CASE REPORT

An Aggressive Evolution of Inverted Sinonasal Papilloma - A Case Report.

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Abstract

Introduction: Inverted sinonasal papillomas (ISP) are benign, but locally aggressive tumour with rare risk potential of malignant transformation referred to as Carcinoma ex inverted sinonasal papilloma (CEISP). The risk factors for malignant transformation include multiple recurrences, incomplete surgical excision and the presence of dysplastic changes in the papilloma.

Case Presentation: 47 year old male presented with nasal obstruction, dry cough, headache with heaviness and had past history of left side nasal polyp removal. CT PNS showed a left large ill-defined lytic soft tissue dense lesion in bilateral ethmoidal air cells causing lytic bony destruction with intracranial extension prompting endoscopic resection of recurrent left sided sinonasal mass. Histopathological analysis of sinonasal mass revealed an inverted papilloma with areas of malignant transformation showing squamous differentiation and evidence of bony invasion.

Conclusion: This case report highlights the complexities in diagnosing carcinoma ex sinonasal papilloma, particularly in the context of recurrence and the importance of meticulous pathological evaluation.

Keywords: Carcinoma Ex Sinonasal Papilloma, Inverted Papilloma, Sinonasal Papilloma, Squamous Cell Carcinoma.

Introduction

Sinonasal Papillomas are rare benign tumors, accounting for approximately 0.5% - 4% of all nasal tumors[1]. They originate from the Schneiderian membrane, the specialized respiratory epithelium lining the nasal cavity and paranasal sinuses1. This epithelium, derived from the embryonic ectoderm, has a unique property that it undergoes both exophytic and endophytic growth patterns, giving rise to different types of sinonasal papillomas.

Historically, Ward in 1854 provided one of the earliest comprehensive descriptions, noting the distinctive morphological characteristics of these growths[2]. Later, in the late 19th century, Billroth credited for his work on sinonasal papilloma and contributed to their classification based on histopathological features, distinguishing between exophytic (fungiform), inverted, and oncocytic (Cylindrical cell) types[2]. The term inverted papilloma was coined by Ringertz in 1938[2], emphasizing the unique growth pattern of these tumors, where they proliferate inwardly into the underlying stroma[3], distinguishing them from the exophytic and oncocytic types.

Among sinonasal papillomas, inverted papillomas are the most common encountered type. They are typically found in adults, with a peak incidence observed between 5th–7th decades of life[2], although they can occur at any age. Sinonasal papillomas often present with symptoms such as nasal obstruction, recurrent nose bleeds or chronic sinusitis like symptoms. Sometimes they may be asymptomatic, which can delay diagnosis or lead to misdiagnosis. Although most sinonasal papillomas are benign, there is risk of malignant transformation, particularly with inverted papillomas. Malignant transformation into squamous cell carcinoma or other malignancies occurs in a small percentage of cases, typically less than 5% to 15%[4]. This aggressive nature was highlighted in the mid-20th century when clinicians began documenting cases of sinonasal papillomas, despite being benign, exhibited traits such as propensity for recurrence, local invasiveness and eventually with malignant transformation[3]. The risk factors for malignant transformation include multiple recur-

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rences, incomplete surgical excision and the presence of dysplastic changes in the papilloma.

The etiology of sinonasal papilloma is not fully discovered. The association between human papilloma virus and sinonasal papillomas was established in 1980s with studies identifying HPV DNA in a significant proportion of these tumors, particularly the exophytic and endophytic types[5]. This discovery provided insights into the potential etiological role of viral infection in the pathogenesis of sinonasal papillomas, and their malignant transformation.

Case Presentation

A 47 year old male came with complaints of dry cough and nose block which gets aggravated during URI for the past two months. He also complained of headache with heaviness. He had a past history of nasal polypectomy 1.5 years ago. On examination of left nostril, a pink polypoidal grape like globular mass occupying the nasal cavity noted. CT PNS showed a left large ill defined lytic soft tissue dense lesion in bilateral ethmoidal air cells, bony destruction of bilateral ethmoidal sinuses, medial wall of bilateral orbit, bony nasal septum and floor of anterior cranial fossa (Figure 1). CT findings revealed the possibility of malignant etiology. Following which FESS procedure was done for tumour removal and sent to histopathological evaluation.

