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Inverted papilloma: Incidence and late results of surgical treatment*

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SUMMARY

The 452,000 inhabitants of the County of Funen are considered to constitute a representative section of the population of Denmark. The county is geographically well-defined, surrounded by sea. Specimens from the two Departments of Pathology in the county have been histologically reviewed. Our incidence material consists of 96 patients suffering from inverted papillomas, during a 14-year period, which corresponds to 1.5 cases per 100,000 inhabitants per year. During the same 14-year period, 67 patients have been operated upon at the ENT Department of Odense University Hospital. In 1992, a clinical re-examination was performed regarding late surgical results. Fourteen per cent (9/67) have developed recurrences from 6 to 56 months after the first operation. No major late surgical complications have been observed. It is our experience that lesions limited to the nasal septum and minor lesions on the lateral nasal wall can be treated primarily by an intranasal procedure. Large lesions on the lateral wall with best results have been treated by lateral rhinotomy.

Key words: papilloma, incidence, treatment, results, surgery

INTRODUCTION

Inverted papilloma is a relatively rare benign tumour arising from the epithelium of the nasal cavity and paranasal sinuses. It has a local, aggressive growth, and may cause destruction of bone by erosion rather than by infiltration. A relatively high rate of local recurrences has been observed, and it is occasionally associated with squamous cell carcinoma. Inverted papilloma in the nasal cavity was first described by Ward (1854) and has to be differentiated from squamous cell papillomas of the nasal vestibule and inflammatory or allergic polyps. The most characteristic microscopical feature of inverted papilloma is the increased thickness of the covering epithelium, with extensive invasion of the underlying stroma. The name "inverted papilloma" is a descriptive term, referring to the histological impression that the surface epithelium inverts into the underlying stroma. Several synonyms are used, e.g. Schneiderian papilloma, Ewing's papilloma, transitional papilloma, and cylindrical cell papilloma. In general, inverting or inverted papilloma is widely accepted (Phillips et al., 1990).

The gross appearance of an inverted papilloma is a grey to red mass, often fairly large, and often of a firmer consistency than the inflammatory polyp. The difficulties in clinically distinguishing between inflammatory polyps and inverted papillomas have been pointed out (Weissler et al., 1986). On the septum the lesions have a tendency to develop a broad-based exophytic growth of smaller dimensions on the septum. The epithelial structural pattern is that of proliferation and metaplasia. The characteristic changes range from pseudostratified columnar, through true stratified columnar and transitional type, to completely metaplastic squamous cell epithelium. The basement membrane always remains intact. Hyams (1971) histologically classified inverted papillomas as inverted, fungiform, and cylindrical cell types. At present, it is widely accepted to use the term inverted papilloma for all the subgroups. The purpose of this investigation was to estimate the incidence of inverted papillomas in the County of Funen, a region representative for the whole of Denmark, and to evaluate where the patients suffering from inverted papillomas has been treated. Furthermore, the purpose was to make a clinical evaluation of late results after surgery at the ENT Department of Odense University Hospital.

AETIOLOGY

The aetiology of inverted papilloma is not known. Allergy, chronic inflammation, environmental toxins and viruses have

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been suggested as aetiological factors. Allergy does not seem to be a causative factor, as a positive history of allergy is not found to be common. Allergic polyposis is characteristically bilateral situated, whereas inverted papilloma usually is of unilateral appearance. Moreover, inverted papilloma does not respond to therapy directed against allergy. Inflammation of the nose and sinuses is a fearly common phenomenon, whereas inverted papilloma accures too rarely for us to be able to establish an etiologic relationship. Hyams (1971) found no evidence to relate inverted papilloma to local chronic inflammation or allergy. Phillips et al. (1990) and Majumdar and Beck (1984) found no correlation between occupational history and inverted papilloma in their study. The most popular theory describes a human papilloma virus to be involved in the development of the tumour. Viruses have been implicated owing to their well-known tendency to produce papillomas elsewhere in the body. Viral inclusion bodies in the stroma of inverted papillomas have been reported (Eggston and Wolff, 1947; Kusiak and Hudson, 1970), but Hyams (1971) was unable to demonstrate viral inclusion bodies and favoured a non-viral cause. Electron microscopical and immunohistochemical studies have failed to reveal virus particles or virus antigens (Furuta et al., 1991), except for one study (Syrjänen et al., 1982). Recently, molecular biology techniques have emerged to support a viral relationship. By using hybridization methods and polymerase chain reaction, several authors (Furuta et al., 1991; Weber et al., 1988; Syrjänen et al., 1987) have found human papilloma virus (HPV) type 6, 11, and 16 in the cells of inverted papilloma. Furthermore, both Syrjänen et al. (1987) and Furuta et al. (1991) developed the issue that HPV type 16 often is present in specimens where inverted papillomas were associated with squamous cell carcinomas. They formed the theory that HPV type 16 could be a high-risk virus regarding malignant coincidence.

