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Original Article

Biphenotypic sinonasal sarcoma with diffuse infiltration and intracranial extension: a case report

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Abstract: Biphenotypic sinonasal sarcoma (BSNS) is a new entity which is a low-grade spindle cell sarcoma with neural and myogenic differentiation and recurrent PAX3 rearrangement. Herein, we present one case of BSNS with diffuse infiltration. We analyzed its clinicopathological features and differential diagnosis. In conclusion, BSNS is a low-grade spindle cell sarcoma. The differential diagnosis includes schwannoma, malignant peripheral nerve sheath tumor, synovial sarcoma, and spindle cell rhabdomyosarcoma. As for the prognosis, BSNS commonly recurs and rarely metastasis. However, it may invade extensively and results in poor prognosis.

Keywords: Sinonasal sarcoma, biphenotypic, PAX3 rearrangement

Introduction

Many kinds of spindle cell soft tissue tumors can involve the sinonasal tract (nasal cavity and paranasal sinuses), including schwannoma, fibrosarcoma, angiosarcoma, malignant peripheral nerve sheath tumor (MPNST), non-classified/non-differentiated sarcoma [1], as well as some location-distinct subtypes including angiofibroma, glomangiopericytoma, and rhabdomyosarcoma [2]. Biphenotypic sinonasal sarcoma (BSNS), a new tumor recently recognized, is a low-grade spindle cell sarcoma that occurs in the sinonasal tract, expressing neural and myogenic markers [3]. It was first described and named low-grade sinonasal sarcoma with neural and myogenic features in 2012 [4]. In 2014, it was found that the tumor had recurrent PAX3 rearrangement and was renamed biphenotypic sinonasal sarcoma [5]. Herein, we present one case of BSNS involving nasal cavity, nasopharyngeal cavity, multiple paranasal sinuses, skull base, and frontal lobe of brain. We analyzed its clinicopathological features and differential diagnosis.

Clinical summary

A 67-year-old female presented with nasal obstruction and right nasal cavity mass for 10 years. She has undergone three surgical procedures for "nasal polyp" over the previous 17, 20 and 23 years. No significant past medical history and family history of cancer were declared. Cranial magnetic resonance imaging (MRI) and computed tomography (CT) scan demonstrated the tumor occupied the right nasal cavity, nasopharyngeal cavity, right maxillary sinus, right frontal sinus, bilateral ethmoid sinuses, and bilateral sphenoid sinuses. The tumor infiltrated the skull base and involved the frontal lobe of brain. Nasal endoscope revealed a pink hemorrhagic polypoid mass obstructing right nasal cavity, resulting in marked nasal septum left deviation (**Figure 1**). She had three biopsies under the nasal endoscopy. The pathological reports were nasal polyps for twice, and the third pathological report was low-grade mesenchymal tumor. The patient underwent an endoscopic surgery combined with craniofacial resection. The tumor was removed completely. However, the patient died of perioperative complications including subarachnoid hemorrhage, multiple cerebral infarction and cerebral hernia because of extensive surgical trauma.

Pathological findings

The specimen was solid, partial polypoid, pale-yellow fragments, measuring 12 cm in overall

