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ORIGINAL CONTRIBUTION

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Experience with endonasal endoscopic resection of non-angiofibroma sinonasal and orbital apex vascular tumours*

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Abstract

Background: Endoscopic endonasal approach for the management of sinonasal inflammatory pathologies and tumours has been a widely accepted procedure and used for many years. The aim of the study is to assess effectiveness and safety of endonasal endoscopic resection in removal of sinonasal vascular tumours and to evaluate outcomes and clinical behaviour of different subtypes with review of the literature.

Material and Methods: A retrospective review of the patients treated for sinonasal and orbital apex vascular tumour was performed. Patient's demographics, surgical approaches, complications, histopathological results, and long-term outcomes were evaluated.

Results: Twenty-two patient included in this study. The mean tumour size ranged from 6 to 100 mm (30.45 ± 22.7 mm). Histopathological examination revealed 8 (36%) capillary hemangioma, 6 (33.3%) cavernous hemangioma, 2 (12%) mixed hemangioma, and 2(12%) vascular leiomyomas. Three (13.6%) patients were diagnosed as glomangiopericytoma and remaining 1 (4.4%) was angiosarcoma. Only in 1 patient with recurrent glomangiopericytoma preoperative embolization were needed. Five patients had preoperative biopsy in office settings. The mean follow-up was 72.9 (± 53.71) months. The recurrence was observed in 3 (13.6%) patients.

Conclusion: Endonasal endoscopic approach for sinonasal vascular tumours is a safe and reliable method for resection. Our study suggested location of the tumour is more important than the size to achieve complete resection. Long-term follow-ups are important to detect recurrences early even after macroscopically complete resections.

Key words: Sinonasal tumours, lobular capillary hemangioma, cavernous hemangioma, glomangiopericytoma, angiosarcoma, endoscopic endonasal surgery

Introduction

The vascular tumours of the nasal cavity and paranasal region that are classified as rarely seen benign, borderline/ low-grade malignant, and malignant soft tissue tumours according to fourth edition of the World Health Organization classification of head and neck tumours [(1)]. Hemangioma arises from vascular endotheliocytes and accounts for about 25% of non-epithelial tumours of the sinonasal tract [(1, 2)]. They have different histologic subtypes such as hemangioma, glomangiopericytoma, angioleiomyoma, angiofibroma and angiosarcoma. Because of rarity, there are only a few published original papers focused on sinonasal non-angiofibroma vascular tumours in the English literature [(6, 7)].

Endoscopic endonasal approach for the management of sinonasal inflammatory pathologies and tumours has been widely accepted procedure and used for many years [(3-9)]. Although open approaches have to be still used in cases that are not suitable for

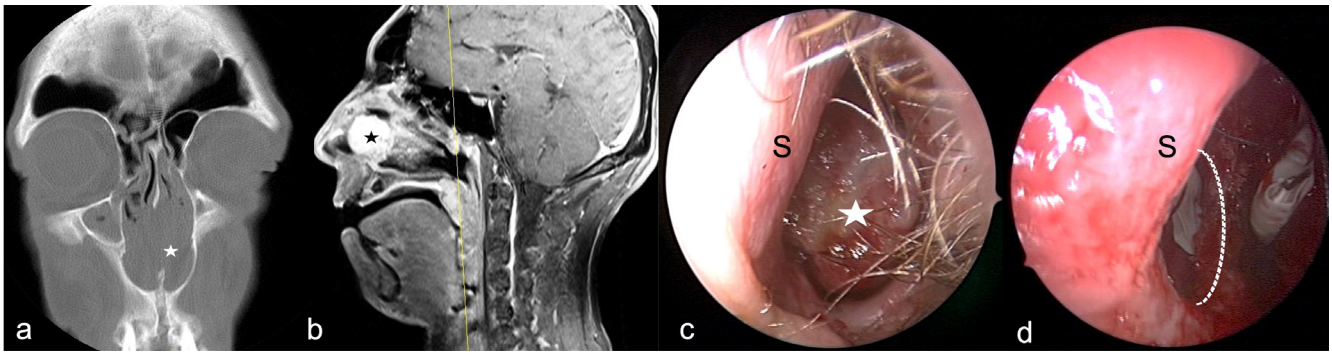

Figure 1. Preoperative a) coronal CT and b) sagittal MRI of the patient with nasal septum anterior originated lobullary capillary hemangioma (LCH) causing septal perforation c) endoscopic view of LCH d) Intraoperative view of septal perforation after complete resection S: nasal septum, * tumour.

