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Case Report

Polymorphous Low-Grade Adenocarcinoma: A Rare Cause of Long-term Epistaxis

Abstract

Polymorphous low-grade adenocarcinoma (PLGA) of the paranasal sinus is an extremely rare disease. PLGA is a minor salivary gland neoplasm that occurs mostly in the junction of the soft and hard palate, followed by the buccal mucosa and upper lip. Only a few cases have been reported in the sinonasal area. PLGA generally follows a benign clinical course with frequent perineural invasion but low metastatic potential.

We report on a patient with PLGA in the ethmoid sinus, which presented as a nasal polyp with epistaxis for more than 2 years. The patient received surgical excision with adjuvant radiotherapy and chemotherapy because of perineural and lymphovascular invasion. One year after treatment, the patient was free of disease. PLGA of the paranasal sinus is an extremely rare disease. Epistaxis as the initial presentation is also uncommon. Local recurrences and distant metastasis are rare if complete excision is performed. Long-term follow-up is required.

Introduction

Polymorphous low-grade adenocarcinoma (PLGA) of the paranasal sinus is an extremely rare malignancy. Being a malignant minor salivary gland neoplasm, PLGA has a predilection for intraoral sites [1]. An extraoral tumor is rare, and nasal tumors constitute less than 1% of cases [2]. Although the neoplasm exhibits an infiltrative growth pattern, which frequently results in perineural invasion, the prognosis is favorable. Local recurrences are uncommon, as are distant metastases [3]. Surgical intervention is the primary option for treating PLGA. Radiotherapy and adjuvant chemotherapy have been used for treating the forms of the disease that are more advanced; however, there is no definite evidence of their advantages [4]. We present the case of a patient with PLGA of the ethmoid sinus, manifesting as a long-term epistaxis.

Case Report

A 52-year-old man presented with a 30-month history of intermittent left epistaxis combined with purulent nasal discharge. He had a history of coronary artery disease and took aspirin regularly. In addition, he had undergone the bilateral Caldwell-Luc surgery for benign maxillary sinus disease previously. He visited different clinics several times for his condition, but it was incorrectly diagnosed as chronic paranasal sinusitis or the side effect of an anticoagulant therapy. Because the treatments did not improve his condition, he visited our department seeking medical help. The physical examination was unremarkable, and no obvious lesions or bleeding over the common meatus, septum, or nasopharynx was observed. However, fiberoptic examination revealed scant crust accumulation inside the middle meatus, and an easily bleeding lesion was identified after removing the crust (Figure 1a). Biopsy was performed, and a histological analysis revealed a basal cell adenoma. However, malignant carcinoma was not ruled out. The patient underwent

computed tomography (CT), which revealed enhanced soft tissue in the left ethmoid sinus and nasal cavity. No skull base invasion was observed. However, the left lamina papyracea was unremarkable, and there was no intraorbital destruction at diagnosis (Figure 1b).

Concerning malignancy, we performed endoscopic tumor excision with medial maxillectomy. The dissection plane was directed toward the skull base and lateral to the periorbita. The structures above this region were intact, and no gross residual tumor was found (Figure 1c).

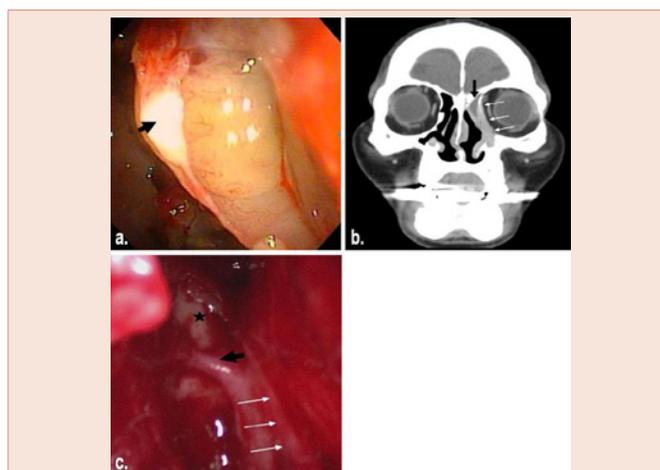


Figure 1: (a) Polyp-like lesion in the left middle meatus (arrow: left middle turbinate); (b) Enhanced soft tissue in the left ethmoid sinus and nasal cavity. The skull base (thick black arrow) is intact; absence of bony density in the left lamina papyracea, and the periorbital contour is smooth (thin white arrow); (c) Dissection to the skull base (asterisk) and periorbita (thin white arrow). The anterior ethmoid artery is identified (thick black arrow). No gross residual tumor is apparent.

The excised tumor specimen measured 3.5 cm × 1.2 cm × 0.7 cm in size. Microscopically, the sections showed a PLGA comprising irregular infiltrating solid nests and cuboidal cells growing in an adenoid cystic pattern arranged in ducts, trabeculae, and tubules (Figure 2a). Under a higher magnification power, most of the tumor cells were bland and relatively uniform. The round and ovoid nuclei were either normal in size or slightly enlarged, and lymphovascular invasion was observed (Figure 2b). Mitoses were infrequent. Perineural, perivascular, and bony invasion, involving nearly all portions of the obtained fragments, was observed (Figures 2c,d).