Grossly, multiple grey brown to grey white soft tissue bits received. Histopathological examination revealed fragments of bone and soft tissue with tumour showing histological features of inverted sinonasal papilloma showing endophytic growth pattern with interconnecting epithelial nest (Figure 2). However there is a foci of nuclear pleomorphism, hyperchromatism with increased mitosis, and foci of necrosis (Figure 3). Atypical mitotic figures noted (Figure 4). Surrounding stroma shows desmoplastic reaction. There are also areas of bone invasion

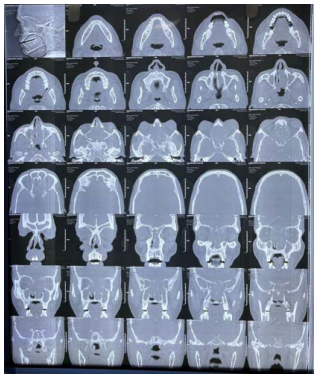

Fig.1: CT PNS showed a left large ill-defined lytic soft tissue dense lesion in bilateral ethmoidal air cells causing lytic bony destruction with intracranial extension

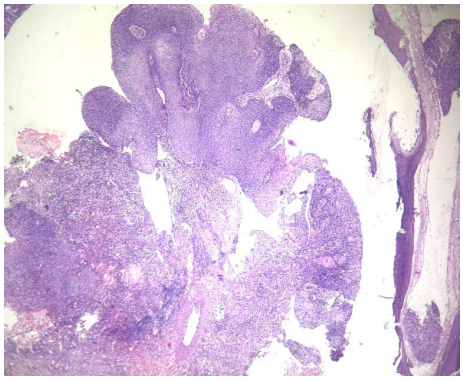

Fig.2: Inverted sinonasal papilloma showing endophytic growth pattern with interconnecting epithelial nests H and E 10X

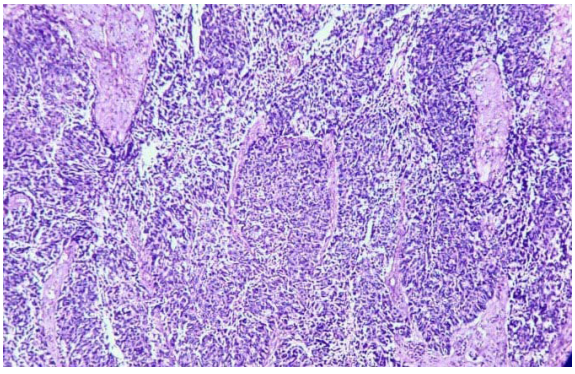

Fig.3: nuclear pleomorphism, hyperchromatism with increased mitosis showing malignant transformation.

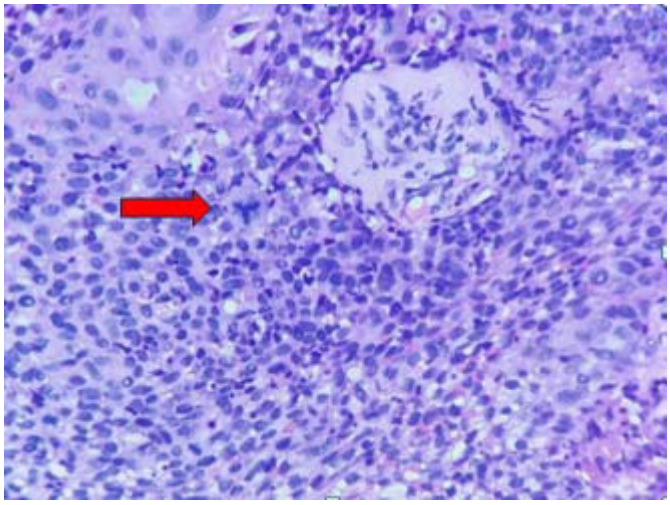

Fig.4: Atypical mitotic figure

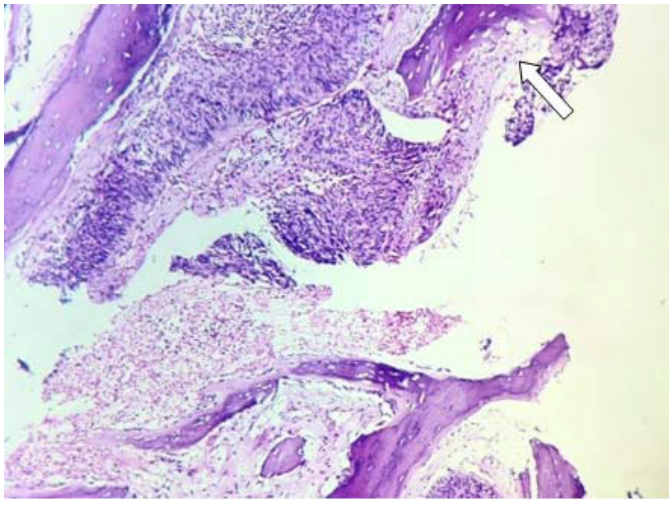

Fig.5: Bone invasion by malignant cells.

(Figure 5) and stromal invasion by isolated malignant cells with areas of squamous differentiation. Lympho-vascular and peri-neural invasion not seen.

