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Diagnostic strategy and therapeutic management of sinonasal inverted papilloma: our experience with review of literature

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Abstract

Background: The sinonasal inverted papilloma is a rare benign tumor, characterized by local aggressiveness, a high rate of recurrence after surgical resection, and the possibility of malignant transformation. The aims of this study are to analyze diagnostic strategy and therapeutic modalities and to evaluate results after surgery.

Methods: We report a retrospective study, including patients operated for inverted sinonasal papilloma in our department. Preoperatively, all patients were assessed by CT scan (computed tomography), 9 of them by MRI (magnetic resonance imaging).

Results: The average age of our patients was 52 years with a male predominance. The most common symptom was unilateral nasal obstruction. The endoscopic appearance was suggestive of inverted papilloma (IP) in 75% of cases. Thirty-two patients underwent an exclusive endonasal endoscopic surgery; one patient was operated with a combined approach. Two patients underwent external approaches. A recurrence was observed in 4 patients (11%).

Conclusion: Preoperative investigation for IP is essentially based on MRI, also required in case of recurrence. Histological examination of the entire tumor is crucial to rule out an associated carcinoma. The "all endoscopic" management is not always achievable for these tumors.

Keywords: Inverted papilloma, Paranasal sinuses, CT, MRI, Endonasal approach

Background

Sinonasal inverted papilloma is a rare tumor, representing 0.5 to 4% of all sinonasal tumors [1]. Despite its benign nature, it is distinguished from other sinonasal tumors by three characteristics that make it a particular tumor: an osteolytic potential, a tendency to recurrence and a possible malignant transformation. Its clinical manifestations are not specific [1]. The management of the IPs presents two challenges concerning the diagnostic assessment as well as therapeutic strategy.

The objectives of our study are to analyze the elements of the diagnostic strategy and therapeutic modalities of the sinonasal inverted papilloma (SNIP) and to evaluate results after surgery.

Methods

We conducted a retrospective study spread over 18 years, involving 35 patients operated for SINP in the ENT department. The diagnosis of IP was made on the basis of clinical, radiological, and especially histological criteria.

We only included patients whose records contain preoperative imaging, with a definitive histological diagnosis of inverted papilloma and having undergone surgery under general anesthesia. Patients with incomplete records were excluded from our study.

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An operating sheet was produced to collect data from medical records and then computerized using SPSS 21.0 software. We expressed the quantitative variables in average and the qualitative variables in number and percentage. We did not analyze power for sample size calculation.

Results

Our study comprised 28 males and 7 females. The average age of our patients was 52 years with a peak of frequency between the fifth and sixth decade. Three patients have a history of sinonasal surgery: two patients were operated for inflammatory polyps and one patient for inverted papilloma (IP) in another establishment. A history of sinonasal polyposis (SNP) was noted in one patient. The mean time of our patients to consult was 26 months.

The most common symptom was unilateral nasal obstruction. This one was bilateral in 2 cases (1 case of bilateral tumor and 1case of unilateral IP associated with SNP). The endoscopic appearance was evocative of an IP in 75% of cases. The tumor had a translucent appearance in 9 patients.

All patients were evaluated by preoperative CT scan of the paranasal sinuses. It revealed in 90% of cases a unilateral soft tissue density mass with an heterogeneous enhancement associated in 11% of cases with calcifications. The tumor origin was predicted by CT scan in 16 cases which concerned in most of cases the middle meatus region (Fig. 1); in 2 cases, the tumor arised from the ethmoid sinus and in 1 case from the sphenoid sinus. The sites that were mostly involved by the tumor were the nasal cavity, the ethmoid, and the maxillary sinus. Among the 13 cases of frontal opacification, CT scan has identified retention in 4 cases. An extension of the tumor to the pterygo maxillary fossa was noted in 1 case.

Bony erosions were observed in 15 patients especially in the lateral nasal wall (LNW) (80%). An erosion of nasolacrimal duct was noted in 2 cases (Fig. 2).

Lyses of the anterior and posterior wall of the maxillary sinus as well as the orbital floor were noted in one case for which an associated carcinoma to IP was suspected. In one case, CT has also suspected an IP within SNP (Fig. 3).