endoscopic technique, most tumours can now be removed by the endonasal route with less morbidity compared to open approaches [9]. Technological advances in endoscopic instrumentation such as computer-assisted navigation systems, microdebrider, microvascular ultrasound doppler probe, and preoperative embolization helping surgeons to avoid complications [9, 10].
The aim of the study is to assess effectiveness and safety of endonasal endoscopic resection in removal of sinonasal vascular tumours, to evaluate outcomes, clinical behaviors of different subtypes and review the literature.

Materials and methods

Medical records of the patients treated for sinonasal vascular tumour and orbital apex vascular tumor at a single tertiary center between January 2006 and November 2021 were retrospectively reviewed. Patient's clinicopathological features including age, sex, medical history, symptoms, tumour origin, tumour size, diagnostic methods, surgery, intraoperative and postoperative complications, histopathological findings, outcomes, and follow-up times were noted (Table 1). Patients underwent purely open approaches or diagnosed with juvenile nasopharyngeal angiofibroma were excluded from the study.

Results

Twelve (54.5%) male and 10 (45.5%) female patient included in this study. The mean age was 54.86 (minimum: 16, maximum: 89, SD: 16.04). The main presenting symptom was nasal obstruction (50%) followed by epistaxis (35%), postnasal drip (15%), diplopia (5%), headache (5%), proptosis (5%), decreased vision (5%), and aural fullness (5%).
The medical history of the patients included hypertension (25%), coronary artery disease (10%), diabetes mellitus (10%), and celiac disease (5%). There was no pregnant patient, and none of the female patients had a history of symptom presented during the time of pregnancy. None of the patient describe trauma but 3 patients had multiple episodes of epistaxis controlled by nasal packing.
The mean duration of the symptoms excluding incidental found cases describing long-term symptoms was 7.94 (minimum: 1, maximum: 36, SD: 9.14) months. The mean tumour size ranged from 6 to 100 mm (30.45 ± 22.7 mm).
The site of origin of tumour was the middle turbinate in 4 (18%), inferior turbinate in 4 (18%), nasal septum in 5 (22.7%) (Figure 1), the lateral nasal wall 2 (9%), the ethmoid cells in 2 (9%), orbital apex in 1 (4,5%), intra-orbital in 1(4,5%), infratemporal fossa in 1(4.5%), (Figure 2), frontal sinus in 1 (4.5%) and the nasal vestibule in 1(4.5%), case. The patient with intra-orbital hemangioma had a surgery history via craniotomy approach for orbital hemangioma 15 years ago. The patient with angiosarcoma had a history of multiple basal cell carcinoma and angiosarcoma of the skin. Other than these 2 patients all patient was primary cases. One glomangiopericytoma, 1 angiosarcoma and 3 capillary haemangioma had preoperative local biopsy in office settings and bleeding were controlled with cauterization and packing with haemostatic agents such as surgicel. In 2 cases, tumours were found incidentally in the surgical specimen of the nasal cavity, and it was not possible to distinguish precisely where they originated from. There was one more case incidentally found hemangioma in the ethmoidectomy specimen.
All patients had undergone computerized tomography (CT) examination. However, 10 (50%) patients got an additional magnetic resonance imaging (MRI) to assess surrounding soft tissue and neurovascular structures. Table 1 summarizes clinicodemographic features of the patients.

Histopathology

Histopathological examination revealed benign vascular tumour in 18 (81,8%) cases consisted of 8 (36%) capillary hemangioma, 6 (27%) cavernous hemangioma, 2 (9%) mixed hemangioma, and 2 (9%) angioleiomyoma. Three (13%) patients were diagnosed as glomangiopericytoma and remaining 1 (4.5%) was angiosarcoma (Table1).

Table 1. Characteristics of the patients with sinonasal vascular tumour.