Discussion

Inverted sinonasal papillomas (ISP) are benign, but locally aggressive tumour present as unilateral mass, often arising from the lateral nasal wall or middle meatus[1]. Mixed anatomic site presentation is also documented such as nasal cavity combined with maxillary, frontal, sphenoid, and/or ethmoid sinus, with possible involvement of nasopharynx and middle ear[6]. Their inward growth pattern contributes to their clinical significance, as it often leads to difficulties in complete surgical removal and contributes to their high recurrence rates which vary widely but are significant, ranging from 15% to 50% and risk of malignant transformation[7]. Carcinoma ex inverted sinonasal papilloma (CEISP), represents a rare but clinically significant entity characterised by the malignant transformation of a pre-existing inverted sinonasal papilloma into squamous cell carcinoma or other malignancies[8]. The pathogenesis of CEISP is multifactorial and not fully elucidated. Chronic inflammation, recurrent ISP, genetic alterations and viral HPV infections particularly high risk types such as HPV 16 and HPV 18 has been implicated as potential risk factors predisposing inverted sinonasal papilloma to malignant transformation[5]. The presence of dysplastic changes within papilloma, incomplete surgical excision and prolonged exposure to carcinogens may also contribute to malignant transformation.

Genetic studies have identified alterations in oncogenes and tumor suppressor genes within ISP tissues, although the specific genetic mechanisms driving malignant transformation are not fully elucidated[8]. Expression of several growth factors and their receptors such as Epidermal growth factor receptor (EGFR) and transforming growth factor-α (TGF-α) are thought to have a crucial role in the progression of tumour.It has been stated that, increased EGFR and TGF-α expression may drives malignant transformation in head and neck cancers[8].

Histologically, ISP is characterized by its distinctive growth pattern, where the epithelial projection grows endophytically into the underlying stroma rather than exophytic pattern. The benign nature of ISP is defined by its orderly papillary architecture with a fibrovascular core, covered by non-keratinizing stratified squamous epithelium. The presence of atypical histologic features most closely associated with malignant transformation are: Lymphovascular invasion, Perineural Invasion, atypical mitoses, desmoplastic stromal reaction, bone invasion, architectural distortion, increased epithelial to stroma ratio, marked pleomorphism, tumor necrosis, increased mitotic figures (>25/10 HPFs), and subtle transepithelial neutrophil elimination[7].

CEISP exhibits a spectrum of features reflecting its transition from benign papilloma to malignant forms. In early stages, the lesion may show areas of dysplasia or carcinoma in situ, characterized by atypical epithelial proliferation confined within the basement membrane without invasion into stroma. As the disease progress, invasive carcinoma develops, with nests or islands of malignant cells infiltrating the stroma. The vast majority of these carcinomas being SCC. The presence of keratin pearls, intercellular bridges, and nuclear pleomorphism further supports the diagnosis of SCC arising from a pre-existing sinonasal papilloma. Other tumor types such as mucoepidermoid, sinonasal undifferentiated carcinoma, and carcinoma- NOS have also been reported 7. Immunohistochemical studies play a crucial role in confirming the malignant nature of CEISP and differentiating it from benign ISP. Markers such as p16, p53, ki-67 and HPV testing can provide additional insights into the molecular alterations and viral etiology associated with malignant transformation[9]. Positive staining for p16 and aberrant p53 expression may suggest HPV associated carcinogenesis in some cases of CEISP. Ki-67 proliferation index, will show a remarkable increase when compared to SP without dysplasia or invasion[10].

Radiologically, CEISP presents as a locally aggressive lesion with potential involvement of adjacent structures such as nasal septum, ethmoid sinuses, orbit and skull base. CT and MRI are essential imaging modalities for evaluating the extent of tumor involvement, assessing bony destruction, and planning surgical management.

The primary treatment for CEISP is complete surgical excision with clear margins. Endoscopic sinus surgery (ESS) has become the preferred approach, allowing for precise visualization and excision of the tumor while preserving sinonasal function. In cases of extensive disease or involvement of critical structures, such as the orbit or skull base, a multidisciplinary approach may be necessary to achieve complete tumor resection. Adjuvant therapies such as postoperative radiotherapy may be considered based on the extent of surgical resection, presence of residual disease and histopathological features suggesting aggressive behavior or high risk features. The role of chemotherapy in the management of CEISP remains limited.

Patients with advanced disease, incomplete resection or lymph node involvement may have a poorer prognosis. Long term follow up with regular endoscopic evaluations and imaging studies are essential for monitoring disease recurrence, assessing treatment response and detecting early signs of metastatic spread.

Conclusion

Carcinoma ex inverted sinonasal papilloma represents a rare entity which is characterised by the malignant transformation of a pre-existing inverted sinonasal papilloma. This case report highlights the complexeties in diagnosing carcinoma ex inverted sinonasal papilloma particularly in the context of recurrence and underscores the importance of meticulous pathological evaluation due to overlapping histological features of benign and malignant components. Understanding the unique histopathological features, radiological insights, clinical implications, management strategies and prognostic factors associated with CEISP is essential for guiding optimal patient care. Continued research into molecular mechanisms driving malignant transformation and novel therapeutic approaches is warranted to improve outcomes for patients affected by this aggressive disease entity.

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