CASE REPORT

Sinonasal angiosarcoma: case report and literature review

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ABSTRACT

BACKGROUND. Angiosarcoma is a neoplastic tumor that originates from endothelial cells, accounting for less than 2% of all sarcomas. The sinonasal localization of angiosarcoma is uncommon. It is a highly aggressive tumor with an increased risk of local recurrence.
CASE REPORT. We present the case of a 24-year-old male patient with 1 month of left side epistaxis, left nasal obstruction, headache and left hemifacial paresthesia. The CT scan of the skull and paranasal sinuses performed with intravenous contrast showed a macronodular heterogenous tissue lesion, partially hyperdense spontaneously, iodophilic, with multiple vascular trajectories apparently of the arterial type, localised in the left maxillary sinus and ipsilateral nasal cavity. The first result from histopathological examination concluded for sinonasal angiofibroma with no signs of malignancy. Even if a wide resection was performed by external and endoscopic approach, a quite quick local recurrence appeared. After the second surgical resection of the tumor, the histopathological examination correlated with immunohistochemical tests and the clinical-imaging aspect concluded on sinonasal angiosarcoma. The proper treatment was delayed because of the histopathological examination misinterpretation.
CONCLUSION. A thorough histopathological examination and immunohistochemistry have an important role for an adequate diagnosis of sinonasal angiosarcoma.
KEYWORDS: sinonasal angiosarcoma, epistaxis, histopathology, immunohistochemistry.

INTRODUCTION

Angiosarcomas are unusual malignant vascular tumors, with rapid growth, which are developed from the endothelial cells. Among all soft tissue sarcomas, they represent less than 2% and less than 0.1% of sinonasal tract malignant tumors[1,2]. Angiosarcoma may occur in any region of the body, but usually appears in the skin and superficial soft tissue of the head and neck, especially the scalp. Primary angiosarcomas involving the nasal cavity and sinuses are rare, only a few cases were reported in the literature[1-26]. Most often, they occur during midlife and the prognosis depends on the size, location and surrounding tissue invasion[18,27].

Clinically, sinonasal angiosarcomas present with similar manifestations as those found in malignant nasosinusal tumors: epistaxis, nasal obstruction and rhinorrhoea. In advanced stages, clinical manifestations depend on the invaded structures such as the brain, the eye, the infratemporal fossa. Usually, the duration of symptoms until the patient comes to an ENT evaluation is between 2 months and 2 years[10]. On nasal endoscopy, the tumor appears as a purple to red polypoid mass, friable, frequently ulcerated with haemorrhage or necrosis associated.

Regarding the management of sinonasal sarcomas, the surgical approach of sarcomas from other regions of the body, such as wide resection, is not suitable for head and neck sarcomas because of the adjacency to the skull base, and to obtain extensive surgical mar-

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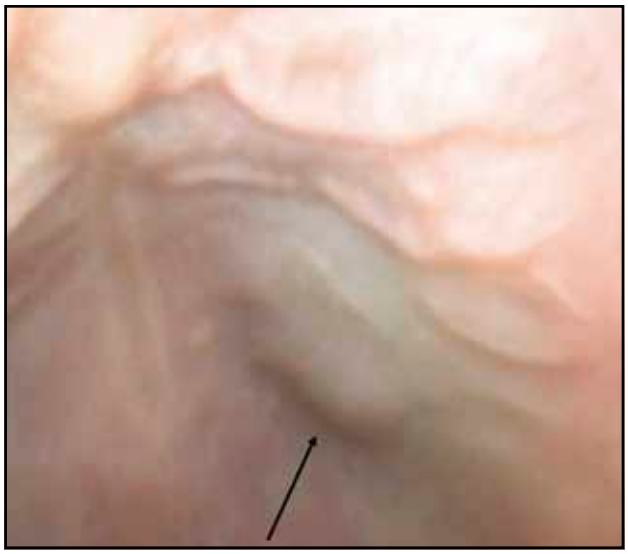

Figure 1. Preoperative endoscopic view of the left hard palate – a bulge of approximately 1/1cm, depressible on instrumental palpation, painless, with an intact mucosa (black arrow).

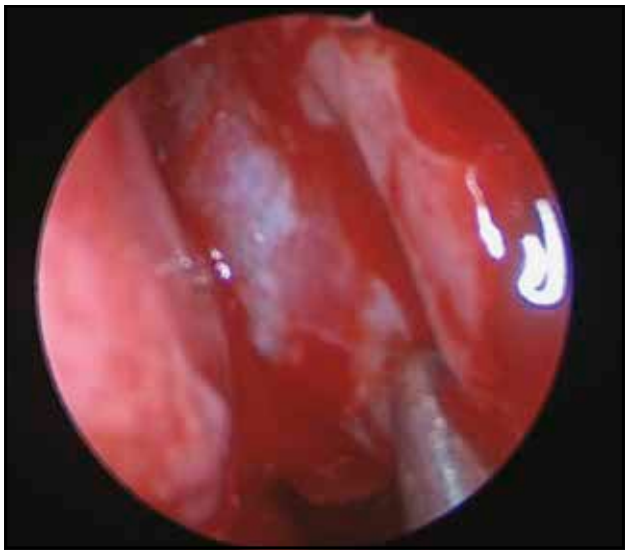

Figure 2. Preoperative endoscopic view of the tumor – reddish voluminous and friable polypoid mass, bleeding on palpation, which completely occupies the left nasal cavity.

gins is often not possible. This may explain the high local recurrence rate and poor survival rate in sarcomas of the head and neck[28,29].