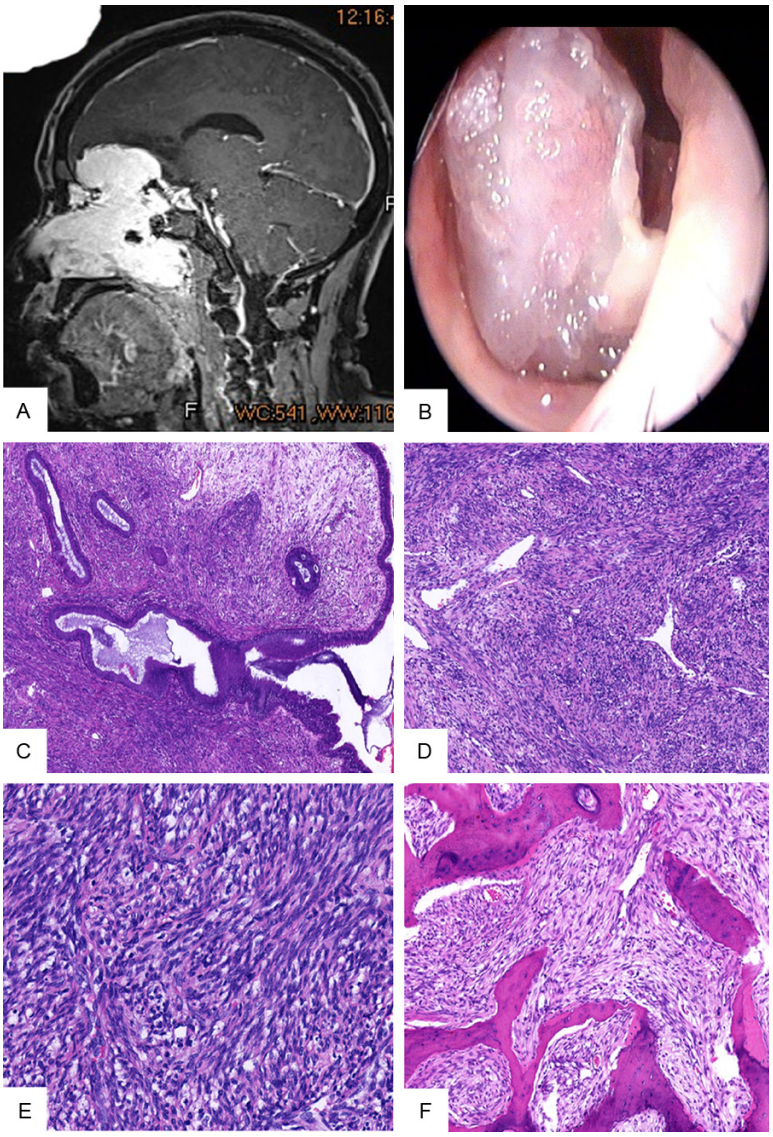

Figure 1. Imaging and nasal endoscope findings and histopathological features of biphenotypic sinonasal sarcoma. A. MRI showed the tumor occupied the right nasal cavity, nasopharyngeal cavity, multiple paranasal sinuses, invaded skull base and involved right frontal lobe of brain. B. Nasal endoscope showed the right nasal cavity was obstructed by polypoid mass. C. In superficial area, tissue presented as inflammatory nasal polyp with scarce tumor cells, HE ×100. D. Disordered bundle structure and "staghorn'' branch vessel were observed in tumor, HE ×200. E. Spindle tumor cells with elongate nucleus and scant cytoplasm, HE ×400. F. Tumor cells infiltrated bone, HE ×200.

diameter. Microscopically, the tumor was composed of homogeneous spindle tumor cells with elongate nucleus and scant cytoplasm. Mitotic figures were scant and tumor necrosis was not found. In some area, tumor cells arranged in "herringbone" pattern, but disordered bundle structure was found in other area. Focally, "staghorn" branch vessel was observed. In superficial area, the tumor presented as inflammatory nasal polyp with scarce tumor cells. In most area, the tumor was cellularity (**Figure 1**). The tumor was non-capsulated, and bone invasion was found in the skull base region, whereas brain parenchyma infiltration was detected in the frontal lobe of brain. Immunohistochemistry staining showed tumor cells were diffusely positive for S-100 protein and smooth muscle actin (SMA), focal positive for desmin and MyoD1, whereas myogenin was expressed only in isolated tumor cell. No EMA or CD34 reactivity was observed. Ki-67 staining demonstrated low proliferation rate, was 1% in most area, and 5% in active region. Fluorescence in situ hybridization (FISH) showed break-apart signal of PAX3 gene in this case (**Figure 2**). Neither FKHR (FOXO1) nor SYT gene rearrangement was found. Based on the clinical, pathological feature, immunophenotype, and FISH detection, we made the diagnosis of biphenotypic sinonasal sarcoma with diffuse infiltration and intracranial extension.

Discussion

BSNS is rare. To our knowledge, only 7 articles about BSNS as case report or series have been reported in English literature [4-10]. BSNS is a locally invasive tumor typically involving nasal cavity or paranasal sinuses. It commonly develops local recurrence without distant metastasis. Only one fatal case has been reported thus far [8, 11]. BSNS usually occurs in middle aged and elderly women, which is a low-grade homogeneous cellular spindle cell tumor with invasive growth pattern, constant expression of both neural and myo-

