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Inverted papilloma of the nose and paranasal sinuses: a fifteen-year review

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Summary
Inverted papilloma is a relatively rare epithelial neoplasm of the nose and paranasal sinuses accounting for 0.5 - 4% of all primary tumours of the nose. This is a retrospective study of fifteen patients with histologically confirmed I.P. of the nose and paranasal sinuses seen from 1986 to 2000 at the Department of Otorhinolaryngology, University College Hospital, Ibadan. The patients ages range from 14 - 65 years, with a median age of 39 years. There were twelve males and three females. Five patients had advanced lesions of which four were bilateral. There was associated synchronous and metachronous squamous cell carcinoma (SCC) in two patients respectively. The surgery offered was based on the clinical and radiological evaluations of these patients. Nine patients had conservative surgery (intranasal clearance/antrostomy and external fronto-ethmoidectomy) while the remaining six patients had radical surgery (lateral rhinotomy/medial maxillectomy) at various times. The two patients with SCC had adjunct radiotherapy/ chemotherapy in addition. Recurrence was observed in those that had conservative surgery only. We therefore advocate radical surgery in our environment as the treatment of choice for effective limitation of recurrence.

Keywords: *Paranasal sinuses; nasal cavity; inverted papillomas; squamous cell carcinoma; medial maxillectomy.*

Résumé
L.I.P. inverse est un neoplasma epithelial relativement rare du mez et de la sinusite paranasale, responsible de 0.5 – 4% de toutes les tumeurs primaires du nez. Ceci est une etude retrospective de 15 patients ayant L.I.P. et la sinusite paranasale histologiquement confirmes, consulte's entre 1986 et l'an 2000 dans le departement d'Otorhinolaryngologie du College Hospitalier Universitaire d'Ibadan. Les patients etaient ages de 14 – 65 ans, avec une mediane de 39 ans, comprenant 12 hommes et 3 femmes. Cinq malades avaient des lesions severe lesquelles quatre etaient bilaterales. Il y avait l'association synchroree et metachronee squameuse de cellules cancerigenes (SCC) chez deux des patients. La chirurgie offerte etait basee sur les evaluations cliniques et radiologiques des patients. 9 des patients ont en une chirurgie modeste (traditionalle) (nettoyage intranasal/antrostomie et la fronto – ethmoi-dectomie externe) alors que les six autres ont en une intervention chirurgicale radicale/) a plusieurs reprises. Les deux maladies ayant SCC ont eu en plus une radiotherapie/cliniotherapie. La repetition etait observee chez ceux qui ont en une intervention chirurgicale traditionalle sentement. Ainsi, nous recommendons la chirurgie radicale dans notre environnement, comme traitement de choix pour la limitation effective des repetition.

Introduction

Inverted papilloma (I.P.) is a relatively rare epithelial neoplasm of the nose and paranasal sinuses. In 1847, this cauliflower like tumour of the mucous membrane was described as a "papillae" by Kramer [1]. This tumour was again brought into limelight by Ward in 1855 [2]. The tumour accounts for 0.5 to 4% of all primary tumours of the nose [3,4]. Many reports have documented this disease entity with various suggestions about its aetiopathogenesis, clinical course and treatment modality with regards to its high recurrence.

The first vivid description of the pathological features of this neoplasm was by Ringertz in 1938 [2]. He revealed the tendency of the squamous or respiratory epithelium to invert into the connective tissue stroma as opposed to the other papillomas that developed raised lesion with the connective tissues drawn upward. Hyams reviewed 315 cases of papillomas from the nose and paranasal sinuses and further sub-classified the papillomas into inverted, fungi form and cylindrical cell types; based on their peculiar histological features [2].

In recent studies, human papilloma virus (HPV) has been accepted as a tumour inducing and promoting virus which has been associated with benign and malignant tumours of the upper aerodigestive tract mucosa. Some of the isolated HPV are 6 and 11 which predispose to benign lesions from stratified epithelium, while HPV 16 and 18 predispose to the development of cancer [5,6].