CASE REPORT

A previously healthy 24-year-old male patient presented to our clinic with unilateral left epistaxis, left nasal obstruction, left side headache and left hemifacial paresthesia; symptoms had started 1 month before.

On clinical examination, the left palpebral split was narrowed, the left trigeminal maxillary point was painful on palpation. In the left half of the hard palate, a bulge of approximately 1/1cm, depressible on instrumental palpation, painless, with an intact mucosa was identified (Figure 1).

Nasal endoscopy showed a reddish voluminous and friable polypoid mass, bleeding on palpation, which completely occupied the left nasal cavity; the endoscope could not pass to reach the nasopharynx (Figure 2).

The CT scan of the skull and paranasal sinuses performed with intravenous contrast showed a macronodular heterogenous tissue lesion, partially hyperdense spontaneously, iodophilic, with multiple vascular trajectories apparently of the arterial type, localised in the left maxillary sinus and ipsilateral nasal cavity with 46/58/58 mm (Figure 3). Also, on the CT scan it was observed a quasi-com-

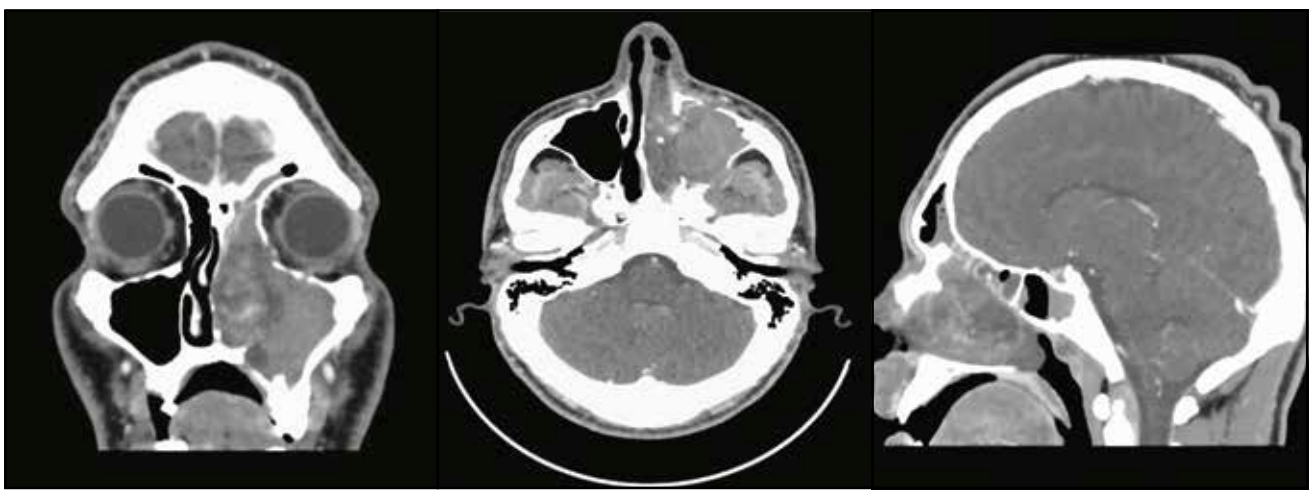

Figure 3. Preoperative imaging – Contrast-enhanced cranio-facial CT scan (coronal, axial and sagittal sections) reveals a macronodular heterogenous tissue lesion, partially hyperdense spontaneously, iodophilic, with multiple vascular trajectories apparently of the arterial type, localized in the left maxillary sinus and ipsilateral nasal cavity.

