery, showed a recurrence rate of 24.5%, whereas *Sun et al.* reported a recurrence rate of 39.2%. [10,11] Multiple staging systems developed by multiple groups staged NA based on whether the tumor was localized, involved adjacent structures, or there was the presence of distant metastasis, which ultimately might guide patient management. [12]

In our patient, the first episode of this disease was managed by preoperative embolization followed by surgical resection, which remains the mainstay of treatment in low-grade NA. External beam radiotherapy may be used as a primary treatment in high-grade tumors as well as in patients with residual tumors. [12,13].Although radiotherapy serves as a therapeutic modality, most of the secondary neoplasms developing in NA were preceded by radiotherapy. [5,14]Hence Sarcomatous transformation in angiofibroma, although a rare entity, is a definite possibility in patients who were treated by radiotherapy. [14]

In our case, however, the patient had no history of radiation exposure as a treatment modality or any occupational exposure to radiation. *Allenswoth JJ et al.* reported the first case of high-grade malignant transformation in a radiation-naive angiofibroma. [15] Reporting NA in a radiation-naive individual opens up the possibilities for medical research into various other hidden etiologies that may be responsible for such a high-grade transformation in a relatively benign neoplasm.

Conclusion :

Nasopharyngeal angiofibroma, though considered a tumor of adolescent males, may occur in any age group and slowly show transformation into a malignant neoplasm. Sarcomatoid transformation needs thorough sampling, and combined radiology, histopathology, and immunohistochemical findings are a must to categorize this high-grade malignant transformation. Given the rarity of sarcomatous transformation in radiation naive NA, awareness of this entity is needed to aid in diagnosis.

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Compliance with Ethical Standards

Research involving human Participants and/or animals :

1. Statement on Human rights : The case was reported in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its latter amendments or comparable ethical standards.
2. Statement on the welfare of animals : This article does not contain any studies with animals performed by any of the authors.

Informed Consent **:** A written informed consent was taken from the patient and all efforts to respect patient confidentiality was maintained. No extra investigation or procedure except the ones needed for patients well being was carried out. In accordance with the Institutional Ethics Committee policy for case reports no formal consent is required.

