

Biphenotypic Spindle Cell Sarcoma: First Report of an Ectopic Occurrence in the Parapharyngeal Space

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ABSTRACT

Biphenotypic sinonasal sarcoma is a rare, locally aggressive disease. This is a site-specific sarcoma that commonly develops in the sinonasal tract. Identifying biphenotypic sinonasal sarcoma is difficult due to the need to assess both the pathological and immunophenotypic characteristics of the tumor. When an unusual presentation occurs at a different site altogether, it may be confusing for the operating surgeon, leading to mismanagement of the patient's condition. We present a rare and unique case of biphenotypic sarcoma of the left parapharyngeal space that has not been previously reported in the English literature because of its site specificity. Occasionally, a biphenotypic sarcoma can develop outside the nasal cavity and paranasal sinuses. Diagnosis and management of this condition are both challenging for pathologists and surgeons.

INTRODUCTION

Biphenotypic sinonasal sarcoma is a newly described tumor of the sinonasal region, as defined in the most recent edition of the World Health Organization's head and neck tumors [1]. Despite its unique dual staining patterns for neural and myogenic markers, it can show some histological overlap with other tumors, such as fibrosarcomas, monophasic synovial sarcomas, peripheral nerve sheath tumors, glomangiopericytomas, and solitary fibrous tumors [2]. In view of the indolent nature of biphenotypic sinonasal sarcoma, it is imperative to determine its exact diagnosis. Immunohistochemistry as well as molecular confirmatory testing would be required to make the diagnosis, predict a course of treatment, and avoid overtreatment or undertreatment. The PAX3-MAML3 fusion is the most common genetic alteration in this tumor (58.6%), but isolated PAX3 rearrangements (19.2%), absence of rearrangements (9.1%), PAX3-FOXO1 (8.1%), PAX3-NCOA1 (4%), and isolated MAML3 rearrangements (2%) have also been reported [3]. Aside from the dual staining pattern, it is also characterized by a highly cellular spindle cell neoplasm with monomorphic histopathology, as well as S-100 positivity and actin positivity on immunophenotyping.

The true nature and full information regarding biphenotypic sinonasal sarcoma are still unknown. This is because it is relatively rare and has been reported mainly in case reports and small case series. Biphenotypic sarcomas have been reported in the English literature at various sites of the nose and paranasal sinuses with intracranial or orbital extensions. This case report discusses the diagnosis and management of the first ectopic site of these tumors located in the parapharyngeal space.

CASE REPORT

A 51-year-old male presented to the outpatient department complaining of diffuse pain on his left side of the neck for the past six years. There was a dull aching pain that was insidious in onset, non-progressive, intermittent, and sometimes radiating to the left forearm. Neither tingling nor numbness was present in the forearm, nor were swallowing difficulties or voice changes reported. The condition was not aggravated or relieved by any factors. In the past six years, the patient had been taking continuous medication (Metformin and Glimpiride) for type 2 diabetes mellitus. Additionally, the patient was hypertensive and had been on continuous medication for the past 10 months (Amlodipine and Telmisartan). A general physical examination revealed no abnormalities, and vital signs were within normal limits.

During the local examination, no swelling was apparent, but upon palpation, a diffuse swelling was palpable over the left side of the neck, which was non-tender, firm to solid in consistency, non-mobile, and had diffuse margins. The overlying temperature was normal. An indirect laryngoscopy using a 70-degree Hopkins rigid endoscope revealed no abnormalities.

The patient underwent radiological investigations including contrast enhanced magnetic resonance imaging cervical spine with screening of whole spine. The results revealed a large lobulated heterogeneous signal intensity mass lesion on the left side of the neck. This mass primarily affected the post-styloid parapharyngeal and prevertebral spaces and displaced the internal jugular vein and carotid artery anteriorly against the left anterolateral vertebral margins of the C2 to C6 vertebrae. There was evidence of muscle involvement in the short-tau inversion-recovery (STIR) sequences, particularly the longus colli, the prevertebral muscles, and the scalene group of muscles with