Patient	Age	Gender	Symptom	Symptom duration (month)	Histopathology	Origin	Complication	Tumor size (mm)	Follow-up time (month)	Recurrence
1	48	F	Nasal obstruction	5	Angiosarcoma	Left middle turbinate	No	40x25	6	Yes
2	16	F	Nasal obstruction, epistaxis	6	Glomangiopericytoma	Left middle turbinate	CSF leak in 2nd revision surgery	100x75	81	Ye
3	72	F	Nasal obstruction	7	Glomangiopericytoma	Left middle turbinate	No	73x53	62	No
4	69	M	Epistaxis	6	Glomangiopericytoma	Left Lateral nasal wall	No	47x37	12	No
5	48	M	Nasal obstruction, postnasal drip	Long time	Cavernous hemangioma	Left nasal septum	Septal perforation	35x32	151	No
6	56	M	Aural fullness	12	Cavernous hemangioma	Right ITF	No	26x17	97	No
7	49	M	Nasal obstruction, postnasal drip	Long time	Cavernous hemangioma	Left lateral nasal wall	No	33x47	74	No
8	89	F	Proptosis	6	Cavernous hemangioma	Left ethmoid cells	No	18x14	44	No
9	46	M	Headache	36	Cavernous hemangioma	Frontal sinus	CSF leak	52x35	42	No
10	52	F	Decreased vision (left)	2	Cavernous hemangioma	Left orbital apex	No	7x7	34	No
11	54	M	Nasal obstruction	2	Capillary hemangioma	Left anterior septum	No	15x10	141	No
12	43	M	Nasal obstruction	12	Capillary hemangioma	Middle of septum base	Septal perforation	27x25	103	No
13	74	F	Epistaxis	24	Capillary hemangioma	Left inferior turbinate	No	15x10	41	No
14	66	F	Epistaxis	1	Capillary hemangioma	Left inferior turbinate	No	20x20	44	No
15	74	F	Nasal obstruction	4	Capillary hemangioma	Left anterior septum	Septal perforation	20x15	37	No
16	20	F	Nasal obstruction	2	Capillary hemangioma	Left nasal vestibule	No	20x16	156	No
17	48	F	Epistaxis	2	Capillary hemangioma	Left middle turbinate	No	16x9	71	No
18	57	M	Orbital pain, diplopia	5	Mixed Hemangioma	Right orbital apex	Frontal mucocele	20x8	145	Yes
19	58	M	Nasal obstruction, postnasal drip	Long time	Mixed Hemangioma	Left ethmoid cells (Incidental)	No	15x20	68	No
20	49	M	Epistaxis	3	Vascular leiomyoma	Right inferior turbinate	No	6x5	184	No
21	52	M	Severe Epistaxis	2	Capillary hemangioma	Right septum posterior	Septal perforation	50x40	6	No
22	65	M	Epistaxis	1	Vascular leiomyoma	Right inferior tubinate	No	15x15	6	No

Surgery

Only one patient with an adolescent onset glomangiopericytoma had preoperative embolization. Preoperative biopsy and intraoperative frozen section were performed in 4 (18%) and 6 (30%) of the cases, respectively. Endoscopic endonasal resection of the tumour including the attachment with a few millimeter margins was performed to most of the cases. If septal deviation that caused nasal obstruction or prevented endoscopic surgery