This disease is mostly unilateral without predelection for any of the nasal cavities. I.P. most commonly arises from the lateral wall of the nose especially in the region of the middle turbinate/meatus [7]. Occasionally, it may arise from the nasal septum. Bilateral cases are very rare. We present our expereices with this tumour in University College Hospital, Ibadan especially as there has not been any previous study of I.P. from Ibadan.

Materials and methods

This is a retrospective review of all cases that were diagnosed histologically as inverted papilloma in patients that presented to the Otorhinolaryngology Department of the University College Hospital, Ibadan within a fifteen-year period (1986 – 2000).

The medical records of these patients were retrieved and reviewed. Data extracted for analysis included age, sex, presenting symptoms and physical and radiological findings. Also included were the number/type of surgical interventions (these were classified into either conservative – intranasal polypectomy, external fronto-ethmoidectomy or radical – lateral rhinotomy/medial maxillectomy) as obtainable in our hospital and the extent of the tumour mass intraoperatively.

Results

A total of fifteen patients with histological diagnosis of inverted papilloma from 1986 to 2000 in the Otorhinolaryngology Department of the University College Hospital, Ibadan were analysed in this review. These cases are summarized in Table 1.

Clinical features

There was a male preponderance (male to female ratio of 4 : 1). Their ages ranged from 14yrs, to 65yrs, with a median age of

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Table 1: Summariezed description of cases

S/No	Hosp. No	Initials	Age Yr	Sex	Duration of sympt.	Symptoms	Signs	Radiological findings	Histology/No
1.	747881	G.K.	38	M	8yrs	Nasal obstruction discharge hyposmia, headache & epiphora	Intranasal polypoidal mass and septal deviation	Soft tissue shadow within cavurt + opaque antrum & ethmoided sinuses (X)	I° feature of inverted papilloma H/142/88
2.	710025	L.A	35	F	4yrs	Nasal obstruction, discharge hyposmia, headache	Intranasal polypoided mass	Soft tissue shadow within nasal cavity + opaque antrum and ethmoidal sinues (X)	I° features of inverted papilloma H/271/89
3.	71795	O.S	65	F	29yrs	Nasal obstruction, discharge anosmia, headache, facial pain.	Intranasal polypoidal mass and septal deviation	Soft tissue shadow within nasal cavity + opaque antrum and ethmoidal sinuses (X)	I° feature of inverted papilloma H/2468/91 and H/1483/00
4.	856113	O.J.	28	M	11yrs	Nasal obstruction, discharge hyposmia, headache and Epiphora.	Intranasal polypoidal mass	Soft issue shadow within nasal cavity + opaque antrum (X)	I° feature of inverted papilloma H/2071/92
5.	836910	R.M	41	M	24yrs	Nasal obstruction*, Epistaxis, discharge, anosmia, nasal mass, headache, epiphora, cheek swelling and diplopia/blurred vision.	**(B) Intranasal polypoidal mass facial asymmetry, Proptosis, hypertelorism and septal perforation.	Soft tissue shadow within nasal cavity + orbitm opaque antrum, frontal, ethmoidal and sphenoidal sinues + bony destruction (X + CT)	I° feature if inverted papilloma + synchronous squamous cell Ca. H/1023/95
6.	867018	O.E.	29	M	4.5yrs	Nasal obstruction *, Epistaxis discharge, anosmia, nasal mass Headache and epiphorea.	**(B) Intranasal polypoidL mass, septal deviation and proptosis.	Soft tissue shadow within nasal cavity + orbit, opaque frontal and ethmoidal sinues (X)	I° feature of inverted papilloma dysplastic changes H/976/96, 1924/97
7.	883507	R.T.	31	M	1.25yr	Nasal obstruction, epistaxis, discharge, hyposmia, headache and epiphora.	Intranasal polypoidal mass	Soft tissue shadow within nasal cavity + opaque antrum and ethmoidal sinuses (X)	I° feature of inverted papilloma H/2553/96
8.	821440	A.B.	27	M	1yr.	Nasal obstruction, epistaxis, discharge, anosmia, headache epiphora and Eyeache	Intranasal polypoidal mass	Soft tissue shadow within nasal cavity + opaque antrum, frontal and ethmoidal sinuses (X)	I° feature of inverted papiloloma H/422/96
9.	932245	U.E.	20	M	1yr	Nasal obstruction, Epistaxis, discharge and epiphora.	Soft tissue shadow within nasal cavity + opaque antrum and ethmoidal sinuses (X)	Soft tissue shadow within nasal cavity + opaque antrum, and ethmoid (X)	I° feature of inverted papilloma H/2808/97
10.	1688	O.J	60	M	2.5yr	Nasal obstruction*, epistaxis discharge, hyposmia, headache, epiphora, eyeache	**(B) Intranasal polypoidal mass and septal deviation	Soft tissue shadow within nasal cavity + opaque antrum, frontal, ethmoidal (X)	I° feature of inverted papilloma H/1663/97
11.	638928	E.E.	14	M	0.75yr	Nasal obstruction, epistaxis, discharge, anosmia.	Intranasal polypoidal mass	Soft tissue shadow within nasal cavity + opaque antrum and ethmoid (X)	I° feature of inverted papilloma H/809/97
12.	815611	A.E	59	M	3yr	Nasal obstruction*, epistaxis, discharge, anosmia, nasal mass Headache, epiphora, eyeache, Diplopia/blured vision, cheek swelling, tinnitus and otalgia	**(B) Intranasal polypoidal mass, septal deviation, facia asymmetry proptosis and hypertelorism.	Soft tissue shadow within nasal cavity + orbit opaque antrum, frontal, ethmoidal and sphenoidal sinuses + bony distruction (X + CT)	I° features of inverted papilloma + metachronous squamous cell Ca. H/949/97
13.	921353	O.A.	57	M	2.5yr.	Nasal obstruction*,-Epistaxis, discharge, Anosmia, nasal mass headache epiphora, eyeache, Diplopia/blured vision, cheek swelling tinnitus and otalgia	**Intranasal polypoidal mass septal deviation, facial asymmetry proptosis and hypertelorism	Soft tissue shadow within nasal cavity + opaque antrum, frontal, ethmoidal and sphenoidal sinuses + slerotic bone (X + CT)	I° features of inverted papilloma H/204/97
14	918683	A.T	24	M	3yr.	Nasal obstruction epistaxis, discharge, hyposmia, headache epiphora and eyeache.	Intranasal polypoidal mass and septal deviation	Soft tissue shadow within nasal cavity + opaque antrum frontal, ethmoidal (X)	I° features of inverted papilloma H/1751/98
15.	677620	A.A	58	F	1.5 yr	Nasal obstruction, epistaxis, discharge, hyposmia, headache, epiphora and eye ache	Intranasal polypoidal mass and septal deviation	Soft tissue shadow witrhin nasal cavity + opaque antrum frntal, ethmoidal (X)	I° features of inverted papilloma H/2925/99