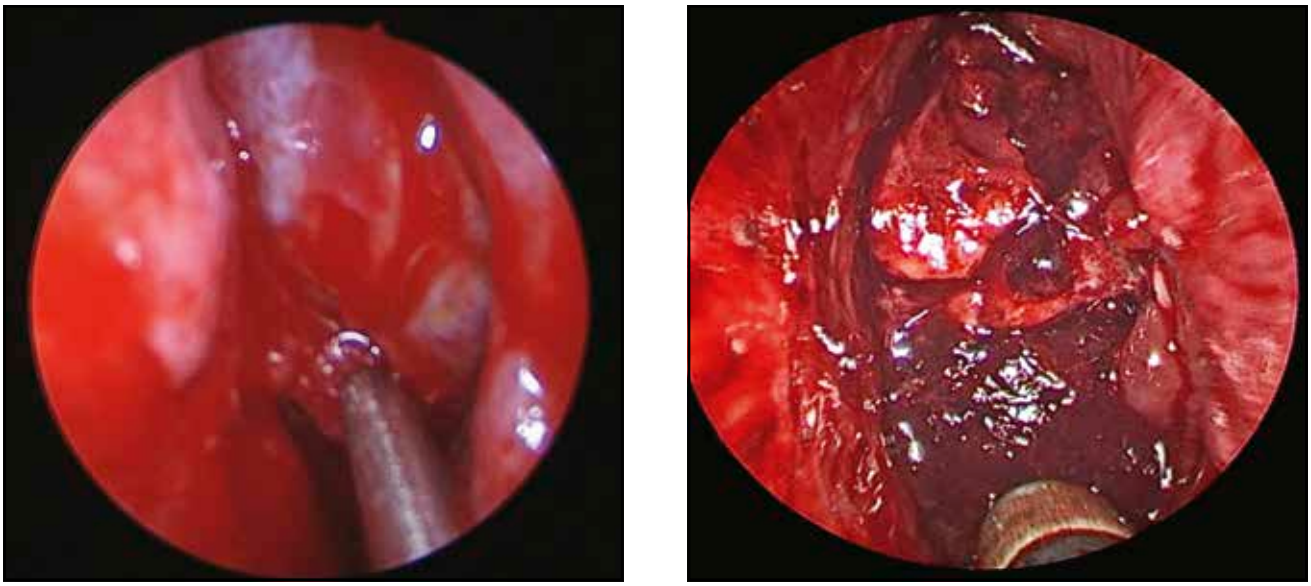

Figure 4. Intraoperative endoscopic view of the tumor.

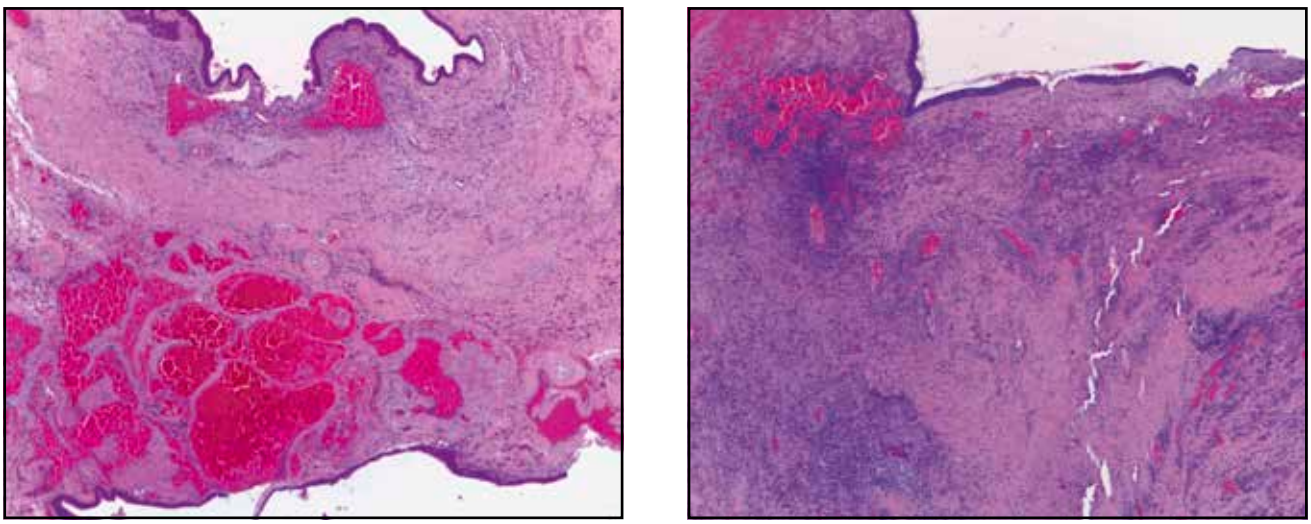

Figure 5. Histopathological images (haematoxylin eosin (HE) staining) - excised tissue areas with no signs of malignancy: diffuse and nodular chronic inflammatory process, haemorrhagic areas, reactive vascular hyperplasia.

plete osteolysis of the left maxillary sinus medial wall, fragmental osteolysis of the anterior sinus wall and fragmental osteolysis of the left lamina papyracea, with posterior protrusion in the nasopharynx.

Due to tumor extension and intense vascularization, the patient underwent angiography with internal maxillary artery embolization, followed by surgical resection of the tumor through combined approach – endoscopic and left lateral rhinotomy (Figure 4).

The microscopic examination revealed a tumor proliferation with an important vascular component composed of dilated vascular structures, full of red blood cells and areas predominantly composed of capillaries compressed by interstitial fibrosis. There was also identified a stromal component formed by stellate, elongated, round oval fibroblasts with areas of fibrosis. The histopathological examination concluded for sinonasal angiofibroma with no signs of malignancy (Figure 5).

One and a half months later, the patient returned to the Emergency Unit complaining about epistaxis that had started 2 days before. On clinical examination and nasal endoscopy, a purple, pulsating tumor mass with the origin at the level of the antero-inferior wall of the left maxillary sinus was identified.