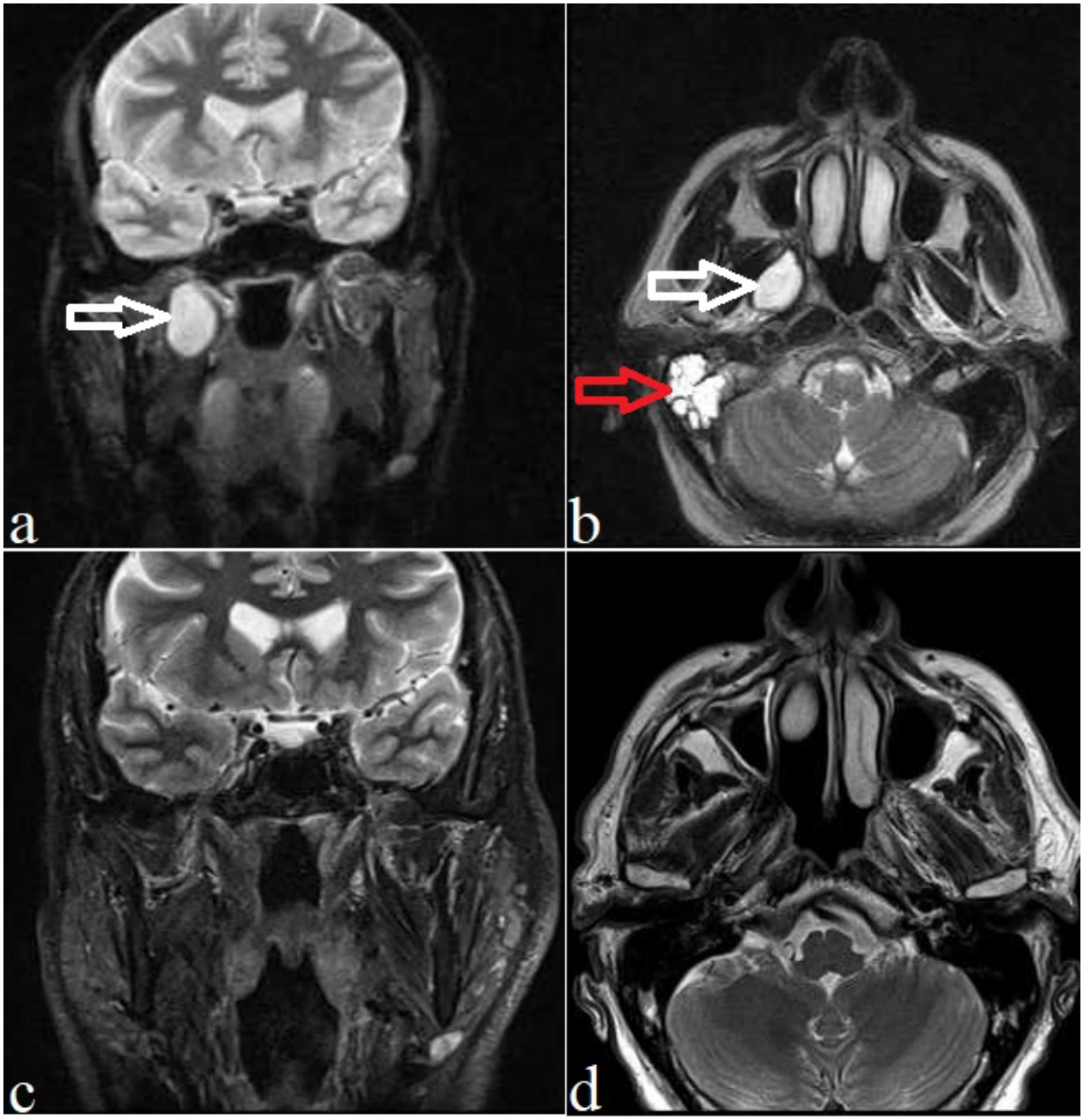

Figure 2. Preoperative a) coronal and b) axial T2-weighted MRI of the patient with Infratemporal fossa cavernous hemangioma which shows a well-defined border and high intensity (white arrow). It also demonstrates otomastoiditis due to serous otitis media (red arrow). Postoperative 1.5 years c) coronal and d) axial T2-weighted MRI of the patient. There was no evidence of recurrence of tumour and otomastoiditis.

was detected, the patient was undergone septoplasty.
One patient with a cavernous hemangioma in the frontal sinus was undergone DRAF3 procedure and endoscopic cerebrospinal fluid leakage repair via endoscopic multilayer reconstruction.
For the patient with a cavernous hemangioma in infratemporal fossa an endoscopic endonasal resection via trans-pterygoid approach (Figure 2) were utilized and unilateral grommet insertion was done. Patient with angiosarcoma a combined approach was performed via infraorbital incision and endonasal DRAF 2b procedure. Patient with intra-orbital tumour was resected via purely endonasal endoscopic approach.
After a mean follow-up of 72.9 (± 53.71) months, ranging from 6 to 184 months| the recurrence was observed in 3 (13.6%) patients. Out of these 3 patients 1 diagnosed as angiosarcoma, 1 hemangiopericytoma and 1 mixed hemangioma (Table 1). Angiosarcoma case had a recurrence 6 months after the surgery and consulted to medical oncology for palliative treatment and died 9 months after diagnosis. The hemangiopericytoma patient had 2 more revision surgery for recurrence and currently living without recurrence for 6,5years (Figure 3). The last case

