Adenofibromatous solitary fibrous tumor:
A new morphologic variant occurring in the sinonasal tract

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Introduction

Solitary fibrous tumor is a mesenchymal tumor that has now been recognized in almost every anatomic site. The morphologic spectrum of this tumor type has expanded from the classical form and hypercellular form ("hemangiopericytoma") to encompass the epithelioid variant[1], the fat-forming variant and the giant cell-rich variant.[2, 3] The distinctive genetic alteration of this tumor is inversion on chromosome 12q13 resulting in *NAB2-STAT6* gene fusion, leading to overexpression of the C-terminal portion of STAT6.[4, 5] We herein describe a new morphologic variant of solitary fibrous tumor occurring in the sinonasal tract, characterized by biphasic morphology due to presence of a prominent adenomatoid component.

Material and Methods

Four cases were studied, including two cases from Queen Elizabeth Hospital and two from the consultation files of the authors. Clinical and follow-up information were obtained from the hospital records or the referring pathologists. Four-micron-thick sections were cut from formalin-fixed, paraffin-embedded blocks and stained with hematoxylin and eosin for light microscopic examination. Immunohistochemical study was performed using automated immunostainers (BOND or VENTANA). Reverse-transcription polymerase chain reaction (RT-PCR) was performed to detect NAB2-STAT6 fusion. Total RNA was extracted from paraffin sections and purified by standard method. RT-PCR was performed using NAB2 and STAT6 gene-specific primers. PCR product bands were purified and subjected to DNA sequencing analysis. NCBI sequence NM_005967.3 (mRNA, NAB2 gene) & NM_001178078.1 (mRNA, STAT6 gene) were used as reference for analyses.

Results

Clinical features

Case	Sex/Age	Clinical features	Treatment	Outcome
1	F/67	2 cm mass in left nasal septum	Local excision	NED 5 years
2	F/34	4 cm polyp in left nasal cavity	Local excision	NED 4 years
3	M/39	1.5 cm mass in left nasolacrimal sac	Local excision	NED 3 years
4	F/69	1.5 cm polyp in right nasal septum	Local excision	NED 2.5 years

NED: no evidence of disease.

Pathologic features

The tumors were firm, oval or bosselated. The cut surfaces were whitish with small cystic spaces. Histologically, the tumors were well circumscribed and showed a fibroadenoma-like architecture. The glandular component, constituting a prominent (cases 1, 2 and 4) to multifocal component (case 3), was represented by dilated ducts and hyperplastic seromucinous acini found throughout or predominantly at the peripheral zone of the tumor. Lined by cuboidal to columnar cells with bland-looking nuclei, the ducts contained eosinophilic secretion and were surrounded by fibrous stroma. The seromucinous acini were arranged in discrete lobules or sometimes merged into the fibrocellular stroma. Focally, connection between the acini and ducts was discernible. In case 2, some glandular structures were lined by respiratory-type epithelium. There was no cytologic atypia or mitotic activity.

The spindle cell component comprised spindly cells arranged in short, irregularly-oriented fascicles interspersed with collagenous to focally myxoid stroma. Keloid-like collagen was readily seen. The spindly cells possessed elongated nuclei, fine chromatin, indistinct nucleoli, and ill-defined eosinophilic cytoplasm that appeared to merge with the collagenous stroma. Mitotic count was less than 1 per 10 high power fields, and there was no necrosis.

Immunostaining showed that the epithelial cells were positive for cytokeratin and negative for p63, SMA, S100, CD34 and STAT6. The myoepithelial/ basal cells around the acini and ducts were highlighted by p63, SMA, and S100. The spindly cells showed diffuse and strong staining for CD34 and STAT6. They were negative for cytokeratin, S100, SMA and calponin, and there was no nuclear staining for beta-catenin. The Ki67 proliferative index was less than 5%.