The cranio-cerebral MRI (magnetic resonance imaging) scan performed with intravenous contrast showed a tumor mass with dimensions of 28/25/35 mm, located in the left nasal fossa and the left maxil-

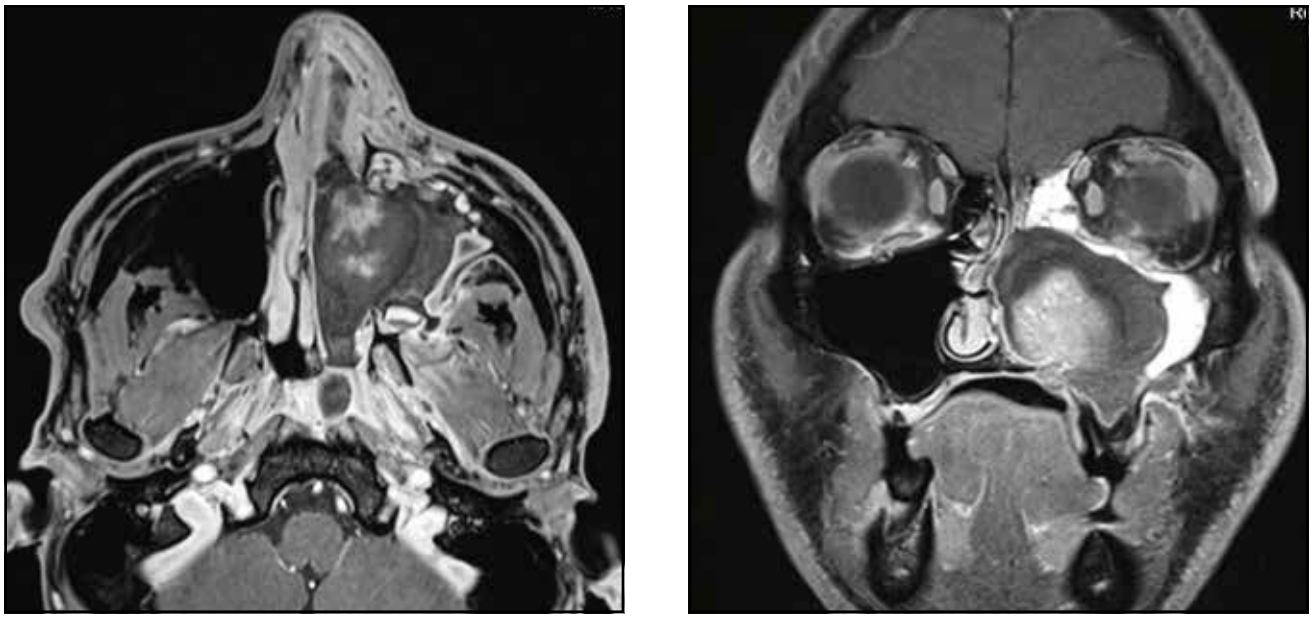

Figure 6. One and a half months after the first surgery: Contrast-enhanced cranio-cerebral MRI (T1 and T2 signal axial and coronal sections) revealed the tumor reoccupied the left nasal fossa and the left maxillary sinus.

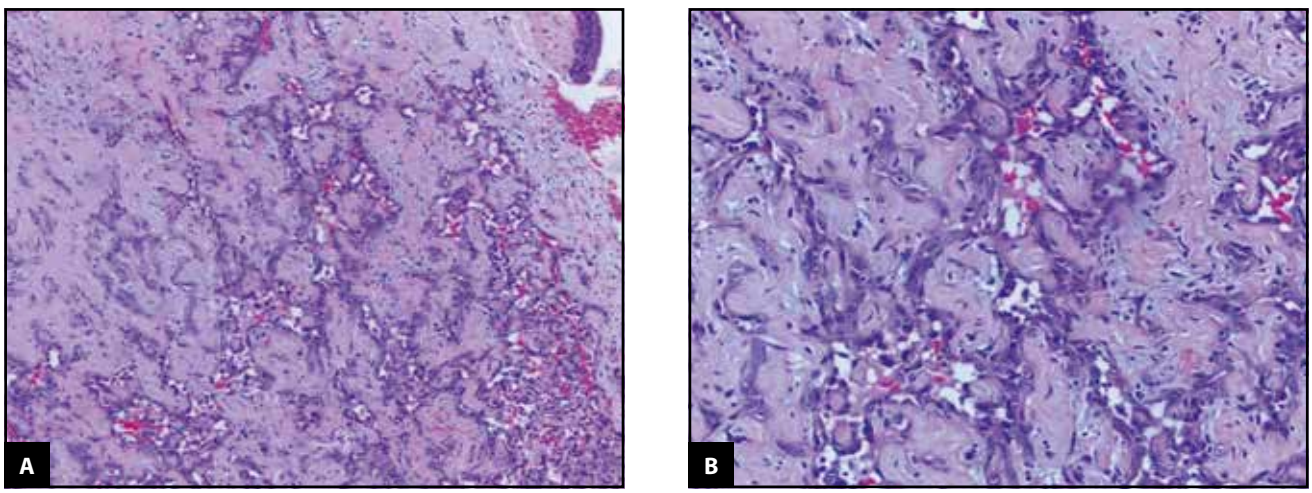

Figure 7. Histopathological exam - masses that include fragments of respiratory-type mucosa; tumor areas with vascular channels lined by atypical, large cells with mitoses and hyperchromic pleomorphic nuclei (HE staining - 10X (**A**) and 20X (**B**)).