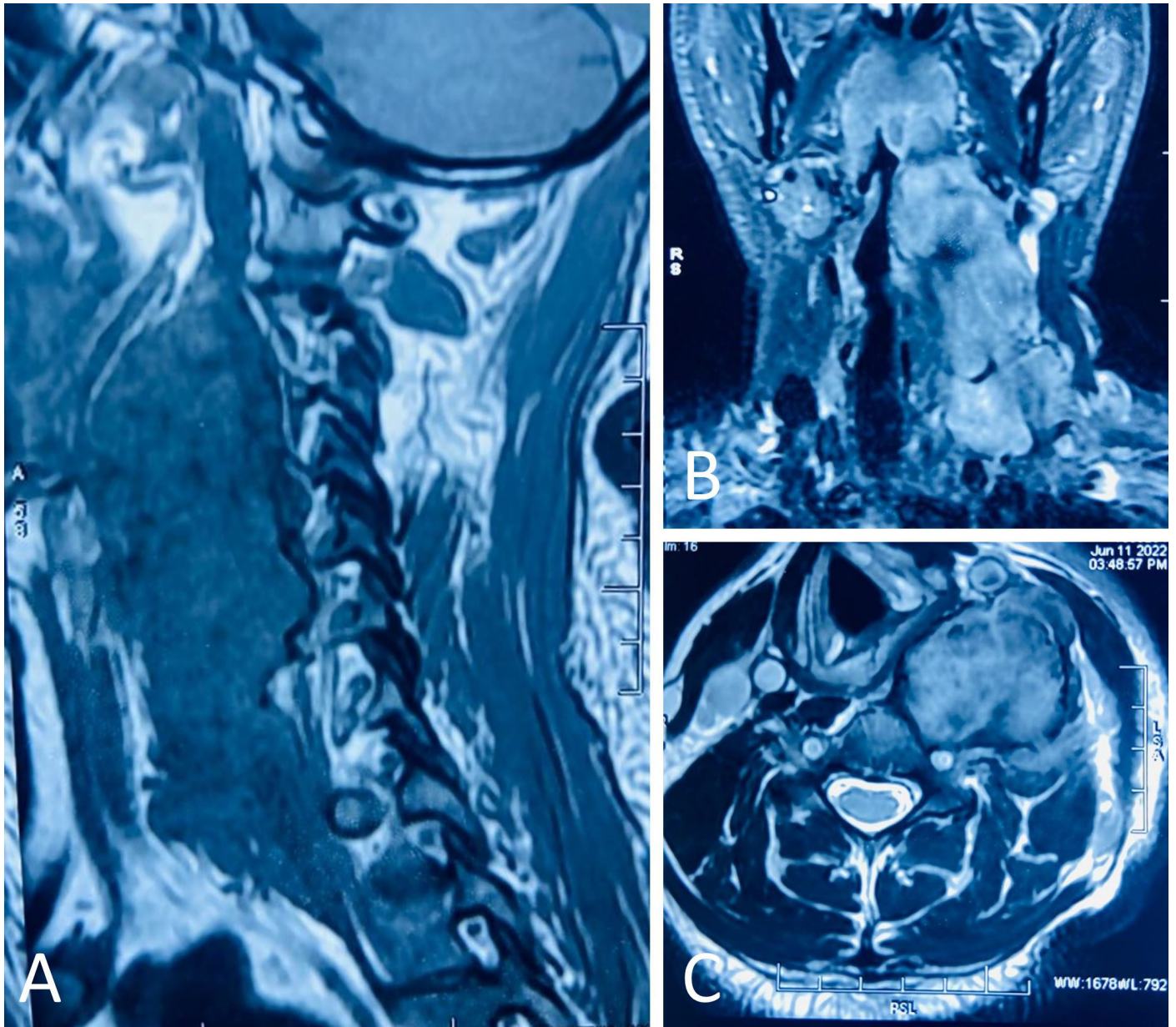


Figure 1. A contrast enhanced magnetic resonance image of the patient's neck reveals a heterogeneous lobulated mass measuring 6 cm x 3.9 cm x 12.8 cm within the perivertebral and post-styloid parapharyngeal regions. (A) A sagittal section of C2 to C6 reveals abutting anterolateral margins (underlying marrow edema and variable cortical flattening in C2 to C5 vertebral bodies, and likely mass extension in C2 to C3). In the perivertebral muscles and the scalene muscles (likely involved), there is a heterogeneous hyperintensity of the short-tau inversion-recovery (STIR) sequences. Coronal (B) and axial (C) sections show the mass in the post-styloid parapharyngeal region and perivertebral areas, displacing the laryngopharynx towards the right without any apparent invasion.