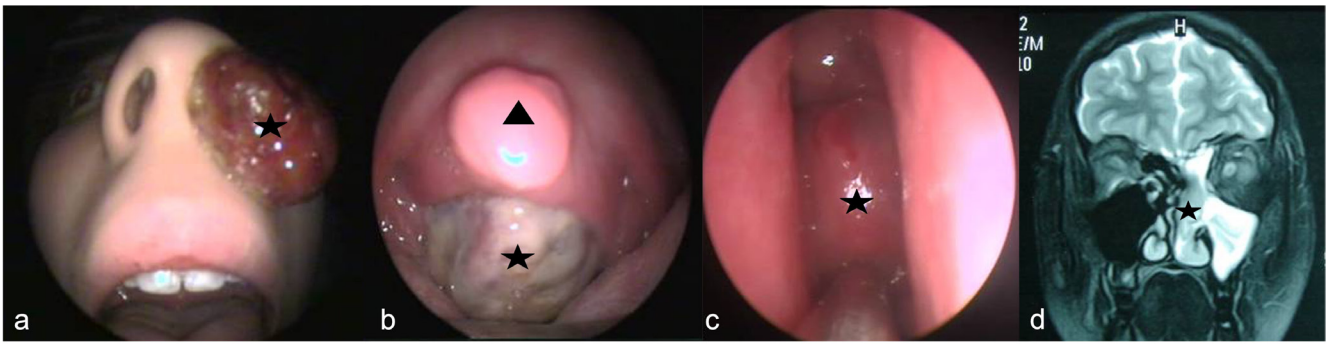

Figure 3. Left sided glomangiopericytoma a) endoscopic view of adolescent patient at presentation b) tumour extending to posterior pharynx endoscopic view inside oral cavity tumour visible in posterior to uvula c) endoscopic view before last revision surgery left side sinonasal mass covered with mucosa d) preoperative MRI before last surgery coronal view showing tumour attaching to the skull base.

was patient with intra-orbital hemangioma. The recurrence was due to incomplete resection to prevent ophthalmoplegia and postoperative visual acuity and eye movements were normal, and there is no complaint for now and following conservatively by otolaryngology and ophthalmology team.

Cerebrospinal fluid leakage was occurred in 2 patient, first patient was patient with a cavernous hemangioma in the frontal sinus. During resection due to invasion of the posterior wall of frontal sinus and CSF leak occurred. Second patient was glomangiopericytoma patient required 2 revision surgery for tumour recurrence, during resection from anterior skull base CSF leak occurred. Watertight closures were achieved in both. Frontal mucocele was occurred in the patient with intra-orbital hemangioma and undergone revision DRAF2b procedure 3 months after resection (Table 1). Septal perforation due to tumour resection was detected in 4 patients. 2 patients had complaints because of perforations and underwent an endonasal septal perforation repair.

Discussion

A wide variety of tumours exist in the sinonasal cavity, as it contains a significant histological diversity [11]. Sinonasal manifestation of vascular tumours are very rare in this variety [1, 2, 4, 5]. There are no randomized clinical trials regarding sinonasal tumours including vascular tumours [7, 12]. Single-center studies and experiences has therefore an important role to define treatment modalities and assess outcomes [12].

Current reports in literature regarding sinonasal vascular tumours are mainly focused on juvenile nasopharyngeal angiofibroma and there is limited study related to other sinonasal vascular tumours [7]. Based on this, in this study, we reviewed non-angiofibroma sinonasal vascular tumours managed with an endoscopic approach. Obtaining preoperative biopsy can be challenging and it could be difficult to manage the bleeding in some cases. Because of the risk of severe bleeding biopsy is not recommended as first choice but unfortunally different sinonasal tumors have same presenting symptoms and it is not always easy to differentiate benign tumours from malignancies and a biopsy is unavoidable [6,13]. Necessary precautions should be taken to avoid catastrophic hemorrhage.

Hemangioma

Hemangiomas are common head and neck tumours in the pediatric population. However, they spontaneously resolve up to 70% by the age of 7 and this may be an explanation for rarity in adults [13]. Nonetheless, sinonasal hemangiomas are rare both in adults and children.

The histological classification of hemangiomas is defined as capillary, cavernous and mixt type according to predominant vessel size at microscopy [14]. It has been reported that cavernous type occurs more likely in adults as capillary form shows more spontaneous resolution than cavernous type [13]. However, capillary hemangioma was the most common form in our cases as with previous studies [2, 6, 13, 15-17] and it may be concluded that capillary hemangioma is the most common form in the sinonasal cavity.

