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Value of a Multidisciplinary Approach in Sinonasal Inverted Papilloma with Extensive Ossification

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Patient: Male, 51-year-old
Final Diagnosis: Sinonasal inverted papilloma
Symptoms: Nasal congestion • nasal mass
Medication: —
Clinical Procedure: —
Specialty: Pathology

Objective: Rare disease

Background: Inverted papilloma is a benign epithelial lesion of the nasal cavities. Although commonly encountered in clinical practice, it rarely presents with extensive ossification and few cases have been described in the literature.

Casa Report: Herein, we describe the case of a 51-year-old man who presented to clinical attention for persistent right nasal obstruction. Magnetic resonance imaging (MRI) and computed tomography (CT) scans of the facial bones showed a lobated lesion with ossification occupying most of the right nasal cavity. The lesion was removed by endoscopic sinus surgery, leaving the surrounding bone structures intact. On pathological examination, mature bone tissue was found within an inverted papilloma. The pathologist contacted the surgeon, who confirmed that no healthy bone tissue was removed during the procedure. Therefore, a diagnosis of inverted papilloma with ossification could be made without the use of ancillary techniques.

Conclusions: Inverted papilloma with ossification is a common lesion with a rare feature. Our report investigates the diagnostic difficulties of a paradigmatic case, highlighting the importance of multidisciplinary teamwork in reaching the final diagnosis.

Keywords: Endoscopy • Nasal Cavity • Ossification, Heterotopic • Papilloma, Inverted

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Background

Inverted papilloma (IP) is a benign epithelial lesion, most commonly located in the nasal cavities and paranasal sinuses, extending into the underlying connective tissue stroma showing a pattern of "inverted growth". It is the most common benign tumor of the sinonasal tract [1] and it often manifests as maxillary sinusitis. The lack of specific symptoms can cause diagnostic difficulties on clinical grounds alone. Therefore, computed tomography (CT) scan of the facial bones has long been considered the criterion standard exam for primary diagnosis and follow-up [2]. Due to its invasiveness, its high degree of recurrence, and a possibility of malignant transformation [3], its treatment consists of radical surgery [4]. Although immunomodulatory therapies have increasingly emerged as a promising new treatment option for advanced malignancies, results from clinical studies of immune checkpoint modulating drugs in this setting have led to mixed results [5-8]. IP usually arises from the lateral nasal wall, in the middle meatus, often extending to the ethmoid and maxillary sinuses [3]. In advanced cases, extension into the ipsilateral peripheral nervous system structures may occur, whereas intracranial growth and dural penetration are rare [9]. The pathogenesis of this lesion remains unclear, although allergy, chronic sinusitis, and viral infections have been suggested as possible causes [3]. Although common in other lesions such as osteoma and ossifying fibroma, bone formation has been rarely reported in IP [10-14]. Herein, we report a case of ossifying IP arising in the right nasal cavity of an otherwise healthy 51-year-old man. A particular focus will be placed upon differential diagnosis and multidisciplinary teamwork, which was of great value in the presence of a common lesion with a striking although rare feature.

Case Report

A 51-year-old man presented with monolateral right nasal obstruction, which had reportedly been present for some months. The worsening of this symptom led him to the attention of an Ear-Nose-Throat specialist, whose clinical evaluation suggested for a polypoid lesion of the right ethmoid sinus. The presence of a lesion was confirmed by a CT scan of the facial bones, which described a solid ossifying lesion occupying most of the right nasal cavity. Erosion of the cribriform plate of the ethmoid bone, septal deviation, and partial dislocation of the medial wall of the right maxillary sinus were also described (**Figure 1A**). On a subsequent MRI, the lesion proved to be hyperintense on T2-weighted images and showed marked contrast enhancement (**Figure 1B**). Based on these findings, endoscopic sinus surgery (ESS) was performed. On endoscopic examination, the lesion appeared to originate from the ethmoid bone, engulfing the middle nasal concha, and was firm and hard on manipulation. Antero-posterior ethmoidectomy was performed and the lesion removed. After surgical removal, lamina papiracea, cribriform plate, and other bone surfaces of the nasal cavity appeared intact and lined by normal mucosa. A frozen section of the lesion was performed, which showed chronically inflamed respiratory mucosa with foci of squamous metaplasia [15].

The remaining lesion was fixed in 10% neutral buffered formalin and sent for definitive examination. On macroscopic examination, the lesion was described as multiple fragments of bony tissue covered by grayish mucosa with a somewhat gelatinous appearance, whose greatest dimension ranged between 0.6 and 3.5 cm. After overnight decalcification, the lesion was sampled in 12 blocks, which were then processed and embedded in paraffin. H&E-stained 3-µm-thick slides revealed an inverted papilloma with extensive ossification (**Figure 1C, 1D**).