heterogeneous hyperintensities. The mass appeared mildly hyperintense on T2 images with peripheral hypointensities. The tumor was isointense on T1 images with focal areas of peripheral hyperintensity, and heterogeneously hyperintense on STIR images, measuring approximately 6 cm x 3.9 cm x 12.8 cm in size. Although the internal jugular vein was compressed, the flow voids in the vascular system remained largely intact. The neck did not exhibit any significant lymph nodes, but subcentimetric lymph nodes with fatty hilum were present bilaterally at levels II and Ib of the neck. The mass indented the laryngopharynx and contralaterally displaced it right laterally, but no obvious invasion was apparent (Figure 1).

Ultrasound-guided fine needle aspiration revealed a spindle cell lesion of possible neural origin with borderline cytological features

that would require histopathological verification. An orthopedic spine surgeon and a plastic surgeon were consulted in order to plan the surgery and provide assistance during the procedure.

As shown in Figure 2A, the patient was then scheduled for excision of the mass under general anesthesia. As the majority of the tumor's bulk lay medial to the sternocleidomastoid and omohyoid muscles, these muscles were cut in the middle in order to expose the tumor (Figure 2B). Upon dissection, the tumor appeared to be bilobed in appearance, extending superiorly just medial to the angle of the mandible and inferiorly until the apex of the pleura. The spinal accessory nerve and the vagus nerve were identified and preserved. The intraoperative examination revealed a few enlarged lymph nodes. A small tumor tissue with two lymph nodes was sent for frozen sectioning in-