** Those with bilateral nasal blockage*
X = Plain radiograph of paranasal sinuses.
*** Those that had the nasal mass visible in the anterior nares*
CT = Computerised Tomographic Scan
(B) - Bilateral cases

39yrs. The duration of presenting symptoms ranged from 9 months to 29 yrs., with a median of 6.5yrs. The age of ocurrence was distributed between the second and sixth decade.

The most common presenting symptoms were unilateral nasal obstruction, nasal discharge, epistaxis, intranasal mass and hyposmia/anosmia. However, five patients had bilateral nasal obstruction and this may be due to the long duration of this disease (from 2.5yrs. to 29yrs.). Other associated symptoms observed were frontal headache, epiphora, eye-ache, diplopia, blurring of vision, cheek swelling, tinnitus and otalgia especially in the two patients that had evidence of malignancy.

In all cases, intranasal fleshy polypoidal masses were noted and these were visible in the anterior nares of nine patients. Bilaterality was seen in four patients. These include two patients with only I.P. (Fig. 1) and one (patient 12) with metachronous malignancy (Fig. 2), who had no evidence of septal erosion or perforation and another (patient 5) with synchronous malignancy who had an evidence of septal perforation. Recurrences were noted in four patients (patient 6 had four with evidence of dysplasia, two patients had three while the one with synchronous malignancy had five recurrences) before presentation at hospital.

