



A pediatric low-grade sinonasal mesenchymal tumor harboring a novel *CHD9::BEND2* fusion

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Abstract

BEND2-rearranged neoplasms represent a newly emerging group of tumors with variable morphology, involving multiple tissue types and anatomical sites such as the central nervous system, bone, soft tissue, and salivary glands. Here, we describe a novel *CHD9::BEND2* fusion in a low-grade spindle cell mesenchymal tumor arising in the sinonasal tract of a 5-year-old girl. Histologically, the tumor exhibited ovoid to spindle-shaped cells with moderate atypia, numerous thin-walled vessels, and focal necrosis. Immunohistochemistry did not indicate a specific line of differentiation, showing focal SATB2 positivity and a low proliferative index. The *CHD9::BEND2* fusion was identified by whole transcriptome sequencing and confirmed by RT-PCR, Sanger sequencing, and break-apart FISH. This case broadens the clinicopathological and molecular spectrum of *BEND2*-associated tumors, suggesting a potential oncogenic role of *CHD9::BEND2* in pediatric mesenchymal neoplasia.

Keywords *CHD9::BEND2* fusion · *BEND2*-rearranged tumor · Sinonasal mesenchymal tumor · Pediatric spindle cell neoplasm · RNA sequencing

Introduction

BEND2 (BEN domain containing 2) encodes a chromatin-associated protein with a BEN domain, mediating transcriptional regulation through protein–DNA and protein–protein interactions. Rearrangements involving *BEND2* have recently been identified in diverse tumor types, including astroblastoma [1–4], sinonasal sarcoma [5], bone-based sarcoma [6], salivary gland carcinoma [7], and phosphaturic mesenchymal tumor [8], and pancreatic neuroendocrine tumors [9]. Reported *BEND2* fusion partners include *MN1*,

YAPI, *EWSR1*, *FUS*, *TCF3*, *MAMLD1*, and *NIPBL* [1, 3, 4, 6, 8–11].

Although functional studies of *BEND2* remain limited, a recent study provided the first experimental evidence for its oncogenic role, particularly within *MN1–BEND2* fusions, by altering transcriptional programs in neural progenitors. *BEND2* contributes to oncogenesis through its BEN domain, which mediates chromatin binding and transcriptional dysregulation [12]. Emerging evidence suggests that fusions involving *BEND2* may contribute to distinct functional effects, including ectopic hormone production in pancreatic neuroendocrine tumors [[9]]. These findings support the role of *BEND2* fusions as recurrent oncogenic drivers.

Despite its recurrent involvement in multiple tumor types, the spectrum of *BEND2* fusion partners across mesenchymal neoplasia remains incompletely characterized. Here, we report the first case of a low-grade pediatric sinonasal spindle cell tumor harboring a novel *CHD9::BEND2* fusion, expanding the clinicopathological and molecular spectrum of *BEND2*-associated neoplasia.

Huiting Wei and Dawei Liu contributed equally to this work.

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Case presentation

A 5-year-old girl presented with nasal obstruction and epistaxis for 1 year, which had worsened over the past month. She was initially diagnosed with a nasal vascular tumor and underwent resection at an outside hospital, but experienced local recurrence after 1 year. Imaging revealed a well-defined tumor mass in the right nasal cavity and ethmoid sinus (70×51×69 mm), exhibiting heterogeneous hyperintensity on T2-weighted images (Fig. 1A, B). Computed tomography (CT) demonstrated bone destruction,

suggesting aggressive biological behavior (Fig. 1C, D). The patient then received a radical resection at our institution.

Grossly, the resected specimen was a gray-white mass with areas of hemorrhage and necrosis on the cut surface. Histologically, the tumor displayed relatively well-circumscribed borders. The tumor cells were oval to short spindle-shaped with moderate atypia. Prominent nucleoli were evident in some cells. Mitotic figures and focal areas of necrosis were observed. The stroma contained numerous thin-walled blood vessels and scattered lymphocytic infiltrates (Fig. 2A–E).