INCIDENCE MATERIAL

All relevant archives at both Departments of Pathology in the County of Funen (Svendborg Hospital and Odense University Hospital) were consulted regarding the 14-year period, 1973–1986. Both departments preserve slides from all tissue examined. Specimens of all epithelial tumours from the nasal cavity and paranasal sinuses, except inflammatory polyps, were histologically reviewed. This served as our basis of incidence calculation. Nasal and paranasal specimens from 2,360 patients were re-examined at the Department of Pathology of Odense University Hospital, and inverted papilloma was found in 97 patients (3.4%).

INCIDENCE RESULTS

Ninety-six patients, 71 males (74%) and 25 females (26%) lived in the County of Funen at the time of diagnosis. Distribution by age and sex is shown in Figure 1. The median age was 56 years (range: 14–87 years). There was no associated malignant cases. Specimens from 81 patients were from the Department of Pathology in Odense, and 10 from the Department of Pathology in Svendborg. Five patients had contributed to specimens at both departments.

The County of Funen is an island which decisively strengthens the incidence calculation. The average population during the period in question was 452,000 (Poulsen et al., 1987). This corresponds to an incidence of 1.5 patients per 100,000 inhabitants per year. The male incidence was 2.3, and female incidence was 0.8. According to the requisition informations forwarded to both departments, the tissues were from 56 patients operated at the ENT Department of Odense University Hospital, and from 11 patients operated at the ENT Department of Svendborg Hospital. (There are two Departments of Pathology and two Departments of ENT in the County of Funen.) In the remaining 29 cases the tissues were exclusively from patients operated by private ENT-specialists. According to the information forwarded to the Departments of Pathology and according to the macroscopic description of the forwarded tissue, all tumours from the private ENT-specialists were small, requiring only limited intranasal procedures and operated in local anaesthesia.

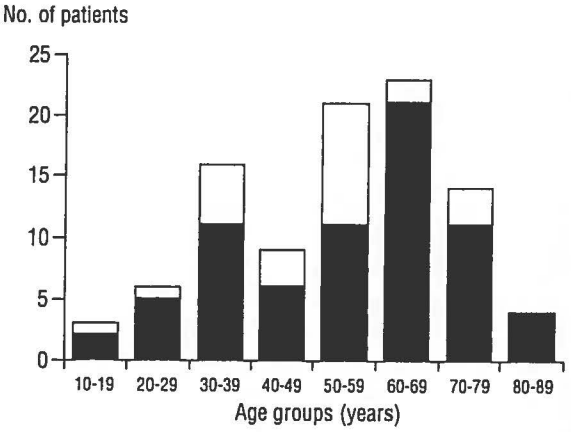

Figure 1. Incidence of inverted papilloma in the County of Funen. Distribution by age and sex (n=96). Open squares: females; closed squares: males.

SURGICAL MATERIAL

Archives from the ENT Department of Odense University Hospital showed that during the very same period, 1973-1986, the period for incidence calculation in the County of Funen, a total of 67 patients were operated upon for inverted papilloma at the ENT Department of Odense University Hospital. Fifty-six of these patients lived in the County of Funen and 11 were referred to the department from other counties. This served as our basis of surgical material. The median age in the surgical material was 58 years (range: 15-87 years); 49 males (73%) and 19 females (27%). Post-operatively, the patients were informed of the risk of recurrence and were recommended an annual check-up for the next five years by the ENT specialists.

In 1992, no less than five years after primary surgery, a clinical re-examination was performed. Thirty-three patients attended the re-examination including endoscopy as well as biopsy, when relevant. Fifteen patients, who had refused to attend the re-examination, answered a questionnaire, which revealed no symptoms of recurrence. Nineteen patients had died due to non-related diseases and without known recurrence. The follow-up time varied from one year to 18½ years, median 9

years and 4 months. The site of the lesions and the extent of the lesions are shown in Table 1.

Table 1. Location and extent of inverted papilloma in 67 patients indicated by single and cumulative anatomical locations.

	single (%)	cumulative (%)
lateral nasal wall and maxillary sinus	16 (24)	55 (82)
ethmoid sinus	0 (0)	19 (28)
frontal sinus	0 (0)	2 (3)
sphenoid sinus	0 (0)	2 (3)
septum	12 (18)	15 (22)

Symptoms

The symptoms at admission are shown in Table 2. None of the patients had bilateral symptoms. The median duration of symptoms was 6 months, range 1 month-25 years.