Inverted papilloma was histologically confirmed in thirteen patients with evidence of dysplastic changes in one that had multiple recurrences. The remaining two patients who also had multiple recurrences later developed histologically confirmed synchronous and metachronous squamous cell

carcinoma of the last biopsies taken before this review respectively.

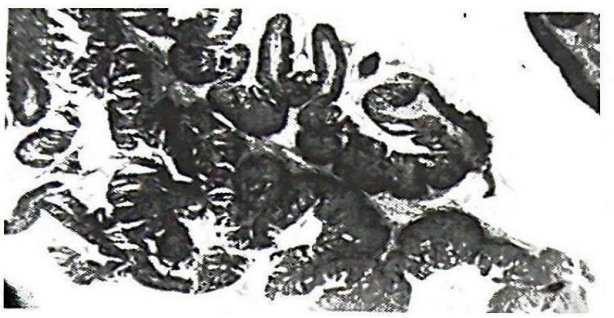

Fig.1: Benign papillary neoplasm displaying endophytic proliferation of metaplastic squamous cells (Haematoxylin and Eosin, x35)

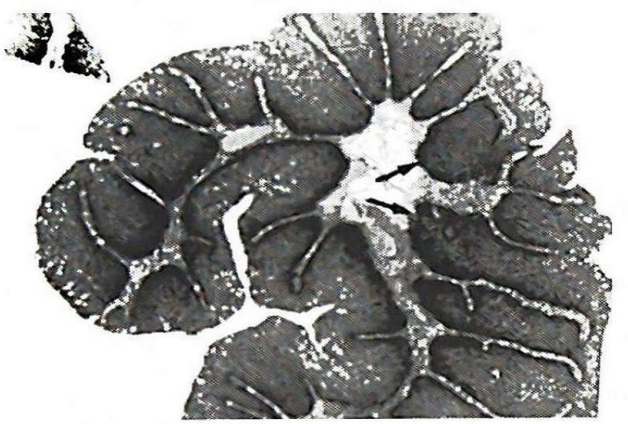

Fig. 2: Inverted papilloma with focal areas of stromal microinvasion by malignant squamous cells (arrowed) (Haematoxylin and Eosin, x35)

All the patients had plain radiograph of the sinuses and the commonest findings were soft tissue shadow within the nasal cavity and opacity of the maxillary, ethmoidal and frontal sinuses; while two showed destruction of the roof and the lateral wall of the maxillary sinus. Three patients had C. T. scan done and the major findings were soft tissue masses within the nasal cavity, maxillary, ethmoidal and spenoidal sinuses with erosion into the orbital cavity. There was associated destruction of the pterygoid plate/ramus of the mandible especially in one patient with synchronous malignancy.

Treatment

Six patients with limited intranasal masses had intranasal clearance /antrostomy. Those with extensive lesion had either external fronto-ethmoidectomy (3 patients) or lateral rhinotomy/ medial maxillectomy (2 patients) or combination of the surgeries (4 patients), especially for those that developed recurrence and malignancy at various times. In all, the origin of the tumour could not be assertained due to the extensive nature of the lesion except in two patients where it arose from the ethmoids and lateral wall of the nasal cavity. Adjunct radiotherapy and/or chemotherapy were offered to those with carcinoma.

Follow up/recurrence

Majority (9 patients) were lost to follow-up after three to four visits at three months interval, thus making it difficult to determine the recurrence rate in our patients. However, none of those that had radical surgery (lateral rhinotomy/medial maxillectomy) had any recurrence as at the time of this review except one that had synchronous carcinoma and another that had conservative surgery (within three and six months of follow-up respectively) while four patients including the one with dysplastic changes are presently on regular follow-up post-treatment without any evidence of recurrence. Minimum follow-up time being one year in these patients.

Discussion

Inverted papilloma (I.P.) is a relatively rare neoplasm of the nose and paranasal sinuses, but its features of aggresiveness, recurrence and the association with malignancy is worthy of note. Various aetiological factors had been advocated some of which are the role of allergy, chronic inflammation, environmental carcinogens and viral infections; but most of them remained unproven.