Magnetic resonance imaging (MRI) with gadolinium was required for 9 patients to better analyze the lesion component in the frontal and maxillary sinus. The tumor was, in the majority of cases, isointense in T1-weighted images and hyper intense in T2-weighted images with heterogeneous enhancement in all patients. The convoluted cerebriform pattern was identified in 75% of cases (Fig. 4). In MRI, the maxillary sinus (MS) was involved in only 44% of cases (Fig. 5) and there were no involvement of frontal sinus or sphenoid sinus.

Nineteen preoperative biopsies were performed under local anesthesia (51% of cases). They were positive for an IP in 15 patients and in 3 patients they concluded to inflammatory polyps. In one case, it detected the presence of carcinoma in situ in a recurrent IP of the MS and affirmed the presence of synchronous squamous cell carcinoma (SSC) in another case.

Using clinical and imaging findings, our patients were graded according to the Krouse classification: 28.5% of

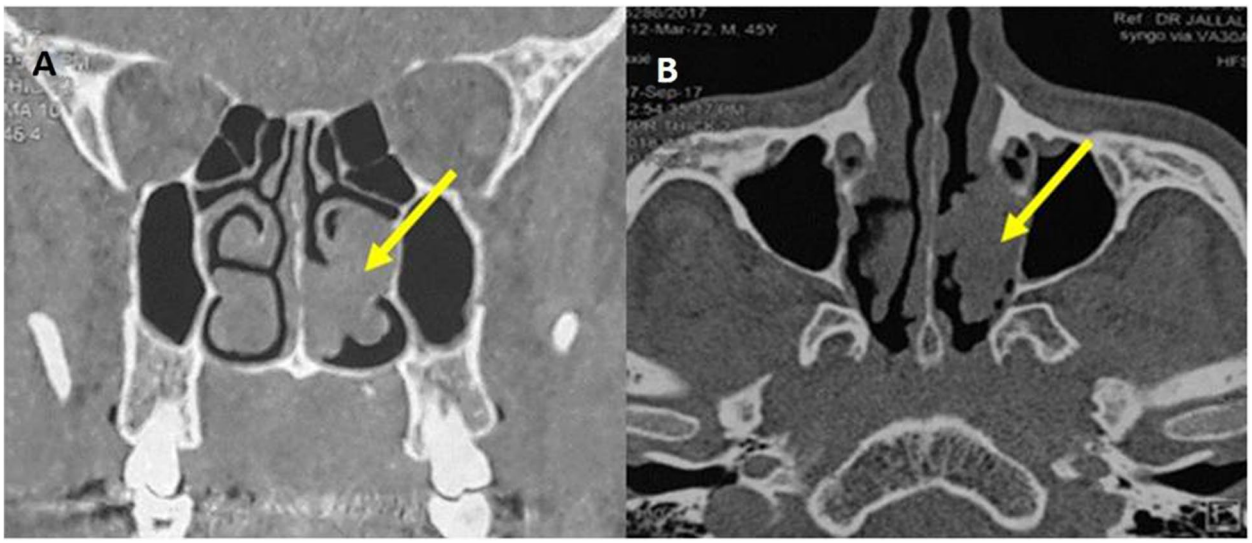

Fig. 1 Sinus CT in coronal (**A**) and axial (**B**) bone window images showing polyploidal mass arising from the left metatal region (arrow) and extending to the homolateral nasal cavity