lary sinus, modelled on the bone spurs remaining from the lower limit of the medial wall of the left maxillary sinus, attached to the anterior wall of the sinus with the important arterial pedicle coming from the infraorbital artery (Figure 6). The loading pattern (restricted diffusion and increased cellularity) argued for a more aggressive version of the tumor, advocating for lobulated capillary haemangioma.

The patient was reoperated by endonasal endoscopic approach, and the resection of the sinonasal mass was performed.

The histopathological result showed masses that included fragments of respiratory-type mucosa at the level of which the tumor areas were represented by vascular channels lined by atypical, large cells with mitoses and hyperchromic pleomorphic nuclei (Figure 7). Immunohistochemical staining (Figure 8) showed endothelial markers positive for CD34, CD31, ERG, D2-40 and proliferation index Ki-67 of 60-70% in the endothelium of tumoral cells. The histopathological examination correlated with immunohistochemical tests and the clinical-imaging aspect concluded on sinonasal angiosarcoma.

The patient started oncological treatment 3

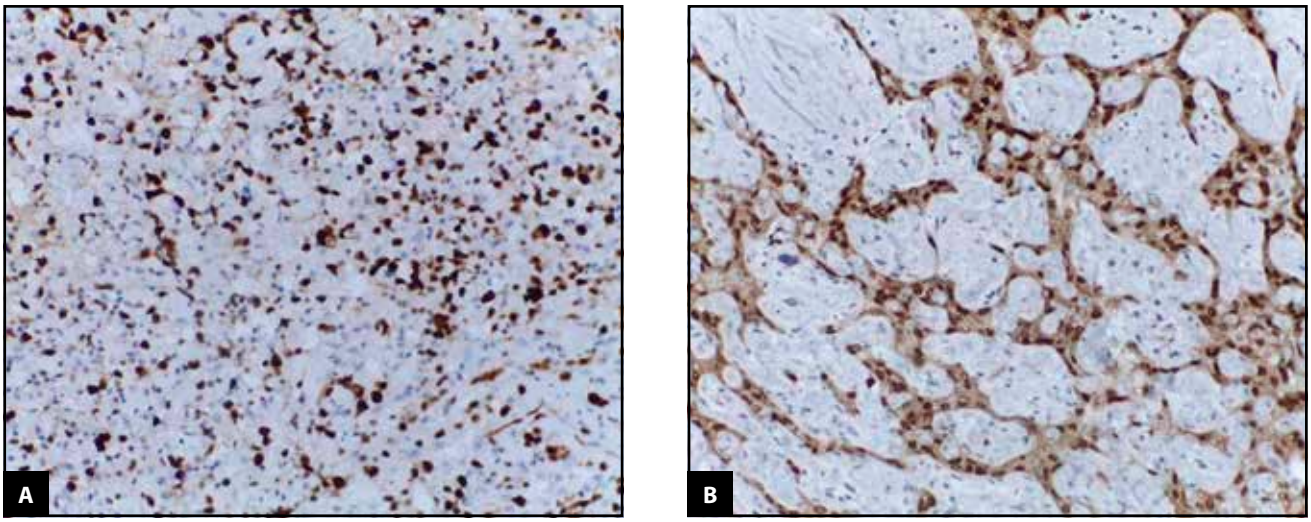

Figure 8. Immunohistochemical staining: **A**. Ki-67 positive 60-70% in tumor cells; **B**. Positive nuclear ERG in malignant endothelial cells (20X).