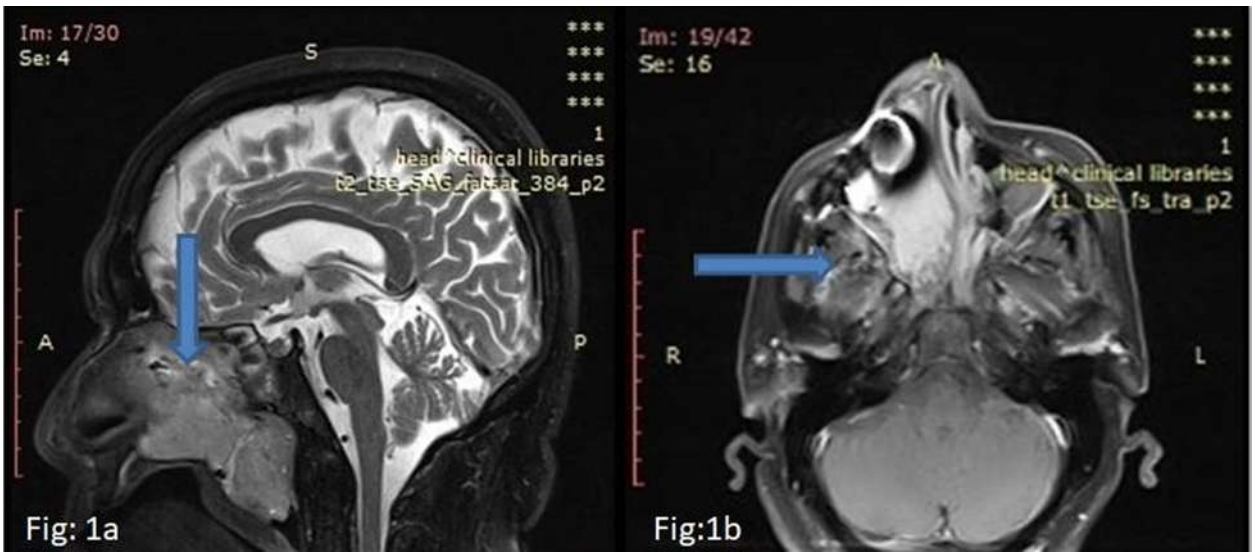

Fig. 1a,b CE-MRI shows a large heterogeneous right nasopharyngeal mass lesion measuring 5.1x3.8x3.2 cm in its main cranio-caudal and axial diameters. The lesion encroaches upon the right para-pharyngeal fat planes and displaces them posterolaterally s/o malignant etiology.

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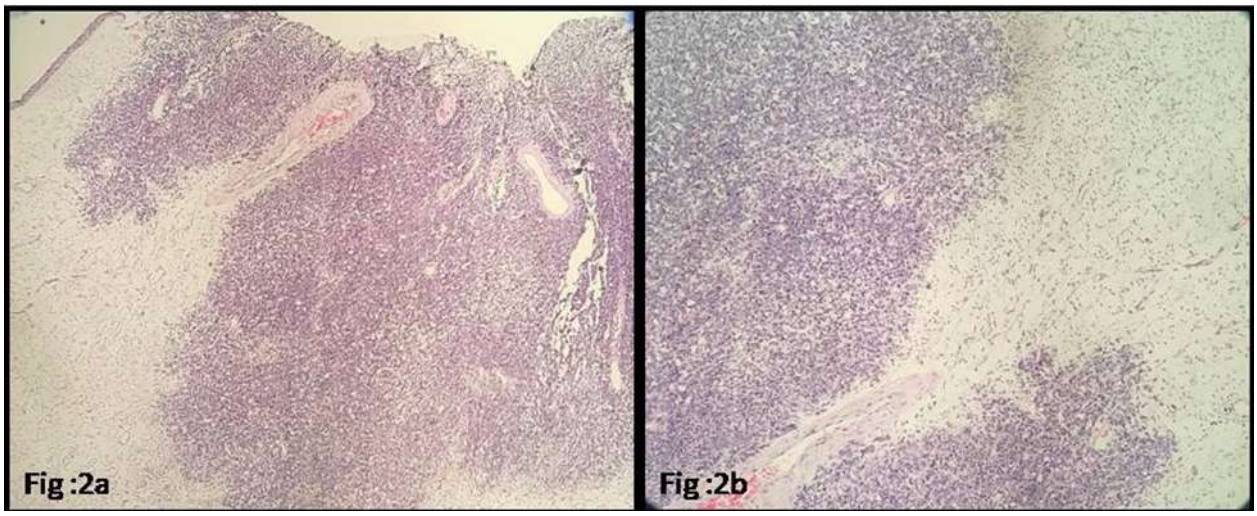

Fig. 2 a, b This figure shows an infiltrative tumor foci with pleomorphic round-oval tumor cells arranged predominantly in nests with scant cytoplasm, coarse chromatin, inconspicuous eosinophilic nucleoli, and atypical mitosis (a. H&E, 10X; b. H&E, 20X)