Discussion

Inverted papilloma (IP) is a non-cancerous sinonasal tumor that mostly affects middle-aged men. It accounts for approximately 0.5-4% of all nasal tumors and is most frequently encountered in patients aged 40-60 years, with a significant predilection for males (M: F ratio from 3: 1 to 5: 1) [16,17]. IP most commonly occurs on the lateral wall of the nasal cavity, most frequently originating from the middle turbinate/middle meatus and maxillary ostium, although it can arise elsewhere in the nasal passage. As the mass enlarges, it results in bony remodeling and resorption. Extension into the maxillary antrum is a common event [18]. Due to its non-specific clinical presentation, with symptoms such as nasal obstruction and chronic sinusitis, the diagnostic process relies heavily on radiology, with CT and MRI scan of the facial bones as criterion standard first-line procedures. On CT scan, IP presents as a solid lobulated lesion causing opacification of the involved nasal cavities or sinuses. Bone involvement is common, in the form of thinning or erosion of bony structures and septal deviation [2]. MRI is slightly more specific than CT and reveals the following typical features: isointense signal on T2-weighted images (T2WI) and so-called "cerebriform" configuration both on T2 and enhanced T1WI [10,19]. Due to extensive bone involvement and to the possibility of malignant transformation, radical surgical excision is mandatory, and is often achieved by endoscopic procedures. Definitive diagnosis is based on pathological examination. On histology, IP typically presents as ribbons and nests of respiratory, transitional, and/or squamous epithelium with smooth outer contours. As suggested by its name, endophytic growth of the epithelium into the stroma is a striking feature, which may be misinterpreted as invasion, leading to an incorrect diagnosis of carcinoma [20]. Although calcification has been described in up to 52% of cases [2], mature bone formation and ossification are rare events in IP. To date, less

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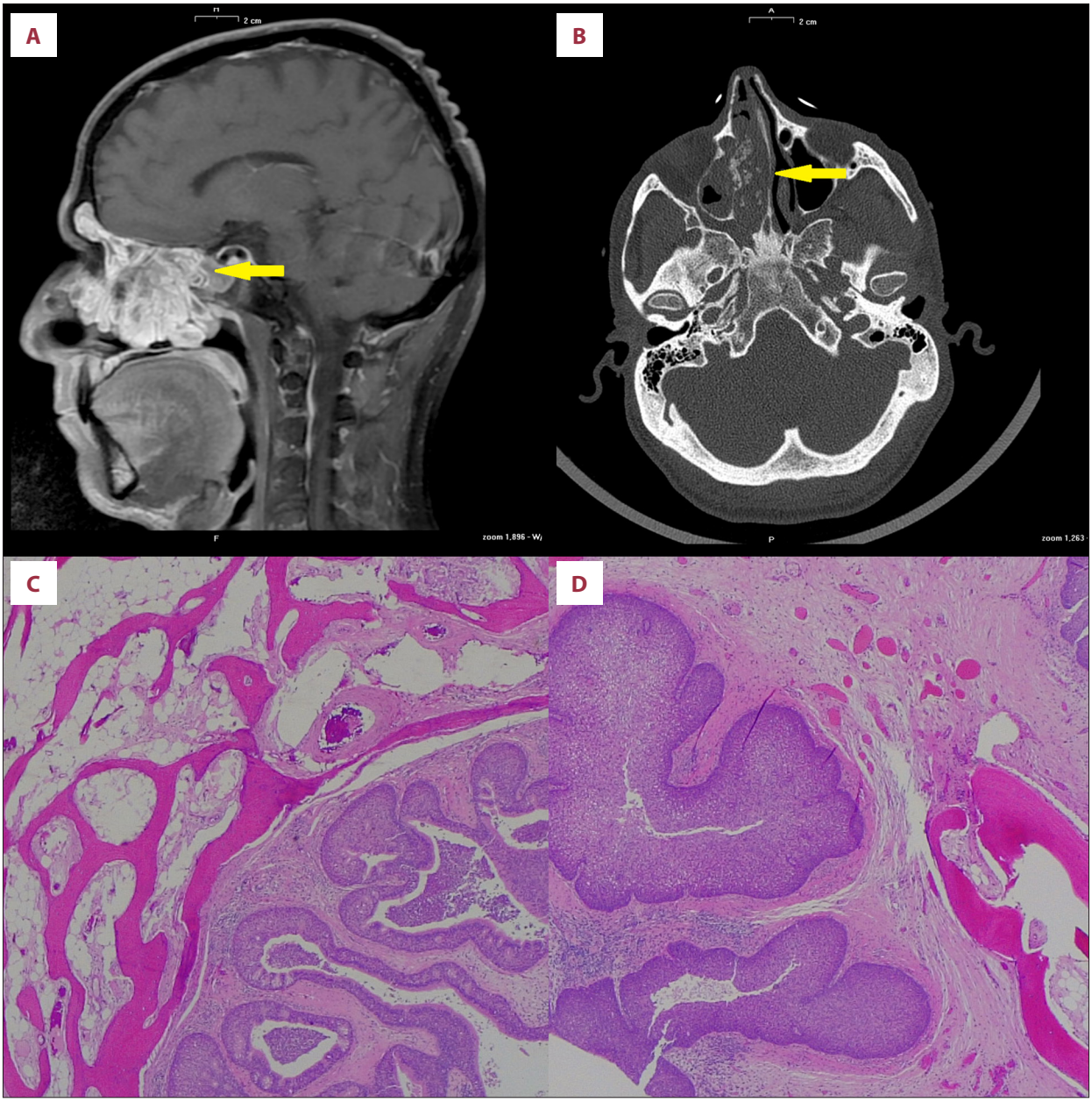

