Case Report: Malignant sinonasal solitary fibrous tumour with clear cell features and BCOR expression

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Introduction

Solitary fibrous tumours (SFTs) are fibroblastic mesenchymal tumours of intermediate malignant potential. They occur uncommonly in the head and neck region, of which the sinonasal tract is the most common location (30%).

SFTs exhibit a wide range of morphology, ranging from the classic “patternless pattern” of spindle cells closely admixed with stromal collagen and associated with dilated “staghorn” branching vessels, to myxoid, epithelioid, and lipomatous features and sarcomatous dedifferentiation. [1] The diagnosis can be confirmed by demonstration of NAB2-STAT6 fusion by sequencing or nuclear expression of STAT6. [2]

BCOR-rearranged sarcomas are recently defined entity which was originally classified as belonging to the Ewing sarcoma family. Unlike Ewing sarcoma, BCOR-rearranged sarcomas consistently show BCOR overexpression. Histologically, BCOR-rearranged sarcomas show round to spindled cells, monotonous nuclei, fine chromatin, delicate vasculature and varying amounts of myxoid or collagenous stroma. [3]

In this report, we describe a case of malignant SFT with BCOR expression. Literature search showed a series reporting BCOR expression in malignant SFT of the kidney. To the best of our knowledge, this is the first report documenting BCOR expression in a malignant SFT with clear cell features in the head and neck region.

Case Presentation

Clinical findings

A female patient in her early fifties presented with nasal obstruction for one month. Past medical history was unremarkable. MRI of the brain and paranasal sinuses showed a contrast-enhancing lobulated mass centred in the right ethmoid and sphenoid sinuses measuring 5x3.3x8.3 cm, extending into the left sphenoid and posterior ethmoid sinuses, the right orbit, right nasal cavity and into the anterior cranial fossa, encroaching the frontal lobes and the cavernous segment of the right internal carotid artery.

Microscopic Findings and Immunohistochemistry

Histological examination showed a proliferation of bland round to spindle cells arranged in sheets with hyperchromatic nuclei, mild pleomorphism, indistinct nucleoli and moderate amount of clear cytoplasm. Gaping thin-walled blood vessels were seen. No adjacent normal tissue was included to assess for presence of infiltration. No mitotic figures, necrosis or sarcomatoid features were identified in the small biopsy. The tumour cells were immunohistochemically positive for BCOR and negative for AE1/3, SMA, S100, CD34, GFAP, CD10, Melan-A, HMB45 and synaptophysin. Retrospective staining for STAT6 showed diffuse nuclear positivity.

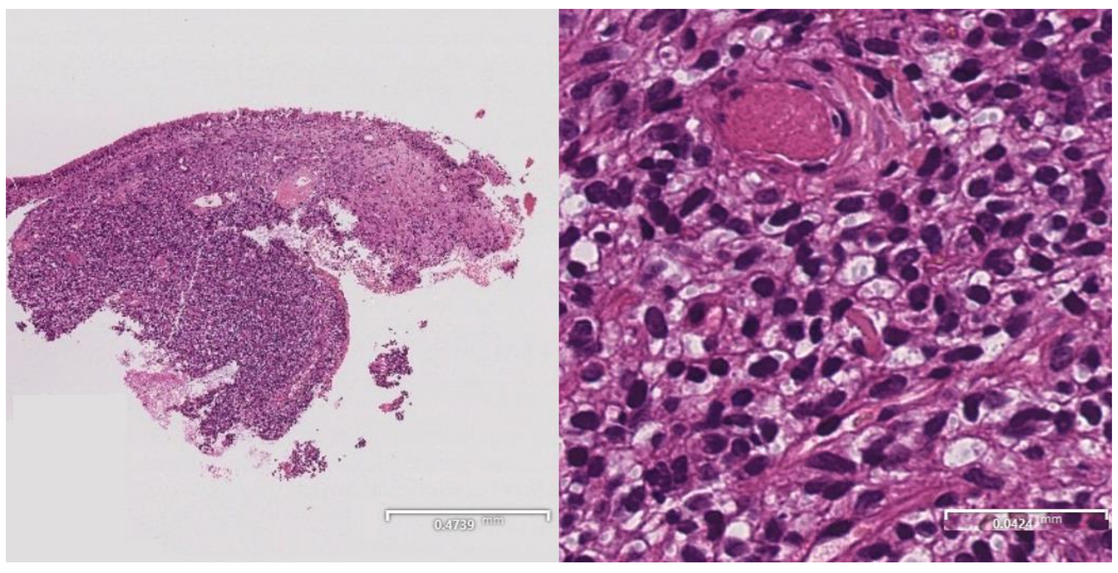

Figure 1. H&E sections of the tumour, low power 2x (left) and high power 20x (right).