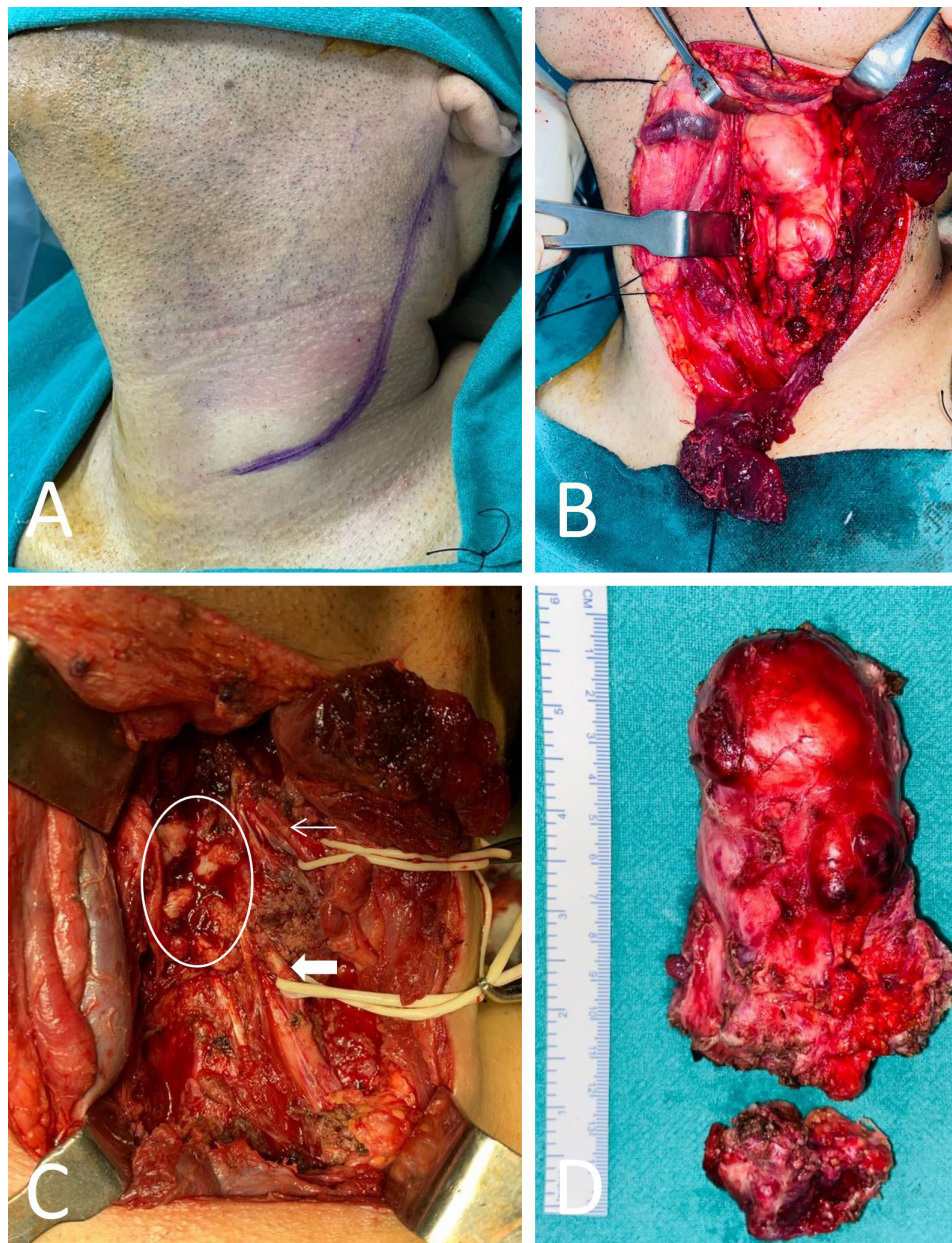


Figure 2. Photographs taken before and during surgery. (A) There is a J-shaped incision on the left side of the neck, and there is no apparent swelling visible on the neck. (B) Upon dividing the sternocleidomastoid muscle, the mass is exposed. (C) An intraoperative photograph following the excision of the tumor. The thin arrow indicates a spinal accessory nerve. The thick arrow represents the vagus nerve. The circle indicates the transverse processes of the cervical vertebrae. (D) Upon excision of the tumor, a specimen is obtained.

traoperatively, which revealed spindle cells with many nuclei. There was no evidence of mitosis or necrosis. In this case, the tissue had neural origins, suggesting that it may have been the result of a neural tumor. However, a section taken from the lymph node demonstrated reactive lymphoid hyperplasia. Following dissection, we found that the tumor was firmly adherent to the body of cervical vertebrae C3-C6 and had extended into the transverse processes of C-3, C4, and C5. By using a chisel and hammer, the tumor was separated from the vertebral bodies from anterior to posterior (Figure 2C). As the tumor extended below the clavicle, the thoracic duct was inadvertently injured during dissection in that area. The specimen was removed in total (Figure 2D).

The wound was closed in layers with a Hemovac drain. The patient was transferred to the Intensive Care Unit for overnight observation and extubated the following day. It was a pleasant surprise to find that

there were no neurological deficits postoperatively, and the patient was discharged on postoperative day five. Serial sectioning of the specimen revealed a grey, white growth measuring 9x4x3 cm³ roughly reaching up to all margins. Microscopically, the growth was composed of spindle cells. It was observed that these cells were monotonous in appearance with an ovoid to elongated nucleus. Pleomorphism was minimal, and there was no mitosis. The tumor had infiltrated adjacent tissues and skeletal muscles, entangling the blood vessels. Hemorrhages were present in certain areas. Immunohistochemistry reveals the expression of Vimentin, Desmin, smooth muscle actin, and S100 in tumor cells. There was no evidence of CD34 or CK expression in tumor cells (Figure 3). There was a strong indication that the tumor was a biphenotypic sinonasal sarcoma based on these features. To determine the condition of the paranasal sinuses and whether a coexisting sinon-