Figure 1. Sagittal MRI scan (**A**) and transverse CT scan (**B**) of the facial bones reveal a solid lobated lesion with extensive ossification, occupying most of the right nasal cavity. Erosion of the ethmoid bone and septal deviation are clearly visible (arrow). Histology shows an inverted papilloma with massive deposition of mature bone tissue. Hematoxylin and Eosin, 25× (**C**) and 100× (**D**) magnification.

than 30 cases of ossifying IP have been reported in the English literature [10-13]. Conventional and enhanced MRI manifestations of 20 ossifying IPs and eight polyps, which were confirmed histopathologically, were retrospectively evaluated by two doctors majoring in head and neck imaging with a significant difference was detected between the two entities for the involved sites. The largest case series has been published by Yang et al, who investigated the CT and MRI features of 20 IPs with ossification and 8 ossifying sinonasal polyps, with a focus on their main differential diagnosis such as osteoma, ossifying fibroma, fibrous dysplasia, and calcified fungal balls [10]. In our case, the patient presented with a months-long history of right nasal obstruction, unaccompanied by other symptoms such as pain or fever, thus raising the suspicion of sinonasal polyps or chronic sinusitis. A CT scan of the facial bones was performed and revealed a solid ossified lesion almost entirely filling the right nasal cavity, with signs of bone erosion in the ethmoid region and nasal septum deviation. A subsequent

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MRI showed hyperintensity on T2WI, which, as previously described, is not a typical feature of IPs. Differential diagnosis included a sinonasal malignancy, a benign lesion with deposition of bone tissues such as osteoma, and a fibrous dysplasia of the facial bones. Due to the lack of specificity of these findings, a definitive diagnosis could not be reached on the basis of clinical and radiological data. Despite this uncertainty, the lesion was considered amenable to complete surgical resection, and the patient underwent endoscopic sinus surgery (ESS). During the procedure, the surgeon noticed that the lesion was hard and firm, suggesting the diagnosis of fibrous dysplasia of the bone or osteoma. After successful removal of the mass, all nasal bone surfaces appeared smooth and intact on inspection. A frozen section was also performed on a sample, but failed to provide a diagnosis, revealing only inflamed respiratory epithelium with foci of squamous metaplasia. On final examination, histology revealed an inverted papilloma characterized by a striking amount of mature bone tissue arranged in trabeculae within the stroma. This feature was so remarkable that the pathologist directly consulted the surgeon, asking whether normal bone tissue of the nasal cavity structures was sacrificed in order to remove the lesion in its entirety. Once a negative answer was provided, a definitive diagnosis of inverted sinonasal papilloma with multiple foci of heterotopic ossification could be made. Common lesions with rare features may be very difficult to diagnose and in this regard our case can be paradigmatic. IP should be kept in mind when a monoliteral sinonasal lesion with extensive ossification is evaluated on CT and MRI. Indeed, IPs have non-specific features on imaging, and heterotopic ossification is so unusual that the correct diagnosis could be easily missed, if not ruled out, in the presence of such a feature. Luckily, IP is readily recognizable on histology, and a definitive diagnosis was possible on H&E slides without the use of ancillary techniques. In this context, communication between specialists again proved to be of fundamental importance in providing the correct diagnosis. The identification of mature bone as heterotopic ossification instead of normal facial bone structures was possible only with direct communication between specialists. The radiologist identified a lesion with massive bone deposition, which was diagnosed by the pathologist as an inverted papilloma with extensive ossification. The presence of mature bone tissue, which was morphologically indistinguishable from that found in normal cranial bones, raised the suspicion that osseous structures could have been damaged during the procedure.