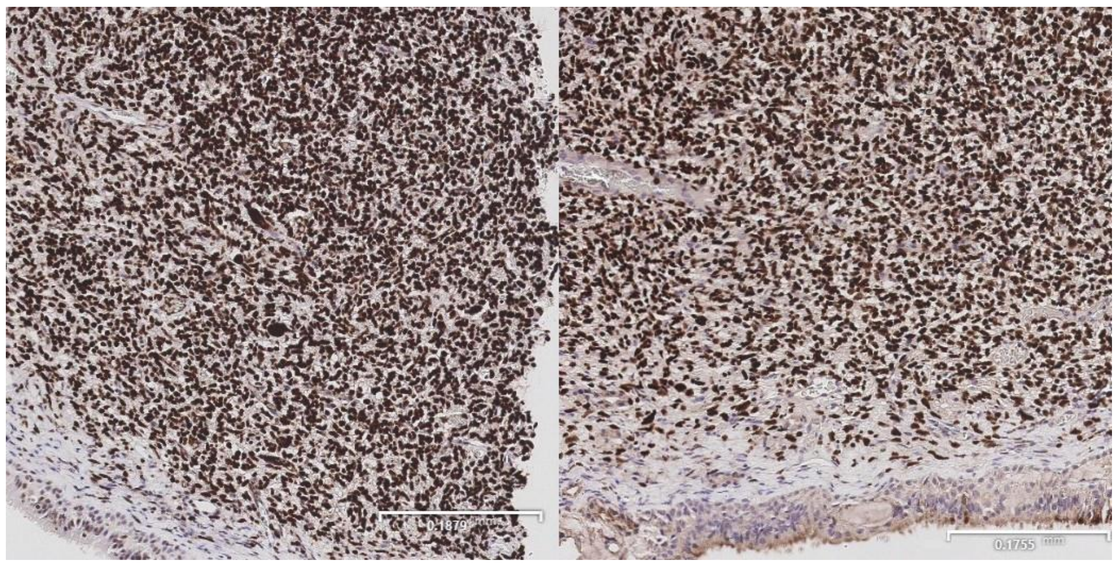

Figure 2. Immunostains show BCOR positivity (left) and STAT6 positivity (right)

Molecular analysis

The tissue was submitted for Illumina Pan-caner RNA sequencing analysis designed to detect fusion transcripts of 1385 cancer-related genes. Briefly, RNA was extracted from the formalin-fixed paraffin embedded tissue. The library prepared was sequenced by NextSeq500/550 mid output v.2 kit at 76bp pair-end on NextSeq500 sequencer (Illumina). The data was analyzed by RNA STAR Fusion pipeline. The raw reads were aligned to reference human genome (hg19) by RNA STAR v.2.4.0d. The fusion transcripts were determined by STAR Fusion software v.0.5.4. The chimeric transcript NAB2-STAT6 fusion was detected. The fusion was created by joining the exon 6 of NAB2 gene and exon 16 of STAT6 gene. The fusion transcript was predicted to be in-frame. BCOR chimeric fusion and BCOR ITD were not detected.

IGV view of NAB2-STAT6 fusion. The fusion was determined by Manta variant caller but missed by STAR Fusion caller. The fusion was joined by fusing exon 6 of NAB2 to exon 16 of STAT6. It is supported by 63 split reads and 54 spanning reads.

Diagnosis and Follow-up

The final pathologic diagnosis was solitary fibrous tumor. Given the large size and extensive invasion, the tumour was managed as malignant SFT. The patient is currently receiving chemo-radiation therapy and shows clinical response with reduction in nasal blockage symptoms and tumour necrosis on serial imaging.

Discussion

SFTs can occur virtually anywhere in the body, including the orbit, oral cavity, meninges, abdominal viscera and genital tract. [4] Most SFTs show benign clinical behaviour, but 5-10% will metastasize.

Morphologically, our case showed monomorphic round to spindle cells with clear cell features, and lacked the classical pattern of SFT. Our differential diagnoses were broad, ranging from primary or metastatic carcinoma to translocation-associated sarcomas. The vast majority (95-100%) of SFTs express CD34. In malignant and dedifferentiated SFTs, a lower but still significant (83%) proportion of cases are positive for CD34 [5]. CD34 was negative in our case, precluding the diagnosis of SFT. BCOR expression instead was positive, hence the possibility of a BCOR-rearranged sarcoma was raised. However, RNA sequencing showed negative BCOR translocation and ITD, and showed NAB2-STAT6 chimeric fusion. Retrospective staining for STAT6 showed diffuse nuclear positivity. STAT6 immunoreactivity is highly (>90%) sensitive and specific for benign and malignant SFTs [2]. The detection of NAB2-STAT6 fusion can be helpful in diagnostically challenging cases.

BCOR expression in malignant SFT with clear cell features was reported in a series of 5 cases which showed nests of round to epithelioid neoplastic cells with fine chromatin and branching capillary vasculature, reminiscent of clear cell sarcoma of the kidney. None of the cases showed the typical bland ovoid fibroblastic cell appearance of SFT, and only 1 case showed haemangiopericytoma-like vasculature and focal ropy collagen deposition. All 5 cases showed strong diffuse nuclear staining for BCOR and STAT6. RNA-sequencing on these 5 cases and additional 20 cases of SFT showed elevation of BCOR mRNA expression relative to 34 common soft tissue sarcomas, and expression correlated with risk of malignancy in SFT. Additional 25 benign and 14 malignant SFTs were evaluated and 92% of malignant SFTs and 44% of benign SFTs showed strong BCOR nuclear staining. [6] Our case adds to the series of BCOR-positive SFTs.

In summary, we present a case of malignant SFT occurring in the sinonasal tract showing round to spindled cells with clear cytoplasm, lacking features of conventional SFT, and showing diffuse nuclear positivity for BCOR and negativity for CD34. Our report draws attention to this diagnostic pitfall for malignant SFT when morphology is atypical and malignant features may not be apparent in a small biopsy. Malignant SFTs may also express BCOR in addition to other known lesions such as clear cell sarcoma of the kidney, high-grade endometrial stromal sarcoma and BCOR-rearranged sarcomas.

References

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