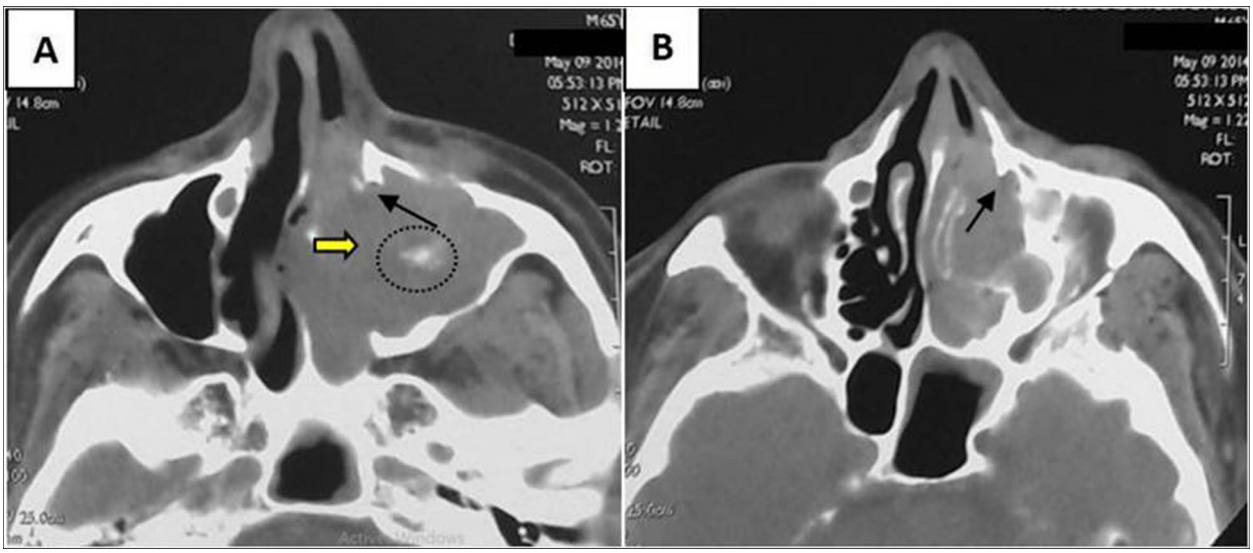

Fig. 2 Axial CT images (**A**, **B**) demonstrating a total opacification of the left MS with central calcifications (circle) with lysis of the LNW (yellow arrow) and nasolacrimal duct (black arrow)

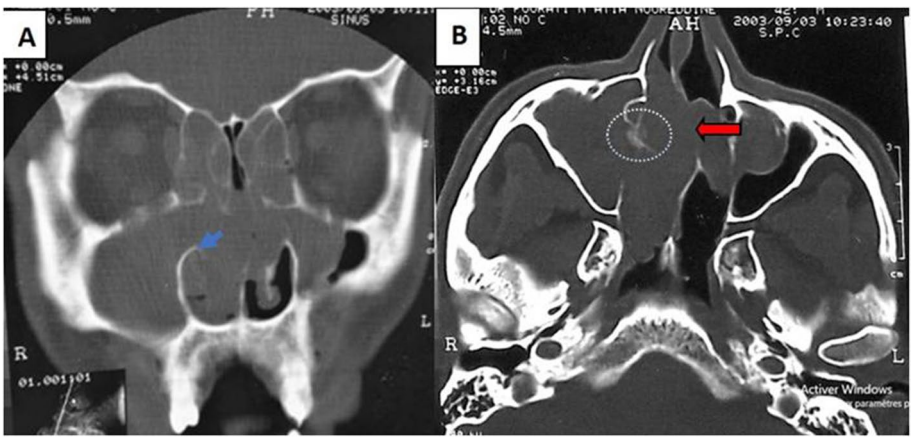

Fig. 3 Coronal (**A**) and axial (**B**) bone CT showing an opacification of the two maxillary sinuses more marked on the right side extending in both sides to the nasal cavity especially on the right side widening the maxillary ostium, noting the lysis of inferior turbinate (blue arrow) a calcification image in the LNW (circle) and nasal septum bowing (red arrow) on the right side: Right IP associated with SNP

cases classified in T1, 57% in T2, 8.5% in T3, and 6% classified in T4.

Intraoperative endoscopic evaluation has determined the tumor pedicle in 75% of cases (24 patients) (Fig. 6), which was frequently located (62%) in the medial wall of MS followed by the ethmoid and posterior wall of the MS. The tumor has originated from the sphenoid in one case. For the tumor extent, there were a predominance of the maxillary involvement (51%) followed by the ethmoid (43%), and the tumor extended from the ethmoid to the frontal recess in one case.

Thirty-two patients underwent an exclusive endoscopic (EE) approach while 2 patients were managed by an open surgery and one patient by a combined approach (endoscopic + Caldwell Luc: CL).

Depending on the site of implantation and the extent of the tumor, a type I endoscopic resection was performed for 15 patients (47%) where the tumor was limited to the middle meatus, the ethmoid, or the sphenoid sinus.