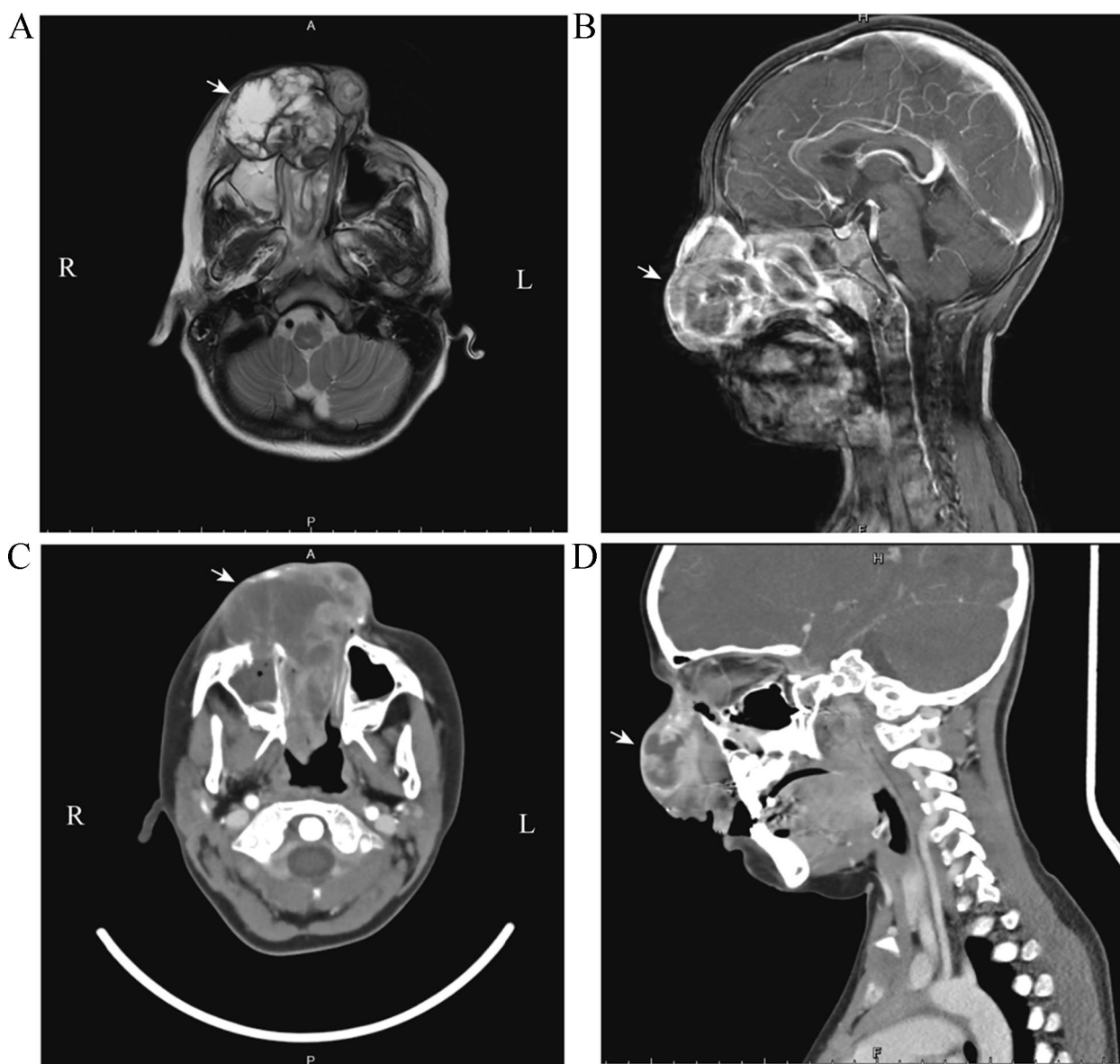


Fig. 1 Imaging features of a *CHD9::BEND2*-rearranged sinonasal mesenchymal tumor. **A, B** Axial and sagittal T2-weighted MR images revealed a large, heterogeneously hyperintense mass centered in the

right nasal cavity and ethmoid sinus. **C, D** Axial and sagittal CT images demonstrated compression and destruction of adjacent bone