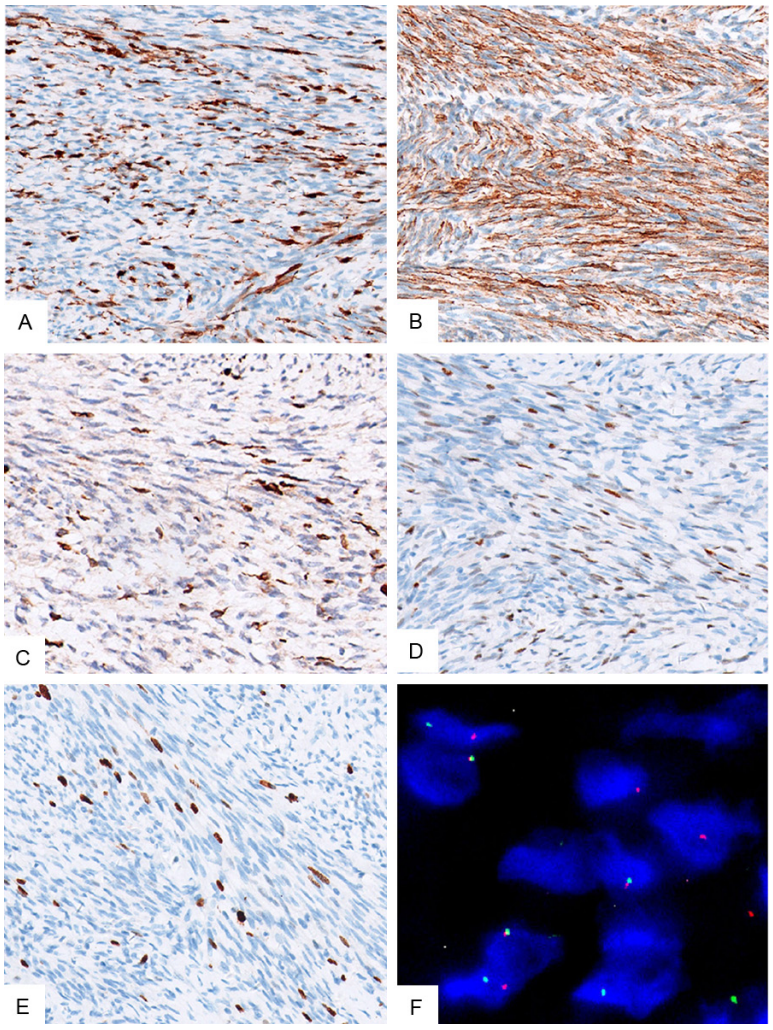

Figure 2. Immunoprofile and molecular alteration of biphenotypic sinonasal sarcoma. Tumor cells expressed S-100 protein (A, IHC ×200), smooth muscle actin (B, IHC ×200), desmin (C, IHC ×200), and MyoD1 (D, IHC ×200). Ki-67 was positive in about 5% of tumor cells (E, IHC ×200). Break-apart signal of PAX3 gene was positive in tumor by fluorescence in situ hybridization (F). FISH ×400.

genic markers, and recurrent PAX3 gene rearrangement [4, 5]. The differential diagnosis includes schwannoma, MPNST, synovial sarcoma, and spindle cell rhabdomyosarcoma before making a final diagnosis of BSNS. Unlike BSNS, schwannoma usually has a thin fibrous capsule, typically is composed of Atoni A and Atoni B without tumor cell atypia and SMA expression. MPNST arises from a peripheral nerve or a pre-existing benign nerve sheath tumor. It is usually a high-grade sarcoma with prominent nuclear atypia, abundant mitotic figures, and necrosis without SMA expression. The present case exhibited haemangiopericytoma-like pattern focally, so synovial sarcoma should be differentiated. Synovial sarcoma usually expresses EMA and has a specific chromosomal translocation t(X;18)(p11;q11) that lead to formation of a SS18-SSX fusion gene. However, our case was negative for SYT gene break apart by FISH. Focal reactivity for muscle markers, especially myogenin and myoD1, may also indicate the diagnosis of spindle cell rhabdomyosarcoma. Spindle cell rhabdomyosarcoma usually has strong and diffuse reactivity for myogenin and myoD1 without S-100 protein expression. Whereas in BSNS, myogenin and myoD1 are usually focal, weak, or scattered [4, 8, 9].

To the present case, patient had three biopsies before surgery, the former two of which were reported as nasal polyps. Indeed, in resected specimen, we found that the surface of the tumor presented polypoid with scanty tumor cells. This reminds us the possibility of misdiagnosis in a small and superficial biopsy if deeply located tumor cells are not sampled. It has been reported that, on the surface of some BSNSs, benign glandular proliferation surrounded by neoplastic cells reminiscent of inverted papilloma, is a distinct feature of BSNS [4, 8]. However, it was not prominent in the present case.

PAX3 rearrangement is a recurrent gene event in BSNS, resulting in increased activation of PAX3 response elements, and leading to the biphenotype of neural and myogenic differentiation [5, 12]. The most common fusion partner is MAML3 [5, 7]. PAX3-FOXO1, PAX3-NCOA1 and MAML3 rearrangement without PAX3 involved have also been identified in several cases, and the former one seems to be associated with focal rhabdomyoblastic differentiation in BSNS [7, 9, 10]. However, whether the molecular phenotype is associated with the

tumor biological behavior and prognosis needs further study in large samples.

BSNS is a locally aggressive tumor, mostly involving the nasal cavity or paranasal sinuses, some BSNS invades the skull base and results in intracranial extension. The present case is the most extensive invasion case of BSNS in the literature, which may be related to the longer duration of the tumor without treatment. It has been reported that almost half of cases with BSNS experienced local recurrences [13]. As for the present case, we could not determine that the present tumor was primary or recurrent since the patient underwent three "nasal polyp" resection previously. However, only pathology report for the third biopsy was low-grade mesenchymal tumor. In addition, there were few cases dead of BSNS, except for one case reported in 2006, dead of second recurrence with intracranial mass [8]. The patient in our case died during the perioperative period, it was closely related to the wide infiltration of the tumor.

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Disclosure of conflict of interest

None.

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