A type II endoscopic resection or an endoscopic medial maxillectomy was performed for 17 patients (53%) for tumors that extended from the middle meatus to the

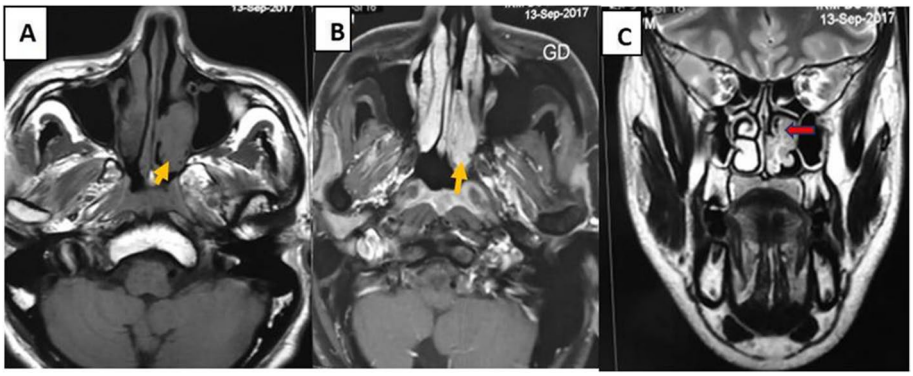

Fig. 4 Axial T1W (**A**), Fat-Sat contrast-enhanced T1W (**B**), and coronal T2W (**C**) MR images showing a mass of the middle left meatus extending to the nasal cavity and homolateral choana (yellow arrow) isointense in T1W, heterogeneously hyperintense in T2W achieving a convoluted cerebriform pattern (red arrow) with moderate and heterogeneous enhancement

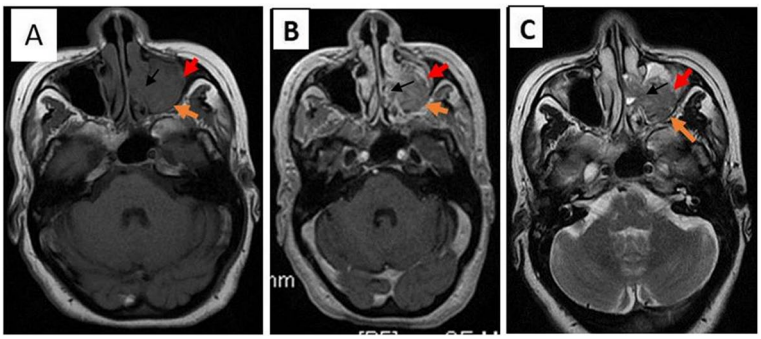

Fig. 5 Axial T1W (**A**), Fat-Sat contrast-enhanced T1W (**B**), and T2W (**C**) MR images showing a tissue mass (red arrow) of the left MS extending to the homolateral nasal cavity involving medial (black arrow) and posterior (orange arrow) walls of MS, hypointense in T1W, with an intermediate heterogeneous signal and moderate and heterogeneous enhancement

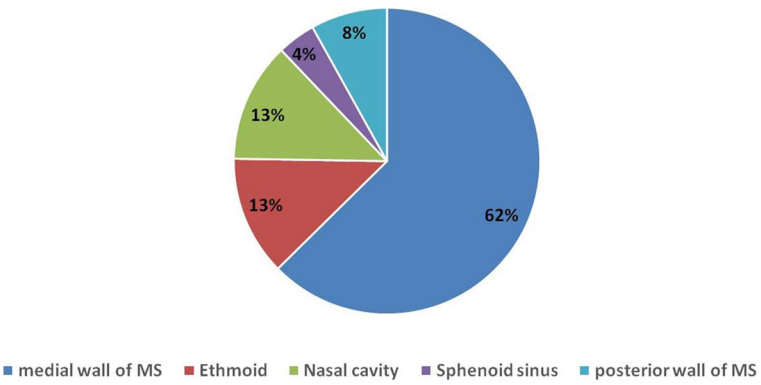

Fig. 6 Origin sites of IP according to surgical findings

maxillary sinus (medial and posterior wall) or tumors invading the lateral nasal wall. A draf IIa frontal sinosotomy was required in case of the involvement of frontal recess. The sphenoidal IP was removed by an endoscopic sphenoidotomy.