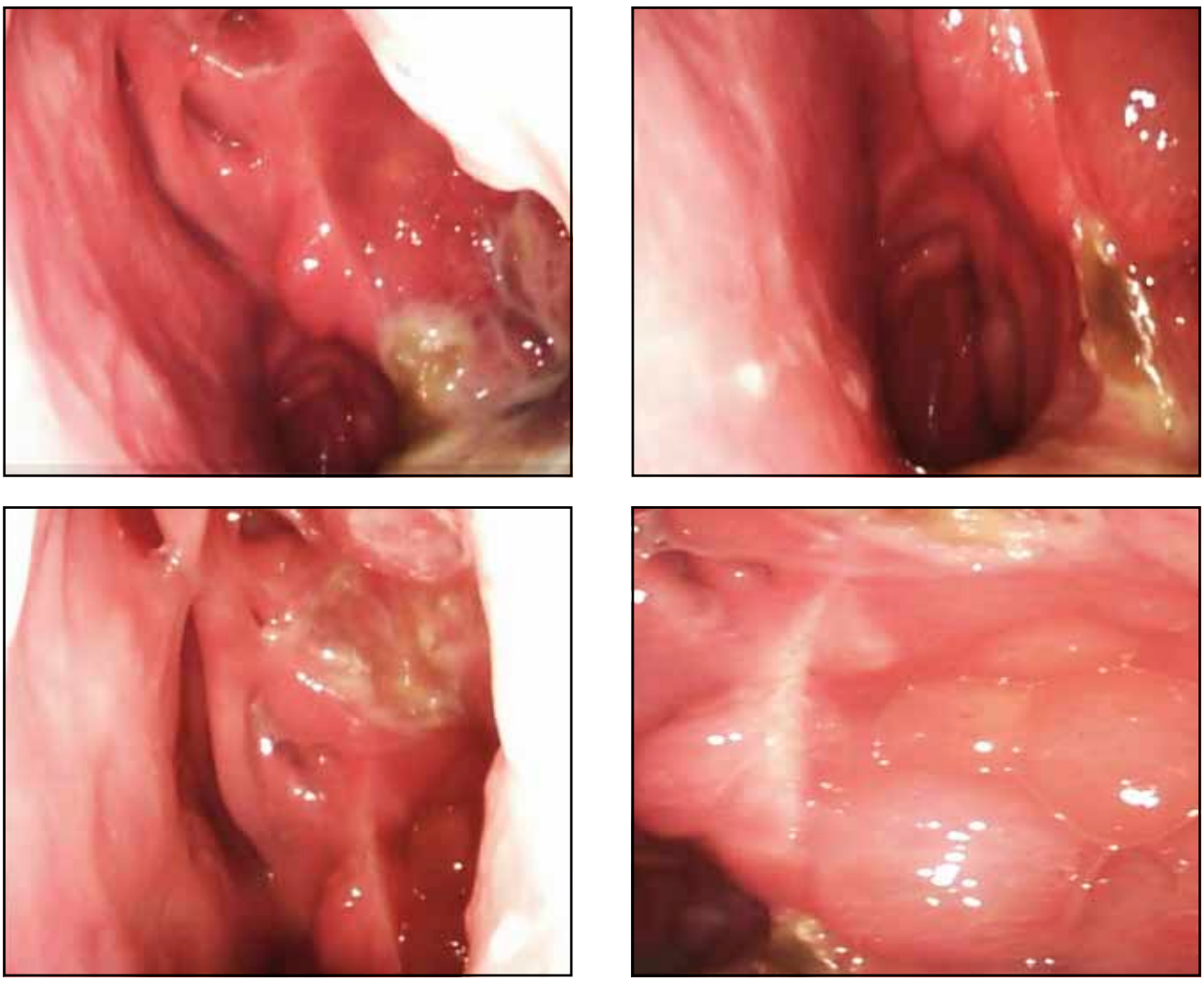

Figure 9. Nasal endoscopy after oncological treatment – crusts and postradiotherapy edema in the left maxillary sinus, no signs of local tumor recurrence.

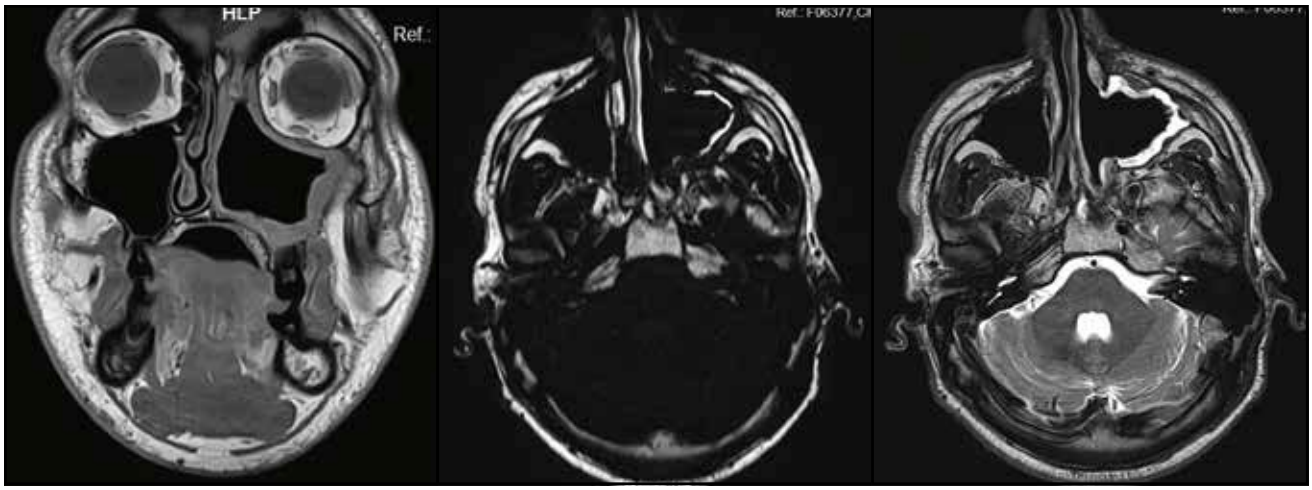

Figure 10. Nine months postoperative contrast enhanced MRI (T1 and T2 signal coronal and axial sections) showing nasal cavity and maxillary sinus with no presence of tumor.