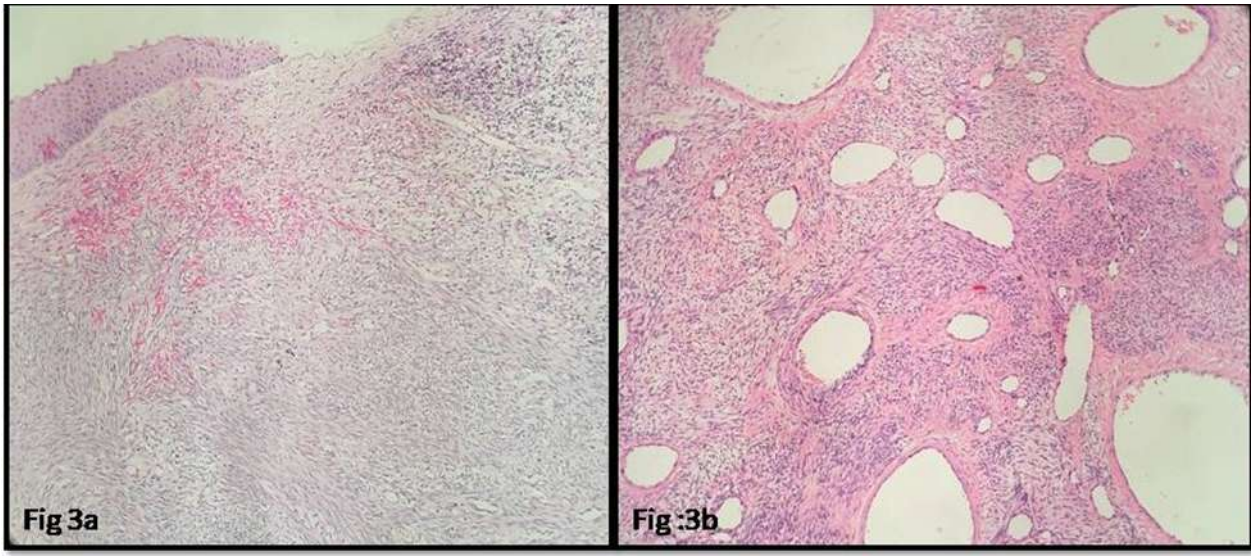

Fig. 3a,b Areas showing blood vessels of various calibers admixed with spindle cells with ovoid-elongated nuclei reminiscent of Nasopharyngeal Angiofibroma (H&E, 10X).

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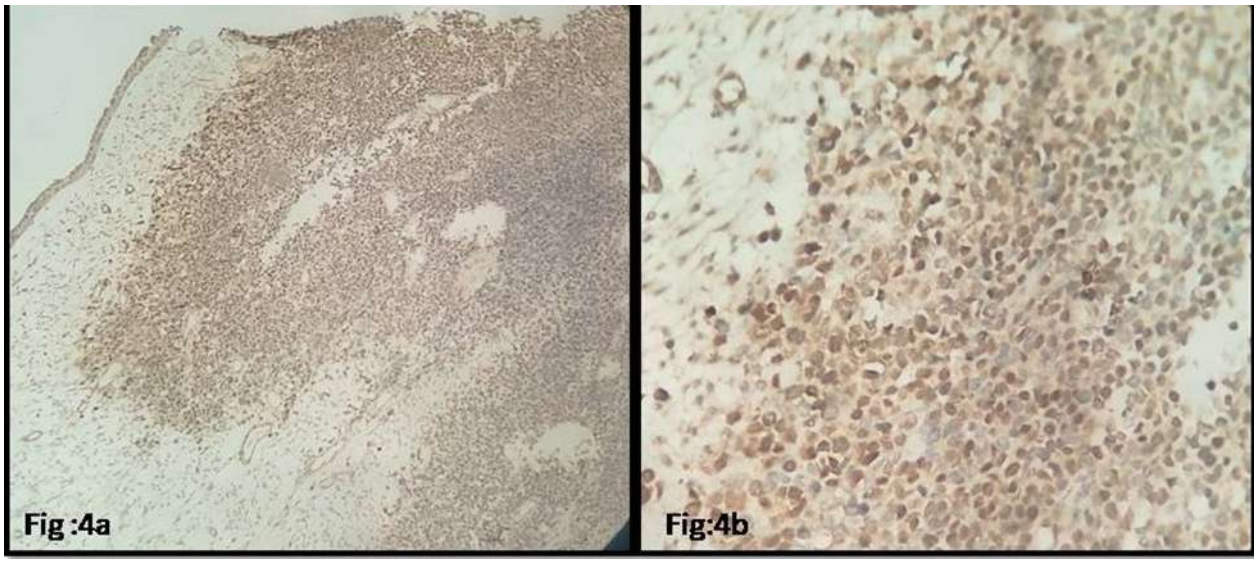

Fig. 4 a Myogenin positive; b MyoD1 positive

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