Table 2. Cumulative symptoms in relation to location of inverted papilloma.

	septum n=12 (%)	lateral wall n=55 (%)
obstruction	7 (58)	44 (80)
epistaxis	4 (33)	6 (11)
nasal discharge	1 (8)	16 (29)
crusting	2 (17)	2 (4)
facial pain	0 (0)	4 (7)
ear symptoms	1 (8)	3 (5)
sinusitis	0 (0)	1 (2)
occasional finding	3 (25)	5 (9)

X-ray findings

Prior to treatment 57 patients (85%) had radiology of their sinuses. Thirty-seven additionally had polytomography and in two a CT scan was performed. Eighty-nine per cent (51/57) had abnormal radiological findings, most often a unilateral mass in the nasal cavity and/or extension to the adjacent maxillary sinus. In 11% (6/57) the radiological investigation was normal; three of those patients had septal, and three had lateral wall lesions without sinus involvement.

METHODS AND RESULTS OF SURGERY

There were 12 patients with lesions limited to the nasal septum. Initially, they were all treated by limited intranasal excision. Two (17%) of the patients developed two recurrences at essentially the same location as the primary lesions. Both patients were followed for 3.5 and 10 years, respectively, and further recurrences were not found.

There were 55 patients with lesions on the lateral wall of the nose and/or the paranasal sinuses. Seven were treated by intranasal limited excision and 48 by an open procedure. The surgical technique and rate of recurrence are shown in Table 3. Seven (13%) of the patients with lesions on the lateral wall and/or the paranasal sinuses developed recurrence after the first surgical intervention; all essentially at the same location as the primary lesion. Five of these patients had one recurrence. One patient developed two recurrences. One patient was found to have developed five recurrences. The patient with five recurrences was primarily treated with lateral rhinotomy, medial maxillectomy, ethmoidectomy, sphenoidectomy as well as frontectomy. At the fifth operation recurrence was found on both sides and a lateral rhinotomy including medial wall maxillectomy, ethmoidectomy, sphenoidectomy and frontectomy were carried out. Four months later a new recurrence was found in both the frontal sinuses. Finally, the patient was treated by an endoscopic technique. He has now been without recurrence for 39 months.

Table 3. Location and surgical procedure in 55 patients with inverted papilloma on the lateral nasal wall. Number of patients with recurrences in brackets.

location/surgical procedure	initial treatment	treatment of recurrence
lateral nasal wall/intranasal limited excision	7 (3)	4
lateral nasal wall + 1 septum/ Caldwell-Luc + medial sinus wall surgery	1 (0)	0
lateral nasal wall + 3 maxillary sinuses + 3 ethmoid sinuses/ Caldwell-Luc + medial sinus wall surgery + ethmoidectomy	3 (0)	0
lateral nasal wall + 23 maxillary sinuses + 12 ethmoid sinuses + 2 septum/lateral rhinotomy + medial maxillectomy + ethmoidectomy	39 (3)	3
lateral nasal wall + 4 maxillary sinuses + 4 ethmoid sinuses + 2 frontal sinuses/lateral rhinotomy + medial maxillectomy + ethmoidectomy + frontectomy	5 (1)*	5

*: this patient developed five recurrences

The seven patients with small lesions on the lateral wall, primarily treated by limited intranasal excision, had developed three (45%) recurrences (Table 3). Two of these recurrences were treated by another intranasal excision and one by a lateral rhinotomy. No further recurrences were seen. The 48 patients with inverted papillomas on the lateral wall and/or paranasal sinuses were treated by an open procedure and four (8%) developed recurrences (Table 3).

Overall, nine (14%) recurrences were found after the first surgical procedure in 67 patients. The first recurrence was found 6–56 months after the primary operation (median: 36 months). The time between the first and the second recurrence was 4–43 months, with a median of 10 months. No correlation between main epithelial type and tendency of the recurrences was observed.

Complications

Per-operative exposure of the dura was noted in five cases. Four patients were treated by a free muscle transplant to close a small

perforation with CSF leak. In the last case a small area of dura exposure without perforation was left uncovered. On the second post-operative day, this patient produced CSF rhinorrhoea and developed meningitis which was successfully treated with antibiotics. The exposed dura was subsequently covered by a free muscle transplant. Yet, one patient developed post-operative meningitis, but recovered after antibiotic treatment. Five patients needed dacryocystorhinostomy owing to epiphora. There was no per- or post-operative mortality.