weeks after surgery. The patient was treated with postoperative concomitant chemotherapy (5 series of 90 mg Paclitaxel) and radiotherapy -Volumetric modulated arc therapy technique (DT = 60 Gray: 30 fractions, 2 Gray/fraction, 5 fractions per week). 8 weeks after the completion of concurrent radiochemotherapy, the patient underwent adjuvant chemotherapy (6 sessions of Paclitaxel 330mg and Carboplatin 550mg).

After the finalization of oncological treatment, the nasal endoscopy revealed some crusts and post-radiotherapy edema in the left maxillary sinus and no signs of local tumor recurrence (Figure 9). At the 9-month follow-up, the MRI scan of the brain and neck revealed linear areas in hyposignal T2 (fibrosis), without signs of local tumor recurrence and without detectable laterocervical or submandibular adenopathies (Figure 10). The patient is currently ten months out from diagnosis, with no signs of tumoral recurrence or metastasis, with full functional capacity.

DISCUSSIONS

Angiosarcoma is rare in the nasal cavity and paranasal sinuses. Only a few cases have been reported until 2024. We performed a research in the Web of Science, PubMed, Science Direct, ProQuest, Wiley online databases in accordance with the following criteria: case reports with sinonasal or nasal cavity angiosarcoma, articles in English with full access. We found only 28 cases of sinonasal angiosarcoma[1-13,15-26]. In this research, the gender predominance was found for male (68% males, 32% females) with ages between 8 and 74 years. Sinonasal angiosarcoma is rarely present in young patients. We found only 6 patients under 30 years old. In our case, the patient was 24 years old.

Most of the patients with sinonasal angiosarcoma (71%) complained about recurrent epistaxis and 25% of patients presented headache besides the recurrent epistaxis[12,15,18,22-24,30]. In addition to the fact that the clinical manifestations are not specific for sinonasal angiosarcoma, it has been observed that sometimes, on the histopathological examination, angiosarcoma can mimic another disease, as it was observed in our case as well as in another 3 of the cases reported in the literature[2,3,15].

In our case, the histopathological diagnosis was not clear from the beginning, and we searched in the literature if there are other cases reported in which the diagnosis of angiosarcoma was delayed. In 3 cases reported in the literature, angiosarcoma was not the first diagnosis[2,3,15]. The first case, presented by Es-Sbissi et al.[2], is a 53-year-old male patient, who was first diagnosed with capillary haemangioma with no associated malignancy signs. The patient presented with tumor recurrence after three and a half months and, after the second surgery, the histopathological examination and immunohistochemistry concluded on sinonasal angiosarcoma. In the case presented by Chai et al.[15], the first histopathological diagnosis was nasal inflammation polyps associated with extensive necrosis. Four months later, this patient presented with tumor recurrence and the postoperative histopathological and immunohistochemical examinations revealed characteristics for sinonasal angiosarcoma (positivity for P16, CD31, ERG (erythroblast transformation-specific-related gene), Ki67). In the third case, a 74-year-old woman, presented by Kimura et al.[3], both the preoperative biopsy and intraoperative extemporaneous histopathological examination described no signs to confirm the malignant lesion. Because the histopathological diagnosis was not clear, a wide resection of the tumor was performed. The histopathological examination of the resected tumor completed with the immunohistochemistry (positivity for ERG) concluded on angiosarcoma[3]. There was a case in

the literature that was initially diagnosed with nasopharyngeal angiofibroma as our patient, but relapsed 2 years after the first surgery and the second histopathological examination revealed nasopharyngeal angiofibroma without signs of sarcoma[31]. Due to the frequent recurrences, the patient underwent radiotherapy. 3 years after the radiotherapy, the patient presented with tumor recurrence, but this time the histopathological examination and immunohistochemistry concluded on leiomyosarcoma[31].

The differential diagnosis of sinonasal angiosarcoma has to be done with intravascular papillary endothelial hyperplasia, nasopharyngeal angiofibroma, sinonasal haemangioma, Kaposi sarcoma and hemangiopericytoma. The microscopic similitude of angiosarcoma with intravascular papillary endothelial hyperplasia or nasopharyngeal angiofibroma, haemangioma or hemangiopericytoma and the probability of misinterpretation has an important significance in the management of the disease.

There are various distinguishing microscopic characteristics that are helpful in contouring the diagnosis of angiosarcoma: anastomosis of vascular channels, which are irregular, tortuous and dissect the stroma by enclosing structures, with rudimentary vessels or cleft-like spaces. The endothelial cells which plate the vascular channels in different layers or papillae are atypical, plump, enlarged and increased in number. These cells may be epithelioid, polygonal or spindle cells. Mitotic activity is present; atypical mitosis can be usually found in most of the cases. Necrosis and haemorrhage may also be present.