An open approach (lateral rhinotomy) was reserved for 2 cases: a maxillary IP with SSC extending to the pterygo

maxillary fossa and a multifocal IP with involvement of the nasopharynx and soft palate. A combined approach (EE + CL) was required for a recurrent IP in the anterior wall of the MS associated with a carcinoma in situ. This approach allowed a complete resection of the tumor verified by intraoperative negative margins. In terms of staging, T1, T2, and T3 (sphenoid/posterior wall of MS) tumors were managed exclusively by endoscopic surgery. In contrast, T3 (anterior wall of MS) and T4 tumors were removed through a combined or external approach. Postoperative radiotherapy was indicated in the case of IP associated with SSC. In the contrast we did not indicate a postoperative radiotherapy for the maxillary IP associated with carcinoma in situ.

The median follow-up was 30 months. Subsequent endoscopic control was performed one month after surgery, every 3 months during the 1st year, every 6 months until the 5th year, and then annually. MRI and biopsy were performed in case we doubted a recurrence or in case of a poor sinus cavity visualization on endoscopic examination. No major postoperative complications were observed in our study.

During follow up, we have detected 4 recurrences (11%,) after 33 months of an average interval after surgery: 3 located in the MS (antero-lateral wall) and one located in the ethmoid roof.

Three of those recurrences occurred after endoscopic surgery (9%). These cases were managed by the same procedure with good results for two cases after 36 months of follow-up. A second recurrence was revealed in one patient located in the anterior wall of MS after 11 years from the second surgery requiring a combined approach with a good evolution.

The patient with recurrent maxillary IP associated with a carcinoma in situ treated by a combined approach has presented a second recurrence in the same primary site which was also associated with a malignancy in situ. We decided to keep the same conservative attitude: re-operating the patient with the same procedure. We did not indicate adjuvant treatment with radiotherapy. No recurrence was noted after a period of 36 months of follow-up.

A metachronous squamocellular carcinoma of the nasopharynx occurred 10 years later in a patient with an ex multifocal IP. This patient was out of sight for a long time. An exclusive radiotherapy was recommended for this case and the patient has died later.

Discussion

Our study suggests that endoscopy and imaging (CT scan and especially MRI) are useful, not in the positive diagnosis of IP, which is histological but in the preoperative assessment by determining the location and extension of the tumor. Thirty-two patients were operated by endonasal endoscopic surgery. Although this technique yielded good results in our study (91% of success), the anterior and lateral walls of MS were its main limitations. In extra-sinus forms or in case of associated carcinoma an open procedure is preferred. Given the risk of recurrence and metachronal malignant transformation, it is essential to inform the patient of the need for endoscopic and radiological follow-up.

Functional symptoms of IP are non-specific and common with the other sinonasal tumors, dominated by a unilateral nasal obstruction [1]. Its bilateral expression was reported by Salomone et al. in a case of bilateral IP. In our study, the nasal obstruction was bilateral in 2 patients: a case of unilateral IP associated with a SNP and a case of bilateral IP. Those two atypical presentations of SNIP (which accounts for 14.1% and 4–5%, respectively) [1, 2] may cause also a delay and misdiagnosis [1, 2]. The endoscopic examination shows a reddish-gray lobulated tumor, firm, and more vascular than an inflammatory polyp, with an irregular friable surface, carrying out the classic "raspberry" aspect [1]. The tumor can be hidden by inflammatory polyps [3] which explain the translucent appearance of the lesion in endoscopic examination in 9 cases of our study.

The lateral nasal wall is the elective site of implantation of the IP in up to 91% of cases, particularly in the region of the middle meatus and the middle turbinate invading the osteo-metatal complex, followed by the ethmoidal sinus (33%) [4]. Rarely, the tumor may arise from the frontal sinus (16%), MS walls (except medial wall) (14%), and more exceptionally from the sphenoid (6%) [4]. A tumor originating in the LNW may secondarily invade the entire nasal cavity or even the adjacent sinuses; maxillary in 70 to 90% of cases, ethmoid in 40 to 70% [1, 4]. Similarly, in our study, the tumor origin was frequently located in the LNW and MS was the most common invaded site followed by the ethmoid.