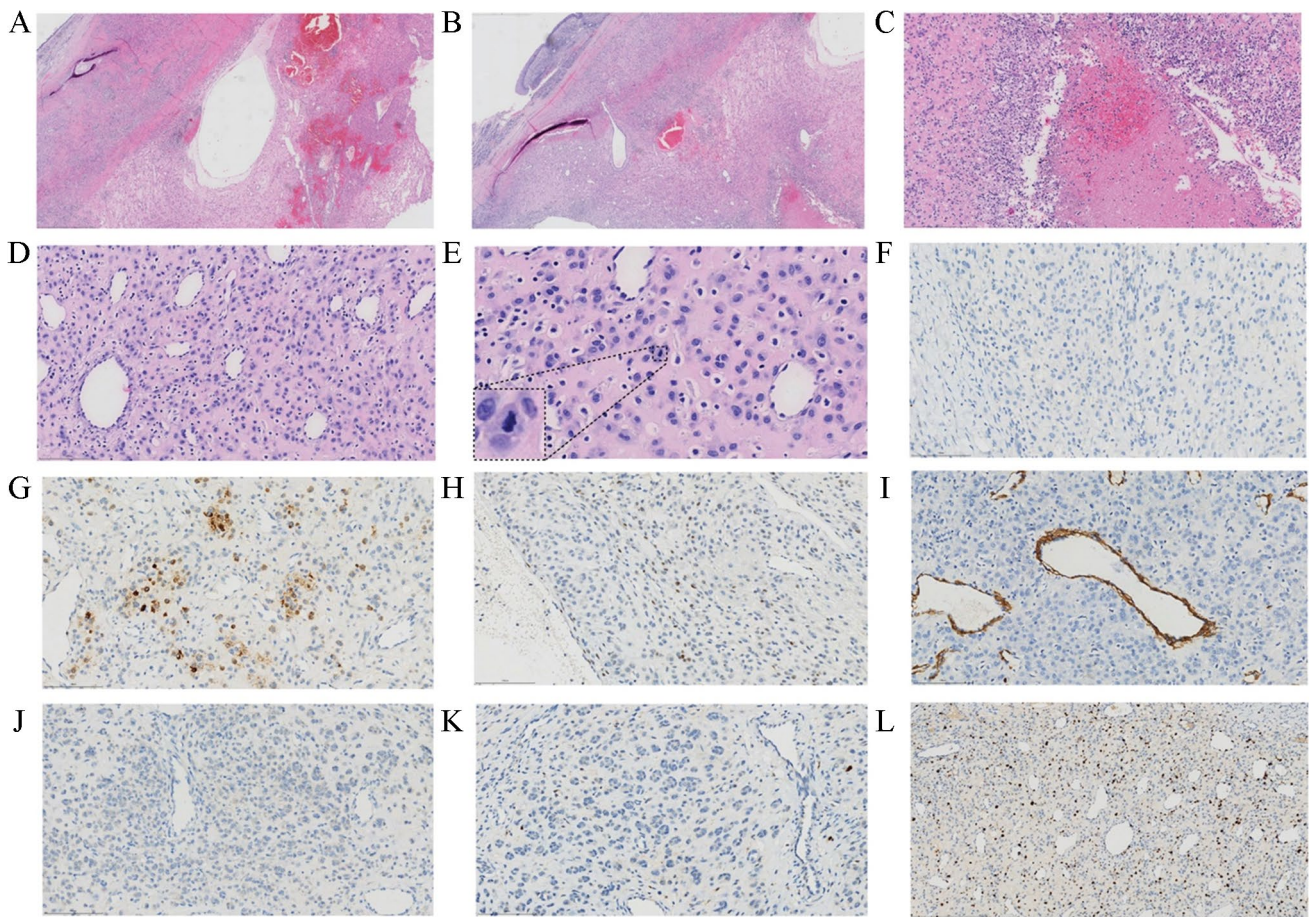


Fig. 2 Histologic and immunohistochemical features of the sinonasal spindle cell tumor with *CHD9::BEND2* fusion. **A, B** Histopathological examination under low magnification revealed a relatively well-demarcated tumor exhibiting hemorrhage and necrosis. **C** Patchy necrosis was present. The tumor is composed of oval to short spindle-shaped cells with mild to moderate cytologic atypia. The tumor cells have pale basophilic to clear cytoplasm, and small but distinct nucle-

oli are present in a subset of cells. Mitotic figures were identified. The tumor stroma is rich in thin-walled blood vessels (**D–E**). Immunohistochemistry showed negative staining for pan-CK (**F**), Actin (**I**), Syn (**J**), S100 (**K**), and focal positivity for EMA (**G**), scattered positivity for SATB2 (**H**), and Ki-67 indicated mildly increased proliferative activity (**L**)