Nasopharyngeal angiofibroma is a vascularised mesenchymal tumor that appears specifically in the nasopharynx, usually in young patients. On histopathological examination, disorganised vessels of different sizes, with irregular muscle substance in a stroma with fibrous connective tissue are identified. In the walls of the vessels, the elastic tissue is lost. Endothelial cells may be round, but not atypical. There are fibroblasts, which are angulated, plump, stellate cells. In the content, the mast cells are frequently abundant[32].

Intravascular papillary endothelial hyperplasia (IPEH) is a vascular tumor defined as a proliferation of endothelial cells besides a thrombus, and it is usually limited to the lumen of the vessels, which are thrombosed, or to vascular malformations. In the histopathological differential diagnosis with IPEH, one can observe: in angiosarcomas, the proliferation is rarely intravascular, usually tending to penetrate the surroundings, while in intravascular papillary endothelial hyperplasia, the proliferation is restricted to the vascular space; mitotic figures are present in angiosarcoma, but in IPEH, these are absent; also, necrosis and solid areas are absent in IPEH[33].

Sinonasal hemangiopericytoma is an unusual tumor of the superior aerodigestive tract and is represented histopathologically by diffuse proliferation of cells that are intimately packed and organized in short connecting fascicles, which are highly vascularized. The vascular channels may have a configuration with multiple bifurcations and, regarding the size, they are from capillary diameter to large spaces. The tumor cells create a packed syncytium of cells from oval to spindle shape. Almost constantly there are extravasated mast cells, erythrocytes and eosinophils[34].

In the literature, a case of sinonasal angiosarcoma, whose initial histopathologic diagnosis was capillary haemangioma, and a case of nasal angiosarcoma originating from a haemangioma were reported[2,4]. Nasal capillary haemangioma usually appears on the nasal septum, turbinates or in the maxillary sinus. On microscopic examination, it is frequently misinterpreted as angiofibroma[35]. The histopathological examination showed proliferating small capillary-sized vessels with a lobular architecture, spindle cells in a stroma with dense fibrosis[2].

In our case, the initial histopathological examination showed features of sinonasal angiofibroma without signs of malignancy (a tumor proliferation with serious vascular component consisting of dilated vascular structures filled with red blood cells and areas with capillaries compressed by interstitial fibrosis; a stromal component consisting of stellate, elongated, round oval fibroblasts with fibrous area). One and a half months after the first diagnosis, when the patient came to our clinic with tumor recurrence, the histopathological examination and immunohistochemical stains revealed the diagnosis of angiosarcoma describing vascular channels lined by atypical, large cells with mitoses and hyperchromic pleomorphic nuclei, the presence of endothelial markers (CD34, CD31, ERG, D2-40) and a proliferation index of 60-70% in the endothelium.

Immunohistochemistry plays a very important role in the differential diagnosis of angiosarcoma, which is positive for CD31, CD34, factor VIII, erythroblast transformation-specific-related gene (ERG). There were cases in which the final diagnosis of angiosarcoma was concluded only when the immunohistochemical stains were associated, the histopathological examination being not clear enough to sustain the diagnosis.

The most efficient therapeutic approach is surgery with complete resection of the tumor, associated with radiotherapy or chemoradiotherapy[3,20,22,27]. There was a case where, even if in the intraoperative quick histopathological examination of the resected tumor the malignancy elements could not be clear and the surrounding tissue was without malignant cells, when the final diagnosis was angiosarcoma, they decided to complete the treatment with postoperative chemoradiotherapy[3]. Patients who underwent radiotherapy (55-60 Gray) and chemotherapy (Docetaxel +/- Gemcitabine) after surgery had a good prognosis, with no signs of recurrence at the 1-year and almost 3-year follow-ups[3,22]. There were also cases who received after surgery only radiotherapy and they did not have local recurrence at the 2-year, 3-year or 4-year follow-ups[8,23,27].

The 5-year survival rate in patients with sinonasal angio-

sarcoma improved over the years. In 2009, it was reported at 22%[27]. In 2024, Kimura et al. reported a 3-year survival rate in patients with sinonasal angiosarcoma of 63.7%[3].

In the first 24 months, 30% of cases may develop distant metastases and 10-15% of patients may develop cervical metastases[27]. Sinonasal angiosarcoma can metastasize in the lung, bone (marrow), liver or spleen. It was observed that patients aged less than 50 years old have a better clinical outcome than the older ones[10]. The most frequent prognostic factors are: the age of the patient, early diagnosis, tumour size, differentiation grade and tumour resectability[10,19,27]. Sinonasal angiosarcoma has a better prognosis than angiosarcoma of another region[20,21].

CONCLUSIONS

The definitive diagnosis of sinonasal angiosarcoma requires a detailed histopathological examination associated with immunohistochemistry, to avoid a delay in the correct approach to the tumor and to prevent distant metastases.

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