The radiological assessment has two main objectives: to establish precisely the extension of the tumor and to localize the site of implantation of the lesion. The aspect on CT is non-specific, with an isodense unilateral homogeneous lesion generally centered on the meatus, with an heterogeneous enhancement [1]. The "macro-lobulated" aspects as well as intra-tumoral calcifications are highly suggestive of IP diagnosis with a sensitivity and specificity of 90% and 97%, respectively [1]. The bone changes related to tumor growth and its local aggressive potential are frequent (up to 93% of cases) and easily studied in CT scan [1]. These can consist of bowing, bone thinning, and erosion. In case of synchronous carcinoma, the destruction of the osseous infrastructure is greater than in benign IP [1, 5].

In our study, using those features, CT scan has suspected a unilateral IP within SNP regarding the presence of bone erosion, calcification, and nasal septum bowing on the tumor side, and in another case, it has detected an associated malignancy in a maxillary IP regarding a great destruction of anterior and posterior walls requiring a preoperative biopsy which contributed to treatment guidance. Moreover, bone changes can include focal hyperostosis or focal osteitis which is useful for predicting tumor origin according to some authors, with a positive predictive value of 40–95%, depending on reports [6].

However, accurate tumor mapping is still unachievable because of inadequate differentiation of tumor from inflammatory diseases. Even though, in theory, tumor enhancement is heterogeneous while it is peripheral in inflammatory disease, an inflamed mucosa also has a soft tissue density which enhances with contrast and may potentially lead to overestimation of the size of some lesions [7]. Sukenik has noted in his study of 90 patients an average CT sensitivity of 69% especially for maxillary sinus and ethmoid against an average specificity of 20% especially for frontal sinus and sphenoid sinus, a positive predictive value of 36%, and a negative predictive value of 64% [8]. These findings emphasize that CT scan is an adequate screening test to detect disease. However, its ability to differentiate between disease and normal membranes is relatively low.

MRI is nowadays requested as a complement to CT [1]. There is no signature pattern of MRI that is suggestive of a specific diagnosis of IP (hypo to iso-intense in T1-weighted images and iso to hyper-intense in T2-weighted images) [5, 9]. There is intense and often homogeneous uptake. A convoluted cerebriform (CC) appearance on T2-weighted images or enhanced T1-weighted images strongly suggests the diagnosis of IP [9]. Nevertheless, this pattern can also be seen in various malignant sinonasal tumors. A focal loss of CC may be suggestive of the diagnosis of IPs concomitant with malignancy [10]. MRI is considered to be superior to CT scanning in distinguishing papilloma from inflammation. It provides excellent demarcation of tumor in contrast to surrounding inflammatory soft tissue and retained secretions [7]. Som et al. reported a 95% MRI sensitivity in differential diagnosis between tumor and inflammatory mucosa [9]. Indeed, in our study, the tumor mapping provided by MRI was consistent with intra operative findings in 78% of cases with high specificity (86%) especially to maxillary and frontal involvement.

The therapeutic decision will depend on the preoperative assessment as well as the surgical team and its experience. The surgeon may start his surgical procedure by the least invasive approach and modify it according to intra operative findings (tumor extension, implantation site). Thus, a combined or external approach should be considered whenever a complete control of the IP by endoscopic technique is impossible. Commonly, for the IP limited to nasal cavity or originating from middle meatus, ethmoid, and sphenoid even lesions protruding into the maxillary sinus cavity without involvement of the sinus's mucosa, a type I endoscopic resection is recommended including ethmoid subperiostal resection, with sphenoidotomy, medial antrostomy, and frontal recess clearance depending on the tumor extension. Unless, the tumor is invading along the lateral nasal wall; in this case, an endoscopic medial maxillectomy is performed [11, 12]. When dealing with the maxillary sinus, it is important to indentify and remove the tumor's pedicle. For tumors involving the posterior or superior wall, tumor resection could be achieved through a large antrostomy or type I resection. The involvement of medial wall usually requires a type II resection or an endoscopic medial maxillectomy [11, 12].