The immunophenotype was non-specific and did not indicate a definite line of differentiation. Markers for epithelial (pan-CK, Fig. 2F), myogenic (Actin, Fig. 2I; Desmin, data not shown), and neural lineages (S100, Fig. 2K; Syn, Fig. 2J) were negative, with only focal EMA positivity (Fig. 2G) and scattered SATB2 expression (Fig. 2H). Ki-67 staining revealed a mildly increased proliferative activity (Fig. 2L). Considering the H&E morphology and immunoprofile, an intermediate or low-grade spindle cell mesenchymal tumor was considered. The differential diagnosis included solitary fibrous tumor (SFT) and *GLI1*-rearranged spindle cell tumor; however, SFT was less likely given that CD34 and STAT6 were negative, and FISH analyses for *GLI1* amplification and rearrangement were negative.

Molecular testing identified a novel *CHD9::BEND2* fusion by whole transcriptome sequencing. The fusion resulted from exon 2 of *CHD9* and exon 5 of *BEND2*,

generating a novel fusion transcript (Fig. 3A). The finding was further validated by RT-PCR using primers spanning the breakpoint, followed by Sanger sequencing of the PCR product (Fig. 3B). Break-apart FISH with *BEND2* probes confirmed the gene rearrangement (Fig. 3C). The patient underwent radical resection without adjuvant therapy and has been under close follow-up.

Discussion

BEND2-rearranged tumors display variable morphologies, including spindle, round, or epithelioid cells, and in some cases, are accompanied by hemangiopericytoma-like vasculature. Our case shared overlapping features, including spindle morphology, hemangiopericytoma-like vessels, and focal SATB2 positivity, features that have also been observed in