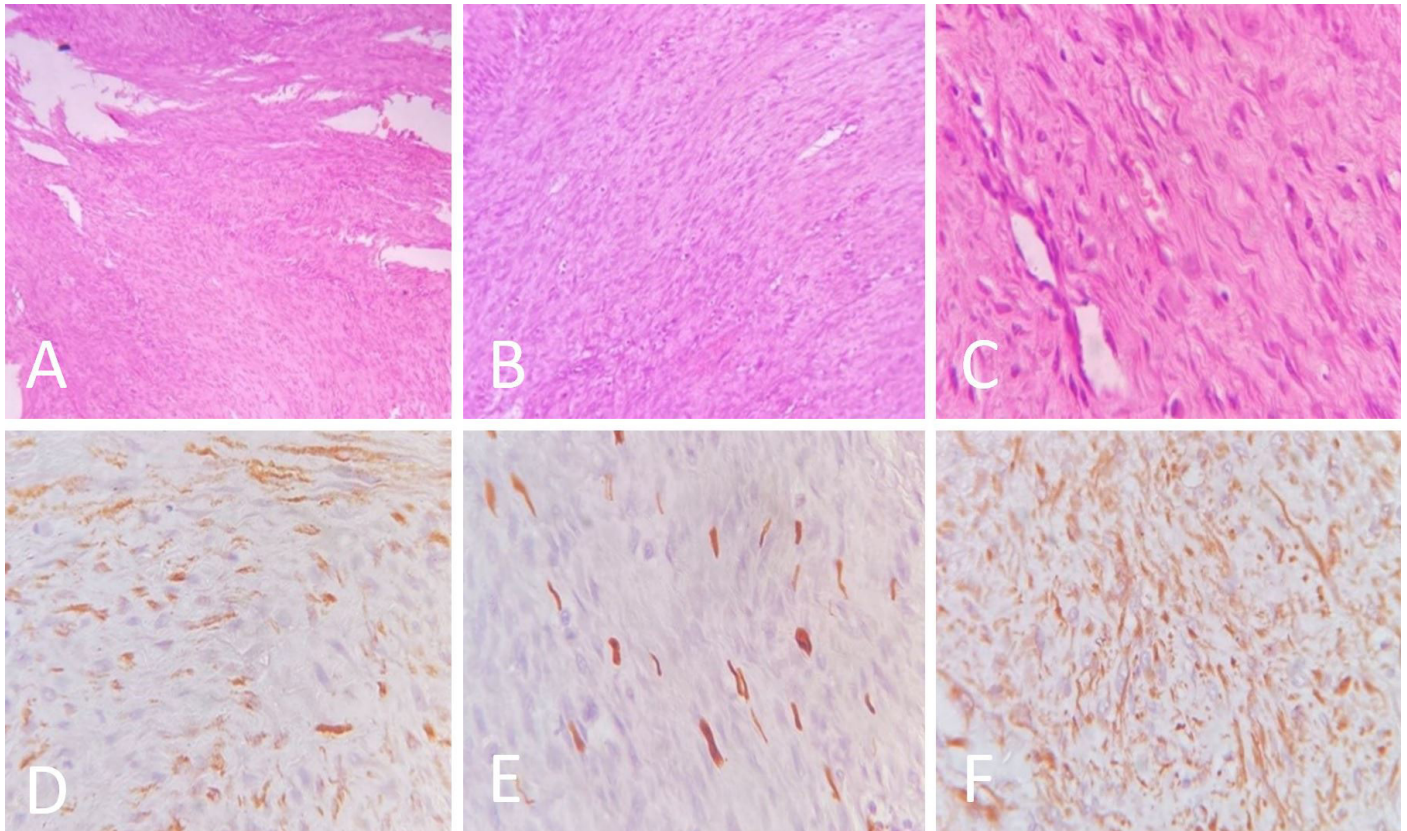


Figure 3. Hematoxylin and eosin-stained sections of the specimen are shown in the image. (A) Monomorphic spindle cells with ovoid to elongated nuclei (40X). (B) Spindle cells with inconspicuous nucleoli (100X). (C) Minimal pleomorphism (400X). (D) Diffuse cytoplasmic and membranous staining with smooth muscle actin (400X). (E) Focal nuclear and cytoplasmic positivity with S100 (400X). (F) Diffuse cytoplasmic positivity with Vimentin (400X).

asal mass was present, the patient was advised to undergo non-contrast computed tomography of the nose and paranasal sinuses. The report revealed that there were no sinonasal masses (Figure 4). Upon being referred to the radiation oncology department, the patient was scheduled for concurrent radiotherapy.