The pathologic staging was pT2Nx, and the patient received radiotherapy with a daily fraction of 200 cGY and a total dose of up to 7000 cGY. UFUR (Uracil 224mg - Tegafur 100mg), 972mg daily was prescribed as chemotherapy for 6 months. Follow-up MRI scans were obtained at 5-month intervals. The MRI obtained 12 months after the complete treatment showed unremarkable results. A fiberoptic examination revealed that the nasal cavity was free of tumors (Figure 3).

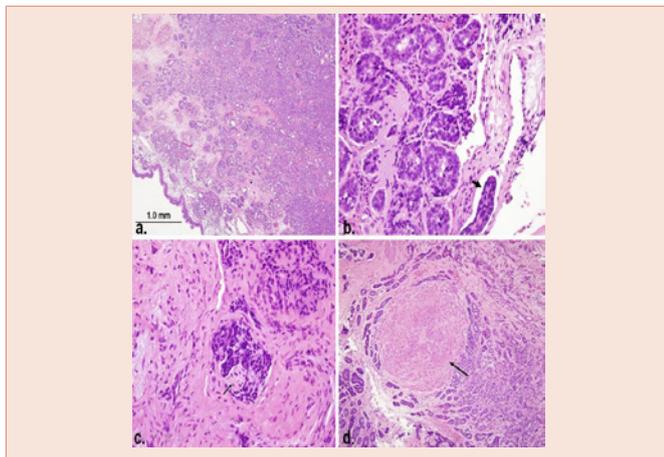


Figure 2: (a) An image of the polymorphous low-grade adenocarcinoma comprising irregular infiltrating solid nests and cells growing in an adenoid cystic pattern arranged in ducts, trabeculae, and tubules; (b) Cytologically bland glandular islands. The nuclei are round and fairly uniform. Tumor cells are apparent in the lymphatic duct (black arrow); (c) Tumor cells arranged concentrically around a small nerve bundle (neurotropism), creating a targetoid appearance (black arrow indicates the nerve); (d) Perivascular invasion (black arrow indicates the thick vessel wall).



Figure 3: The nasal cavity is free of tumors 1 year after treatment. (White asterisk: the skull base; white arrow: the orbital wall).

Discussion

The incidence of nasal tumors is as follows: papillomas (33%), soft tissue tumors (20%), and glandular tumors (19%), discovered according to the Armed Forces Institute of Pathology (AFIP) [2]. In glandular tumors, the distribution is as follows: high-grade adenocarcinoma (29.9%), mixed tumors (23.4%), low-grade adenocarcinoma (including those of acinic cells, 21.5%), adenoid cystic carcinoma (17.3%), and mucoepidermoid carcinomas (5.4%); the remaining were PLGA (2.5%) in only a few case reports [5].

In 1984, Evans and Batsakis first used the term PLGA to describe this specific salivary gland adenocarcinoma [4]. Histologically, the most common pattern is a formation of tubular, trabecular, solid, and cribriform structures. Because of the prominent neurotropism of the cells, perineural infiltration is a frequent finding. A histopathological overlap may occur with pleomorphic adenoma and adenoid cystic carcinoma (ACC), which complicates diagnosis when the biopsy is small [8].

The cells in PLGA tend to exhibit an infiltrative growth pattern, particularly neurotropism, which is not found within pleomorphic adenoma. Distinguishing PLGA from ACC is crucial. Perineural spread is more common in PLGA than in ACC. However, PLGA has a more favorable prognosis and fewer local recurrences. Regional lymph node and distant metastases have been documented in rare cases [6,7].

PLGA occurs over a wide age range but mostly at the ages of 50 and 70 years [8]. Most PLGA cases have been observed in the oral cavity, and over 60% arise from the palate (hard and soft), followed by the buccal mucosa or the upper lip [4]. Nasal cavity and nasopharyngeal involvement are rare (1% and 0.5%, respectively) [2], and only a few cases have been reported to date [2,9-12]. PLGA is an indolent, slow-growing, locally invasive tumor. Clinical symptoms last from a few days to 40 years, with an average span of 27 months [8]. Pain, bleeding, or ulceration does not aggravate the disease. The local recurrence rate is approximately 9.1%–24% [8,11], and regional lymph node metastasis develops in 6%–9% of cases [7,8,13]. Distant metastasis is rare and has been reported only in patients suffering from the papillary variant [6,14].

The appropriate treatment for PLGA is wide but conservative surgical resection, because treating a recurrent disease is rarely effective [4]. Neck dissection is not necessary unless there is a clinical evidence of positive lymph nodes. The benefits of adjunctive chemotherapy or radiation have not been reported [6]. However, in case of unclear marginal, perineural, or perivascular spread, radiotherapy is recommended [15].

James T. Castle reported an average of 7.2 years for recurrence [8]. Some authors have suggested that patients must be followed for more than 5 years [16].

Conclusion

PLGA is a minor salivary gland disease that rarely occurs in the sinonasal region. Although the perineural spread is common in PLGA, it generally follows a benign clinical course that manifests as a

slow-growing mass. Patients may be asymptomatic or merely present insignificant signs for a long time, and physicians can disregard these signals. Complete surgical excision is the appropriate therapy. The role of adjuvant therapy in a more advanced disease is uncertain. Local recurrences and distant metastasis are uncommon. Long-term clinical follow-up is suggested.

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