This lesion from our study has a male preponderance with a ratio of 4:1 which is comparable with those quoted in the literatures (i e. 2:1, 3:1 and 5:1) [1,7]. However, our sample size was very small compared with those in the early reports . I.P. could occur in all age groups as evident in its distribution in this review even though its peak incidence is noted between the fifth and sixth decades [8,9]. It has also been observed to be more common in the caucasians than other races in the world [10]. Late presentation is the major feature observed in this review with the minimum duration being nine months at first presentation, although this was within the quoted range of two months to twenty years in the literature [10,11].

It is a known fact that clinical evaluation may be unreliable because the clinical features of this neoplasm which are non-specific could mimic any other lesions like benign polyp, nasoantral or nasopharyngeal tumours [8]. However, the main presenting symptoms noted were mostly unilateral nasal obstruction, nasal discharge, epistaxis, hyposmia/anosmia and epiphora. Other recorded symptoms though negligible were headache, eyeache, cheek swelling, proptosis/blurred vision and otalgia especially in those that developed malignancy.

The lesion is mostly unilateral, but in this review three patients had bilateral involvement without any evidence of septal erosion or perforation. This is in contrast to the mechanism of direct spread through the nasal septum as noted by Weisslier and co-workers [7]. However, direct spread was only noted in a patient with synchronous carcinoma. This highlights the peculiarity of bilateral presentation of this tumour especially in our environment. Athough it may not be as common as the benign nasal polyps, there is need for further research into the aetiological and/or the predisposing factors responsible for the observed increase in the prevalence of this lesion in our patients.

Momose and co-workers concluded in their study that there were no specific findings on radiological evaluation pathognomic of inverted papilloma, since other disease state like chronic sinusitis, mucocele of the sinuses and other neoplasms could show similar features [12]. This was found to be true in this review. Although C.T. scan may be specific for delineating the extent of the lesion as well as a guide to the best

surgical approach to offer, the high cost involved limited its use in our patients. We therefore depended mostly on the clinical evaluation and high index of suspicion in the diagnosis of this lesion.

The tendency for malignancy arising either synchronously or metachronously ranges from 2 to 53%.[8]. This is the reason why all tissues obtained must be subjected to histological evaluation no matter how many times the biopsies were obtained. Diagnosis could be improved upon if multiple biopsies are taken from different sites particularly in an office set-up by using the nasal endoscope [8]. This could further help in early identification of those with synchronous or metachronous carcinoma and those with recurrence. However, this may not be feasible in our patients due to their late presentation at the hospital and the advanced nature of the lesion.

Some authors deduced inadequate surgical excision as being responsible for recurrence while others claimed this may be due to the multicentric/multifocal origin of this lesion [2,11]. However, surgery is still the mainstay of treatment having in mind the need for adequate exposure and complete excision of the lesion with very good functional result. This also helps to reduce the recurrence rate and possible malignant transformation from repeated excision. When available, endoscopic resection of I. P. is advantageous because of precise determination of tumour extent, preservation of normal mucosa and bony sructures and avoidance of external scars [13]. This is applicable in small lesions and may not be feasible in our environment where our patients present late with massive lesions.

Recurrence rate of 41 – 78% has been noted in patients offered conservative management while it is 0 – 29% in those offered radical surgery [11,14]. This is very difficult to assess in our patients since most of them were lost to follow-up after three to four visits post-surgery. However, it was observed in this review that the failure rate was high especially in those who had multiple surgeries with one developing recurrence within the first three months post-surgery. Whereas those offered radical surgery so far had no evidence of recurrence except one patient with synchronous carcinoma who had recurrence after six months. This showed the effectiveness of radical surgery in extirpating the lesion over conservative surgery as advocated by some authors [7-10,15].

Close endoscopic follow-up is advocated to ensure early recognition and treatment of recurrent diseases but when used indiscrimately may result in a high recurrence rate with the inexperienced surgeon [13]. Radical surgery is therefore recommended for patients in this environment. From the observed findings, it is pertinent to intimate any patient with inverted papilloma of the need before discharge from the wards for regular follow-up. This is to allow for early detection of any recurrence of the lesion or any malignant transformation especially in those with dysplastic changes histologically. However, their not showing up may be a pointer to the fact that these patients have remained disease free.

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