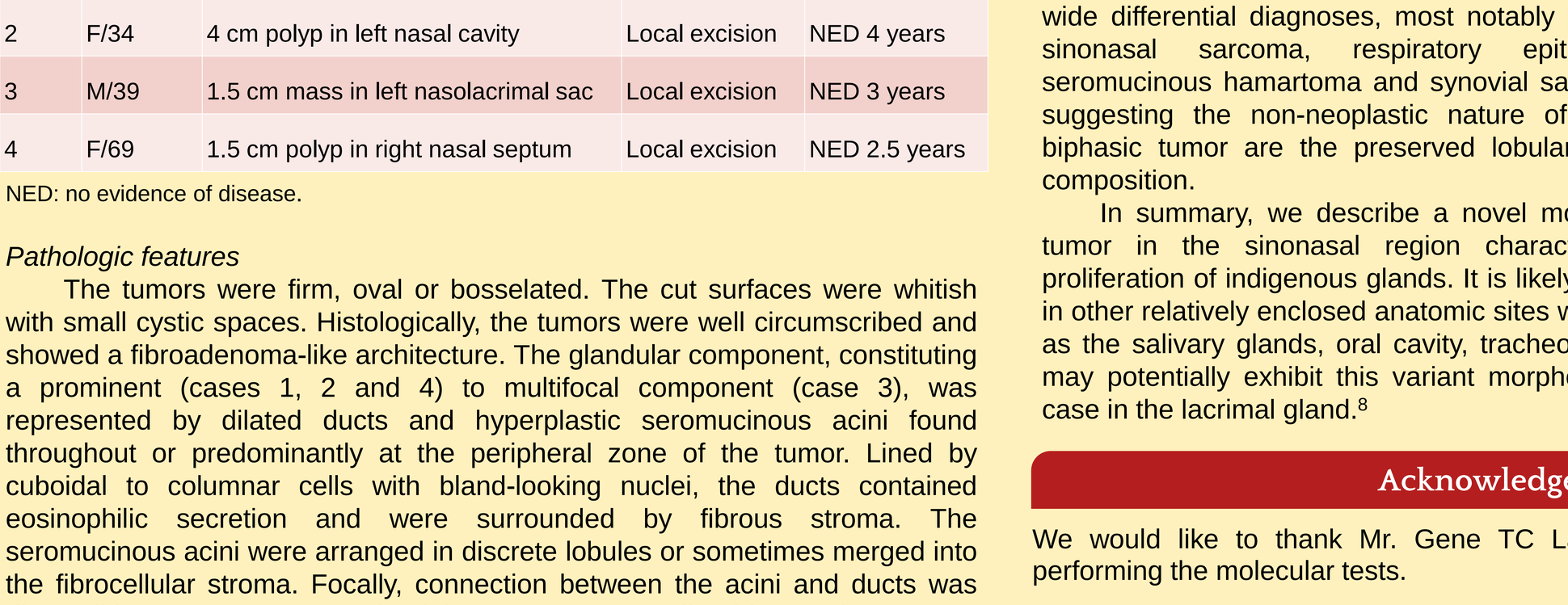
RT-PCR revealed *NAB2-STAT6* gene fusion in all cases. The breakpoint was identified between exon 4 of *NAB2* and exon 2 of *STAT6* for cases 1 and 2, and between exon 3 of *NAB2* and exon 18 of *STAT6* for case 3. For case 4, in addition to a major fusion transcript between exon 6 of *NAB2* and exon 17 of *STAT6*, there was a minor transcript joining exon 5 of *NAB2* and exon 19 of *STAT6*, with breakpoint located within exons.

Discussion and Conclusion

The epithelial component features dilated ducts and hyperplastic acini which do not appear to be neoplastic because of preserved lobular architecture, maintenance of the ductal-acinar organization and luminal-abluminal cellular architecture, as well as lack of nuclear STAT6 staining. They most likely represent a hyperplastic process in response to the tumor, similar to that seen in granular cell tumor, which is commonly accompanied by striking mucosal epithelial hyperplasia.[6, 7] The morphologic features of the spindly cells are otherwise typical for solitary fibrous tumor, and the diagnosis is confirmed by positive staining of CD34 and STAT6 and the presence of *NAB2/STAT6* gene fusion.

In this series, the indigenous minor salivary acini, ducts and surface respiratory epithelium of the sinonasal tract undergo exuberant hyperplasia in the solitary fibrous tumor, resulting in a biphasic appearance that can evoke wide differential diagnoses, most notably pleomorphic adenoma, biphenotypic sinonasal sarcoma, respiratory epithelial adenomatoid hamartoma, seromucinous hamartoma and synovial sarcoma. The most important features suggesting the non-neoplastic nature of the glandular proliferation of the biphasic tumor are the preserved lobular architecture and dual cell-layered composition.

In summary, we describe a novel morphologic variant of solitary fibrous tumor in the sinonasal region characterized by intratumoral exuberant proliferation of indigenous glands. It is likely that solitary fibrous tumor occurring in other relatively enclosed anatomic sites with indigenous mucosal glands, such as the salivary glands, oral cavity, tracheobronchial mucosa or lacrimal gland, may potentially exhibit this variant morphology, as exemplified by a reported case in the lacrimal gland.[8]



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References:

1. Warraich I, Dunn DM, Oliver JW. Solitary fibrous tumor of the orbit with epithelioid features. *Arch Pathol Lab Med.* 2006;130:1039-1041.
2. Gengler C, Guillou L. Solitary fibrous tumour and haemangiopericytoma: evolution of a concept. *Histopathology.* 2006;48:63-74.
3. Fletcher CDM, Bridge JA, Lee JC. Extrapleural solitary fibrous tumor. In: Fletcher CDM, Bridge JA, Hogendoorn PCW, et al., eds. *WHO Classification of Tumors of Soft Tissue and Bone*. Lyon: International Agency for Research on Cancer; 2013:80-82.
4. Chmielecki J, Crago AM, Rosenberg M, et al. Whole-exome sequencing identifies a recurrent NAB2-STAT6 fusion in solitary fibrous tumors. *Nat Genet.* 2013;45:131-132.
5. Robinson DR, Wu YM, Kalyana-Sundaram S, et al. Identification of recurrent NAB2-STAT6 gene fusions in solitary fibrous tumor by integrative sequencing. *Nat Genet.* 2013;45:180-185.
6. Desimone RA, Ginter PS, Chen YT. Granular cell tumor of the breast eliciting exuberant pseudoepitheliomatous hyperplasia. *Int J Surg Pathol.* 2014;22:156-157.
7. Lack EE, Worsham GF, Callihan MD, et al. Granular cell tumor: a clinicopathologic study of 110 patients. *J Surg Oncol.* 1980;13:301-316.
8. Cho NH, Kie JH, Yang WI, et al. Solitary fibrous tumour with an unusual adenofibromatous feature in the lacrimal gland. *Histopathology.* 1998;33:289-290.