The etiologic factors of the hemangioma are still controversial [2, 13, 17]. Nevertheless, nasal trauma, hormone related situations such as pregnancy and oral contraceptive use, viral oncogenes are the possible causes that may have a role in the pathogenesis [2, 6, 13, 17], however, none of them were present in our study population. On the other hand, whatever the etiology is, it is possible that mucosal inflammation and related changes of the levels of vascular endothelial growth factors may have triggered the formation of hemangioma [2]. However, it is unknown that why hemangioma develops in some patients and not others. Although hemangiomas are benign tumours, they have a potential for local recurrence up to 42% [3].

Three of patients with hemangioma had hypertension and hypertension was the most common medical condition in our study compatible with Kim and Kwon's study [6]. They also suggested that hypertension may be considered as a possible cause of

hemangioma in the elderly [6]. However, our data is not enough to support this suggestion even hypertension is the most common concomitant medical disease in our cases.

Hemangiomas can occur at any age [1]. In our study, patients' ages ranged from 20 to 89 (mean: 55.6 ± 16.03) compatible with Lim et al. 's study [17]. In our study, capillary and cavernous form showed female and male predominance, respectively as with Kim and Kwon's study [6]. However, there is no consensus in the literature about gender dominance [13, 14, 17, 18].

Although unilateral epistaxis and nasal obstruction are the main symptoms of sinonasal hemangioma as with our study, the patients can refer with fewer common symptoms such as headache, facial pain, vision changes, diplopia, and aural fullness due to location of the tumour [6, 16, 17]. However, these symptoms do not differ between capillary and cavernous types [17].

Previous studies [2, 6, 13, 17, 18] showed that the nasal septum and inferior turbinate are common sites of the sinonasal hemangioma followed by middle turbinate, nasal vestibule, maxillary, or ethmoid sinuses and incidentally found cases. In contrast, 5 (33.3%) of 15 cases were in these locations. Unlike other studies, ours included very uncommon locations i.e., pterygopalatine fossa, and orbital apex [19, 20]. Although, there were several cases intraosseous frontal hemangioma, we found only one case with frontal sinus hemangioma in a child in the English literature [21].

The relationship between site of the origin of the tumour and histopathologic features are controversial. While Lim et al. [17] found no significant difference between them, Kim and Kwon [6] detected that capillary hemangioma is more likely located in the septum and inferior turbinate ($p < 0.01$) as with our study.

The first step in the diagnosis is endoscopic examination which shows typical red or purplish appearance of the hemangioma [2]. CT and/or MRI demonstrate anatomical structures, the extent, and characteristics of the tumour [2, 6, 13, 17, 18]. Kim et al. [18] compared the radiological findings of capillary and cavernous hemangioma. They found that while capillary form showed early strong enhancement and delayed wash-out, there were centripetal and multifocal nodular appearance in the cavernous form. They also detected that bony destruction and remodeling occurred more likely in the cavernous form, particularly hemangioma larger than 2 cm. Similarly, bony destruction was observed in two of 15 cases which were larger than 2 cm in our study. The histopathological examination reveals certain diagnosis and typing of the tumour. Preoperative biopsy was undertaken in 3 of our cases as compatible with other studies. However, we performed intraoperative frozen section in 6 patients with a 100% accuracy of the results. The risk of uncontrolled nasal bleeding after biopsy should bear in mind, although it facilitates the diagnosis and treatment planning [6, 13, 17] and this may be the reason why preoperative biopsy is not preferred. Intraoperative frozen section may be an option in case of the suspect of malignancy.

The differential diagnosis may include inverted papilloma, angiofibroma, malignant sinonasal tumours, nasal polyposis, and organizing hematoma [6, 13].

Endoscopic endonasal subperichondrial or periosteal excision of the tumour including the attachment of the hemangioma is the treatment of most of the cases [2, 17]. Incomplete excision is the main cause of the recurrence. Similar with in literature [2, 17], one (6.6%) of our patient with intra-orbital hemangioma showed recurrence due to incomplete resection. To achieve complete resection, endoscopic sinus and skull base surgery including DRAF procedures and CSF leakage repair may be needed due to location and/or bony destruction as with our cases. Preoperative embolization may be useful when the tumour are supplied from branches of external carotid artery [10]. We only need preoperative embolization in a. case with recurrent glomangiopericytoma. Intralesional bevacizumab (anti-vascular endothelial growth factor monoclonal antibody) injection, steroid injection, cryotherapy, sclerotherapy, or laser ablation are other treatment methods for the hemangioma [17,22].