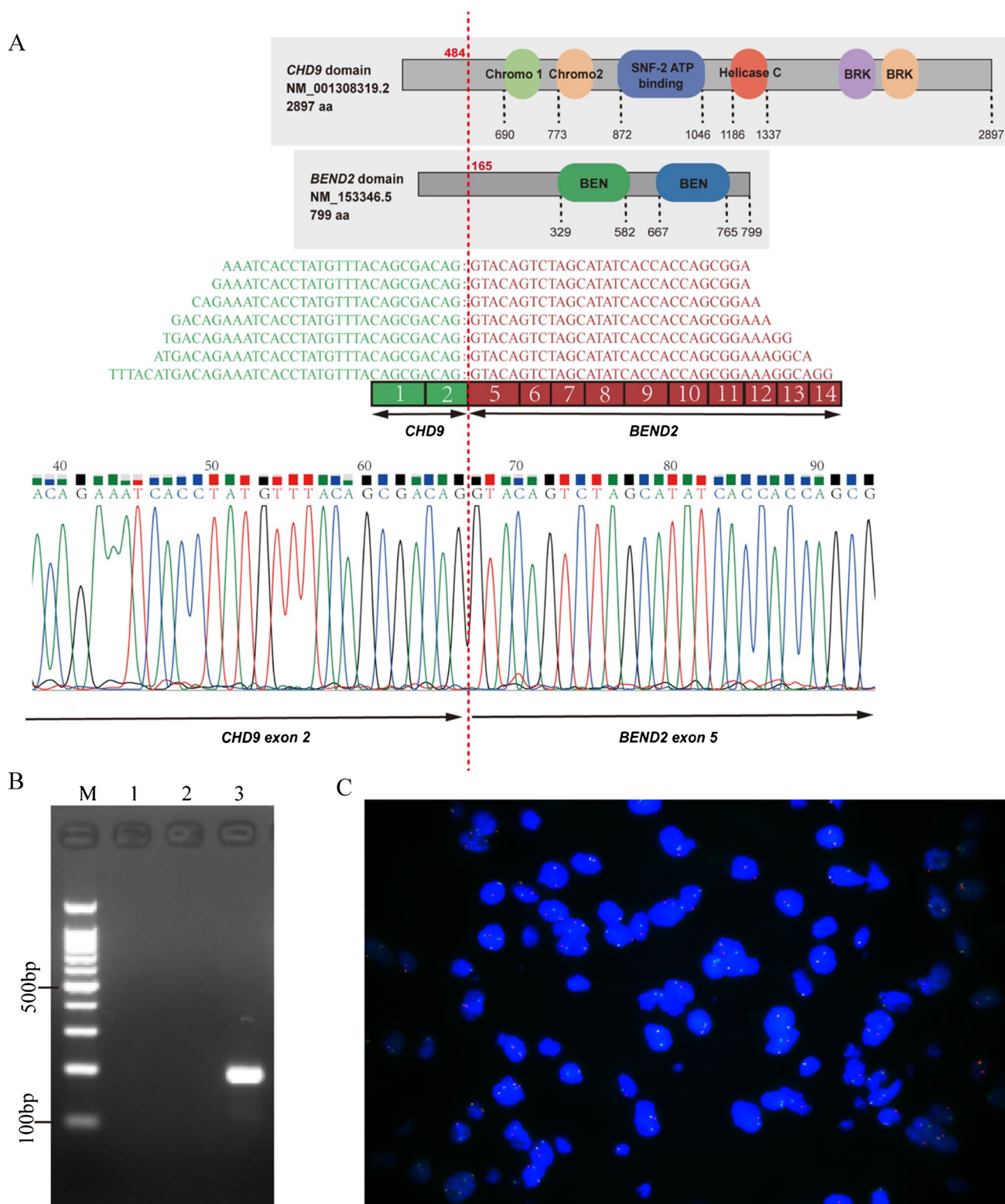


Fig. 3 **A** Whole transcriptome sequencing identified the *CHD9::BEND2* fusion, which was confirmed by Sanger sequencing. **B** RT-PCR with *CHD9* and *BEND2* primers amplified a fusion-

specific product. Lane 1: negative control; Lane 2: wild-type; Lane 3: patient sample. **C** Break-apart FISH with *BEND2* probes showed split signals, indicating *BEND2* gene rearrangement

the *EWSR1::BEND2*-rearranged sinonasal sarcoma reported by Palsgrove et al. [[5]].

BEND2 encodes a BEN domain protein that regulates chromatin structure and transcription. Accumulating evidence supports its role as an oncogenic driver when fused with diverse partners in tumors. Beyond its oncogenic roles, full-length *BEND2* is dispensable for male fertility but essential for establishing the ovarian reserve, highlighting the broader biological relevance of this gene beyond tumorigenesis [[13]].

Importantly, the novel *CHD9::BEND2* fusion identified here expands the repertoire of *BEND2*-associated partners. *CHD9* (Chromodomain Helicase DNA Binding Protein 9) encodes an ATP-dependent chromatin remodeler within the CHD family, which modulates nucleosome positioning and transcriptional regulation [[14]]. The role of *CHD9* in human cancer is poorly understood. Our discovery of a *CHD9::BEND2* fusion suggests a novel, previously unrecognized mechanism by which *CHD9* may be involved in tumorigenesis.

Given the convergent functions of *CHD9* and *BEND2* in chromatin regulation, the *CHD9::BEND2* fusion may act through epigenetic dysregulation to promote tumorigenesis; however, this mechanistic hypothesis requires validation in functional models.

In summary, our case highlights a novel *CHD9::BEND2* fusion in a pediatric sinonasal spindle cell tumor, thereby broadening the molecular spectrum of *BEND2*-rearranged neoplasia and underscoring the importance of molecular testing in the diagnosis of diagnostically challenging pediatric mesenchymal tumors.

Author contribution Huiting Wei and Dawei Liu contributed to the study design, data interpretation, and manuscript writing. Anjia Han designed the study, supervised the work, and made the pathological diagnosis. Huijuan Shi and Sheng Xiao provided guidance and supervision. Yanan Li performed molecular analyses confirming the *CHD9::BEND2* fusion. All authors read and approved the final version of the manuscript.

Data availability The nucleotide sequences of the *CHD9::BEND2* fusion transcript validated by Sanger sequencing have been deposited in the GenBank database under accession numbers PV992632–PV992635. These sequences are currently under embargo and will be released on August 1, 2026, or upon publication, whichever comes first.

Declarations

Ethics approval Ethical approval for this study was granted by the Institutional Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University, with a waiver of informed consent (Approval No. [2025]493).

Conflict of interest The authors declare no competing interests.

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