For some authors, the endoscopic access of anterolateral and inferior walls is considered to be difficult and inadequate for a complete tumor resection [13] requiring an adjuvant vestibular approach (Caldwell-Luc or mini endoscopic Caldwell-Luc technique). In addition to the anterior wall, this technique offers a complete control of the three recesses (lacrymal, orbital, and zygomatic) of MS [14]. Others have developed new surgical strategies in order to access to these problematic regions while limiting the surgical procedure such as trans-septal approaches [15] and prelacrimal approach [16]. In our experience, we required a combined endoscopic/Caldwell-Luc approach for the treatment of the anterolateral wall involvement. The management of SNIP originating from the frontal sinus is the most challenging [11]. Tumors prolapsing into the sinus or involving the medial or posterior wall can be managed endoscopically through DRAF type sinosotomy. On the contrast, an external (frontal osteoplastic flap) or combined external/endoscopic approach is envisaged in case of massive lateral supraorbital attachment of the lesion in laterally pneumatized frontal sinus or anterior wall involvement [17]. Some authors suggested a treatment strategy according to krouse's staging. There is no doubt that T1 and T2 IP can be managed endoscopically. Nevertheless, the classic open or combined approaches may be best appropriate for some specific T3 and T4 Krouse IP [18].

Treatment of IP associated with prevalent carcinoma should involve surgical treatment by external approach (most commonly paralateronasal) and postoperative radiotherapy. In case that the carcinoma is discovered on final histological examination, the attitude is controversial. It depends whether it is an invasive carcinoma or

a carcinoma in situ. For the invasive type that is limited to one site without multiple dysplasia foci, an additional radical surgery of the area in question with an adjuvant irradiation will be proposed. Otherwise, in case of carcinoma in situ, a simple monitoring is recommended [14, 19].

Cases of IP associated with malignancy in our study were treated by external or combined surgery. We did not indicate a postoperative radiotherapy in case of IP with carcinoma in situ neither after first recurrence nor after second recurrence with good evolution after 36 months of follow-up. This attitude was adopted for many reasons: first, in the light of a complete tumor resection histologically verified, and second, as long as a close and prolonged follow-up was guaranteed; therefore, facilitate the endoscopic surveillance in order to detect further recurrence earlier, and finally regarding a risk of transformation to an invasive carcinoma relatively low (2.7%) according to Mirza [19]. In the opposite, Yuan et al. in a study of 22 cases of recurrent IP associated with carcinoma suggested that a radical strategy is the optimum treatment in this case [20].

Recurrence's rates reported in the literature range generally between 10 and 20% [1], even lower between 0 and 8% in recent studies [16]. Endoscopic endonasal surgery has reduced significantly the rate of IP recurrence below that it was observed in external surgery, and it is actually considered the gold standard [1, 16, 21]. In a meta-analysis, Kim et al. showed that the endoscopic procedure reduces the risk of recurrence to 44% [22]. However, some authors explained this difference in recurrence rate between open and endoscopic surgery by the fact that cases with more advanced disease (T3 and especially KrouseT4 IP), which are correlated with higher recurrence rate, are those most often reserved for an open or combined approach [18, 23]. Risk factors for relapse still the subject of debate [24]. T3 tumors as well as maxillary and frontal location, for some authors, are incriminated in recurrences [24, 25]. However, incomplete removal remains an indisputable factor. In our series, recurrences occurred in 75% of cases in T3 patients and were located especially in MS.

Conclusion

At the end of this study, we can retain that the preoperative investigation is essentially based on MRI, also required in case of recurrence. Histological examination of the entire tumor is essential to rule out an associated carcinoma. The "all endoscopic" is not always achievable for these tumors. The anterior wall of the maxillary sinus and the latero-frontal extension are the main limitations of this approach.

Abbreviations

CT: Computed tomography; MRI: Magnetic resonance imaging; IP: Inverted papilloma; SNIP: Sinonasal inverted papilloma; SNP: Sinonasal polyposis; LNW: Lateral nasal wall; MS: Maxillary sinus; SCC: Synchronous squamous cell carcinoma; EE: Exclusive endoscopic; CL: CaldWell Luc.

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Authors' contributions

RB corrected the manuscript. AF analyzed and interpreted the patient data. AM performed the imaging exams and correction of the radiologic part. NK contributed to the bibliographic search. AeK contributed to the bibliographic search. MF contributed to the bibliographic search. KH revised the manuscript. Jk revised the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The data are analyzed during the current study and are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study poses no ethical problem and received a favorable opinion from institutional research ethics committee of Faculty of Medicine of Monastir [IORG 0009738/0990–0279]. Consent to participate was not required as it is a retrospective study with a retrospective collection of files over a period of 18 years.

Consent for publication

Not applicable (images included respect identity of patients).

Competing interests

The authors declare that they have no competing interests.

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