Angioleiomyoma (Vascular Leiomyoma)

Vascular leiomyoma, also known as angioleiomyoma, that is a benign mesenchymal tumour of skin and mostly subcutaneous, is very rare (<1%) in the sinonasal area. Histopathologically, they contain well differentiated smooth muscle cells with vascular channels. They generally originate from turbinate followed by nasal orifices, septum, and lateral nasal wall. The symptomatology, diagnosis and treatment of vascular leiomyoma are similar with hemangioma [23].

Glomangiopericytoma

Glomangiopericytoma, also known as hemangiopericytoma, is a borderline and low-malignant-potential soft tissue of the sinonasal tract [1]. Although demographic and clinical features are similar to hemangioma, it should be considered that glomangiopericytoma may metastasize even after a long period of treatment [24]. Glomangiopericytoma, has a high incidence of local recurrence (8-53%) and metastasis (35-57%) rates (4). Park et al. [24] reported that positive surgical margin ($p = 0.036$) and adjuvant chemotherapy/radiotherapy ($p = 0.003$) has a strong correlation between recurrence/metastasis. Sinonasalmanifestation of glomangiopericytoma rarely occurs and accounts for <0.5% of all sinonasal neoplasms [1, 4].

Our study was included three patients with glomangiopericytoma. Two of them showed no recurrence during follow-ups. But in a patient with an adolescent onset glomangiopericytoma first recurrence was detected just in 5 months after initial surgery, and she showed more recurrence at 2 years interval. For now, she is at about 6.5 years follow-up with no evidence of recurrence. All glomangiopericytoma patients had CT and MRI preoperatively unfortunally radiologist are unable to differentiate glomangiopericytoma from other vascular tumors neither with

CT nor with MRI. One of these tumours was bigger in size despite the suspicious of a vascular tumour we decided to perform biopsy to differentiate from malignancy.
Endoscopic endonasal treatment of glomangiopericytoma is widely used approach however, in some cases it may be necessary to combine it with open approaches to achieve negative surgical margins. Also embolization should be considered in selected cases [25].

Angiosarcoma

In this study, there was one patient with angiosarcoma who had a multiple basal cell carcinoma and angiosarcoma of the skin. The recurrence was detected 6 months after surgery.
Angiosarcoma is a malignant tumour originating from endothelial cells and represents <0.1% of all sinonasal neoplasms [1, 5]. Angiosarcoma is characterized by a very poor prognosis of about 22% five-year survival rate [26]. There was no consensus on standard treatment modality in the literature due to rarity of the tumour. We performed endoscopic endonasal and infraorbital incision and referred to medical oncology for adjuvant therapy however, the patient died 9 months after diagnosis.
The main limitation of this study was a retrospective design at a single-center institution. However, the rarity of these tumours does not allow to arrange prospective cohort studies with larger populations. Nevertheless, the authors of this study consider that these studies may be a steppingstone for potential future multicenter studies and meta-analyses to facilitate defining optimal treatment modalities for different variants of sinonasal vascular tumours.

Conclusions

Sinonasal vascular tumours are rare entities. Endonasal endoscopic approach for sinonasal vascular tumours is a safe and reliable method. Total tumour removal is possible in most of the cases without causing any morbidities. Surgeons should be aware of that complete resection is crucial and key point of the surgery. Our study suggested location of the tumour is more important than the size to achieve complete resection without complication. Long term follow- ups are important to detect recurrences early even after macroscopically complete resections. However, especially for angiosarcoma more studies are needed to assess combine surgical and medical treatment modalities to increase survival rates.

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Authorship contribution

HB and CM wrote the protocol. HB collected the patient data, analyzed and interpreted the patient data. Final critical review was done by CM. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by the institutional ethics committee (Nr: İ10-650-21 Year 2021) and conducted in accordance with the related privacy statements and applicable regulatory requirements.

Availability of data and materials

The datasets used and/or analysed during the study are available from the corresponding author.

Conflict of interest

The authors declare that they have no competing interest.

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