After direct consultation with the surgeon who performed the procedure, this event was ruled out. This process highlighted once again the importance of a multidisciplinary approach.

Conclusions

Although sinonasal inverted papilloma is commonly encountered in the context of head and neck pathology, extensive ossification is an extremely rare feature. Our report investigates the diagnostic difficulties of a paradigmatic case, highlighting the importance of multidisciplinary teamwork in reaching the final diagnosis.

Department and Institution Where Work Was Done

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Statement

All figures were obtained by the authors using Leica Application Suite and Eyelite software and are not published elsewhere. The patient consented for the use of such pictures after anonymization.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Lawson W, Ho BT, Shaari CM, Biller HF. Inverted papilloma: A report of 112 cases. Laryngoscope. 1995;105(3):282-88
2. Dammann F, Pereira P, Laniado M, et al. Inverted papilloma of the nasal cavity and the paranasal sinuses: Using CT for primary diagnosis and follow-up. Am J Roentgenol. 1999;172(2):543-48
3. Khandekar S, Dive A, Mishra R, Upadhyaya N. Sinonasal inverted papilloma : A case report and mini review of histopathological features. Oral Maxillofac Pathol. 2015;19(3):405
4. Atan D. An unusual sinonasal inverted papilloma originating from superior turbinate and extending to epiglottis. Turk J Ear Nose Throat. 2017;27(1):39-42
5. Girolami I, Pantanowitz L, Barberis M, et al. Challenges facing pathologists evaluating PD-L1 in head & neck squamous cell carcinoma. J Oral Pathol Med. 2021;50(9):864-73
6. Eccher A, Girolami I, Troncone G, Pantanowitz L. Digital slide assessment for programmed death-ligand 1 combined positive score in head and neck squamous carcinoma: Focus on validation and vision. Front Artif Intell. 2021;4:684034
7. Munari E, Marconi M, Querzoli G, et al. Impact of PD-L1 and PD-1 expression on the prognostic significance of CD8+ tumor-infiltrating lymphocytes in non-small cell lung cancer. Front Immunol. 2021;12:680973
8. Munari E, Mariotti FR, Quatrini L, et al. PD-1/PD-L1 in cancer: Pathophysiological, diagnostic and therapeutic aspects. Int J Mol Sci. 2021;22(10):5123

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

9. Miller PJ, Jacobs J, Roland JTJ, et al. Intracranial inverting papilloma. Head Neck. 1996;18(5):450-53; discussion 454
10. Yang BT, Wang YZ, Sun FR, Dong JY. Ossifying inverted papilloma and ossifying polyp of the sinonasal tract: Comparison of CT and MRI features. Clin Radiol. 2017;72(1):84-90
11. Dadas B, Ercan İ, Başak T. Inverted papilloma with new bone formation in ethmoidofrontal region. Otolaryngol Head Neck Surg. 2006;134(2):343-44
12. Unlu HH, Songu M, Ovali GY, Nese N. Inverted papilloma with new bone formation: Report of three cases. Am J Rhinol. 2007;21(5):607-10
13. Tsuzuki K, Nishigami T, Takebayashi H, et al. Inverted papilloma with osteogenesis in the anterior ethmoid and frontal sinuses. J Laryngol Otol. 2010;124(2):230-33
14. Okamoto T, Kodama S, Nomi N, et al. Expression of bone morphogenic protein in sinonasal inverted papilloma with new bone formation. Allergy Rhinol. 2011;2:16-20
15. Cima L, Brunelli M, Parwani A, et al. Validation of remote digital frozen sections for cancer and transplant intraoperative services. J Pathol Inform. 2018;9:34
16. Jeon TY, Kim H-J, Chung S-K, et al. Sinonasal inverted papilloma: Value of convoluted cerebriform pattern on MR imaging. Am J Neuroradiol. 2008;29(8):1556-60
17. Yousem DM, Fellows DW, Kennedy DW, et al. Inverted papilloma: Evaluation with MR imaging. Radiology. 1992;185(2):501-5
18. Momose KJ, Weber AL, Goodman M, et al. Radiological aspects of inverted papilloma. Radiology. 1980;134(1):73-79
19. Russo C, Elefante A, Romano A, et al. A multimodal diagnostic approach to inverted papilloma: Proposal of a novel diagnostic flow-chart. Curr Probl Diagn Radiol. 2021;50(4):499-504
20. Goldblum JR, McKenney JK, Lamps LW, Myers JL. Rosai and Ackerman's surgical pathology. Elsevier Health Sciences; 2017

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