The patients were asked about cosmetic complaints. One patient developed alar retraction after lateral rhinotomy, which was later corrected at our department. One patient complained about minor web-formation near the medial canthus, and one patient had developed a minor retraction, corresponding to the resected nasal bone. None had essential cosmetic complaints.

Eleven patients complained of minor nasal crust-formation. Four of these patients had septal involvement, and one developed a septal perforation. In three cases oedematous tissue was found in the cavities. Biopsies only showed inflammation. No recurrences were seen at the follow-up. Complications such as diplopia, mucocele or fistula were not seen.

DISCUSSION

We have made a study dealing with the incidence of inverted papilloma over a 14-year period in the County of Funen, and a study of late results of surgery in the very same period at the ENT Department of Odense University Hospital. Odense University Hospital is a referral hospital and one of the two ENT Departments in the County of Funen. Owing to the conditions within the Danish health care system none of the patients have probably been treated outside the County of Funen, and no specimens have probably been histologically examined outside the County of Funen.

In the literature, the frequency of inverted papilloma is estimated to represent 0.4–4.7% of the surgically removed nasal tumours (Batsakis, 1980), in our study 3.4%. In the present report, the incidence of 1.5 cases per 100,000 inhabitants per year is relatively high. Buchwald et al. (1989) in their study from another Danish county stated an incidence of only 0.6 cases per 100,000 inhabitant per year, but only tissues from 600 patients were examined. Perhaps a more thorough investigational design for our study could explain the difference.

The mean age in our incidence study was 56 year, which corresponds to that reported in other studies. Also, the male predominance is in agreement with other studies (Lawson et al., 1989). There is no known cause of this difference. Majumdar and Beck (1984) found no correlation between occupational history and inverted papilloma.

The basic problem in treating inverted papilloma is the coincidence with squamous cell carcinoma and the tendency to recurrence. The coincidence rate between inverted papilloma and squamous cell carcinoma varies, from less than 2% to more than 53% (Lawson et al., 1989). The great variability probably reflects difficulties in distinguishing between atypia and malignancy (Batsakis, 1980; Weissler et al., 1986). Additionally, most of the reported studies are from referral centers, which are supposed to attract problem cases, and an overestimation of coincidence could be the result. This was also found in our study. None of the 96 patients with inverted papilloma in our incidence material from the County of Funen had associated squamous cell carcinoma. The only one patient with squamous cell carcinoma and associated inverted papilloma in our surgical material were referred to the ENT Department of Odense University Hospital from another county. The majority of recurrences occurred within three years, but tumours have been reported to reappear after more than 10 years. We observed no recurrence more than four years and seven months after treatment.

The reported recurrence rate of inverted papilloma ranges from 6-78%, and is related to the surgical technique and underestimation of the extent of the lesion (Cummings and Goodman, 1970). Fifty-five of our patients had lesions involving the lateral nasal wall. Eight per cent (4/48) had recurrence after open procedure, most often lateral rhinotomy. Fourty-three per cent (3/7) had one recurrence after intranasal excision, presumedly because of underestimation of the extent of the lesion. Cummings and Goodman (1970) reported a 13% recurrence rate after lateral rhinotomy, compared to a 73% recurrence rate after more conservative transnasal procedures. During recent years we have employed endoscopic surgery, when the tumour could be visualized sufficiently, otherwise lateral rhinotomy was performed. Waitz and Wigand (1992) published a series of patients with inverted papilloma, treated endoscopically. They found recurrence in 17% (6/35) after at least a 1-year observation period (mean 46 months).

Our incidence study has shown that over a 14-year period 96 patients with inverted papillomas were diagnosed, all living in the County of Funen. As part of our incidence study we discovered that many patients (29 out of 96) have been managed exclusively outside hospitals with small intranasal procedures. Our surgical material showed that in the very same 14-year period, 56 patients from the County of Funen, and a further 11 patients with extended lesions referred from counties outside Funen have been operated at the ENT department in Odense. It is clearly seen that a referral hospital as Odense University Hospital have attracted patients with extended lesions. This means in every case in our study that clinical material from a referral hospital does not reflect the real severity of inverted papilloma. The same could be true for other reports. Our study showed that septal lesions could be managed by limited intranasal excisions. Lesions on the lateral nasal wall should be managed depending on their extent, judged by endoscopic examination and /or a CT scan. Minor lesions on the lateral nasal wall could be managed by intranasal procedures. Larger lesions have been treated in our study with best results by lateral rhinotomy.

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