DISCUSSION

Initially described by Lewis et al. in 2012, biphenotypic sinonasal sarcoma was described as a low-grade sinonasal sarcoma with neural and myogenic features [4]. Furthermore, they observed histological similarity between this group of cases and adult fibrosarcoma, monophasic synovial sarcoma, and malignant peripheral nerve sheath tumor (MPNST). The tumor was renamed biphenotypic sinonasal sarcoma in 2014 due to its recurrent genetic rearrangement in PAX3 [5]. It is imperative to note that the tumor is locally invasive and may affect adjacent areas including the skull base frontal lobe and the opposite side sinuses if diagnosis or treatment is delayed [6]. We also found that the tumor infiltrated the prevertebral fascia in our case. It has a female to male ratio of 2:1, indicating a preference for women, whereas our case report refers to a male patient. It is typically associated with multiple sinonasal subsites, with the superior nasal cavity and ethmoid sinus being the most commonly affected, followed by the sphenoid sinus [7]. In a case of biphenotypic sinonasal sarcoma of the nose and paranasal sinuses, the most common symptoms are nasal obstruction and midfacial pressure; however, patients may also experience epistaxis, epiphora, rhinorrhea, and re-

current sinusitis [3]. However, none of these symptoms were present in our case. Friche et al. reported the largest series of biphenotypic sinonasal sarcomas, including 44 patients, all of whom had a disease affecting either their nose or their paranasal sinuses [8]. In a series of 41 cases reported by Loarer et al. in 2019, all of the cases originated from the nose and paranasal sinuses, and none of them presented as ectopic [9]. Clinically, a biphenotypic sinonasal sarcoma may resemble a schwannoma in both appearance and presentation. In our case, ultrasonography-guided fine needle aspiration cytology revealed a spindle cell lesion with borderline cytological characteristics.

The surgical excision of the case was planned accordingly. The intraoperative appearance of the case was similar to that of a schwannoma and appeared to arise from the brachial roots. However, the surgical management of such tumors may require the cooperation of a multidisciplinary team since the tumor was located near the vertebrae and brachial roots. In order to reduce the risk of neurovascular injuries during surgery, otolaryngologists, orthopedic spine surgeons, and plastic surgeons should be present during surgery. To accurately diagnose biphenotypic sinonasal sarcoma, immunophenotyping and/or molecular analysis are required. In histological terms, biphenotypic sinonasal sarcoma is characterized by highly cellular spindle cell neoplasm with monomorphic features on histology as well as immunophenotyping positive for both S-100 and actin.

Biphenotypic sinonasal sarcomas are generally reported to originate from the nasal cavity, sinuses, and adjacent tissues; however, this was not the case in our case. An unusual presentation was observed in our patient. He complained of diffuse left-sided neck pain not previously described in the English literature. A radiograph-

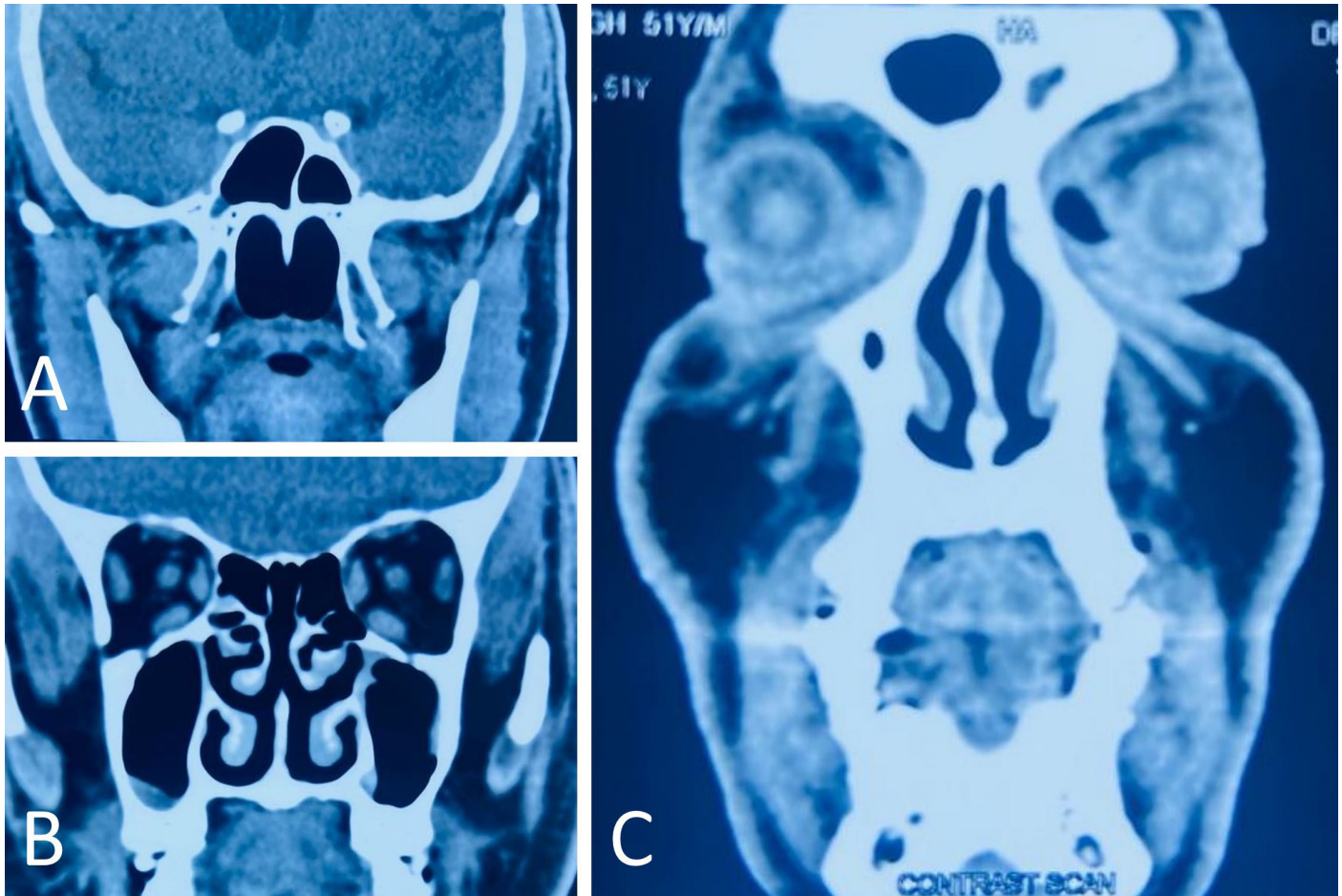


Figure 4. A non-contrast computed tomography examination of the nose and paranasal sinuses reveals that no masses are found in the sinonasal cavities (A-C).

ic examination revealed that the tumor was not involving its usual sites, namely the nose and paranasal sinuses. It was noted that the tumor mass was located in the left parapharyngeal space and that it involved the pre- and perivertebral spaces. A cytological examination revealed spindle cells with neural origins. It appeared that this tumor had infiltrated the surrounding tissues and skeletal muscles, entrapping blood vessels along the way. In immunohistochemistry, tumor cells were found to express Vimentin (a marker of mesenchymal tissue), S-100 (a marker of neural tissue), as well as Desmin and smooth muscle actin (representing muscular origins) [10,11]. There is a tendency for biphenotypic sinonasal sarcomas to recur, and the recurrence rates between surgical excision alone and surgical excision with radiotherapy are equivalent. Indications for postoperative radiotherapy include positive or close surgical margins, high-grade tumors, perineural invasion, or concerns regarding surgical margins. Typically, radiotherapy is used to target the tumor bed, resection cavity, and areas that are at high risk of harboring microscopic disease [12].

It is pertinent to note a few salient points. First, biphenotypic tumors can be challenging to diagnose both for clinicians and pathologists. Therefore, it is imperative that the specimen be reviewed by an experienced pathologist in order to plan appropriate surgical management. Second, biphenotypic tumors should be considered among the differential diagnoses for neck swelling. Third, such tumors should be managed by a multidisciplinary team.

CONCLUSION

Biphenotypic sinonasal sarcomas are rare sinonasal tumors that are generally not found in ectopic sites such as the parapharyngeal and paravertebral space. To make an accurate diagnosis and to manage the case effectively, cytology and histopathology must be thoroughly examined by an experienced pathologist.

ARTICLE INFORMATION

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