Pathophysiology of sinonasal polyps

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R4

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The commonest benign nasal mass (70%)

mostly are benign semitransparent nasal lesions, pink to pearly white, that arise from the mucosa of the nasal cavity or from one or more of the paranasal sinuses, often at the outflow tract of the sinuses, connected to normal mucosa with a flaccid crus
- Can be single or multiple, unilateral or bilateral
- Antrochoanal vs Ethmoidal
- Antrochoanal polyp
  - Solitary
  - Arises from maxillary antrum
  - Has three components
  - Common in young adolescents

- Ethmoidal polyp
  - Multiple
  - Arises from ethmoidal sinus
  - Has only one component
  - Common in adults / elderly
The following conditions are associated with multiple benign polyps:

- Bronchial asthma – In 20–50% of patients with polyps
- CF – Polyps in 6–48% of patients with CF
- Allergic rhinitis
- AFS – Polyps in 85% of patients with AFS
- Chronic rhinosinusitis
- Primary ciliary dyskinesia
- Nonallergic rhinitis with eosinophilia syndrome (NARES) – Nasal polyps in 20% of patients with NARES
- Aspirin intolerance – In 8–26% of patients with polyps
- Alcohol intolerance – In 50% of patients with nasal polyps
The overall incidence of nasal polyps in children is 0.1%;
Among adults, the incidence is 1–4% overall
Causes life affecting symptomatology (usually NO epistaxis)
❖ GALEN study
Etiopathogenesis of nasal polyps

Chojnowska S.1*, Kępka A.2, Waszkiewicz N.3, Kołodziejczyk ZP.4, Konarzewska-Duchnowska E.5, Ościłowicz K.4, Cabaj-Wiater I.6, Sowizdraniuk J.7, Dziecioł J.8, Ładny JR.5, Zwierz K.4, Szajda SD.5
Etiology

- Mainly by damage to nasal mucosa epithelium (infection, irritant subs.. )
INFECTION FACTOR → GM-CSF → MACROPHAGE → TISSUE DAMAGE → POLYP

UNINFECTION FACTOR → GM-CSF → NEUTROPHIL → SECONDARY INTENT → EDEMA

LYMPHOCYTE → IL-6 → EDEMA

GROWTH FACTORS → MEDIATORS → TISSUE DAMAGE

MEDIATORS → EDEMA
Theories of polyp formation

- *Polyps as an allergic reaction theory (1970)*
  - **Supports it:**
    - Edema and eosinophiles
  - **Locally produced IgE**
  - **Contradicts it:**
    - 5% of patients with allergic symptoms have polyps, EXCEPT FOR AFRS (85%)
  - In patients with CRS, reaction to fungal antigens is IgE INDEPENDENT
Polyps as a stage of long term development of non allergic rhinitis with eosinophilic syndrome (NARES) theory:

- 1 – eosinophiles migrate to mucosa
- 2 – accumulation
- 3 – polyps form

Doubts it:
- Only 30–40% of pts with NARES have polyps
Polyps as a stage of chronic hyperplastic sinusitis development theory:

- Chronic hyperplastic sinusitis is accompanied by large local and peripheral eosinophilosis.
- **Confirms it:**
  - in polyp's tissue, interleukin 5 (Il-5) has been observed, enabling the migration of eosinophiles to mucosa.
  - Il-5 is responsible for BA in patients with chronic hyperplastic sinusitis (accumulation of eosinophiles in pulmonary tissue)
Polyps as a stage of inflammatory bioelectric changes development theory (Bernstein & Yankaska 1994):

- Turbulent air flow >> inflammation >> ulceration of mucosa >> electrical changes of Na and Cl channels
- Impaired (incl.) Cl secretion, increased Na & water reabsorption intracellularly & interstitially
- Altered mucosal composition >> thickening >> altered ciliary function
- Edema >> polyps
Confirms it:

- Polyp epithelium has more ability to reabsorb Na and more Cl secretion than normal chonchal mucosa.
- Impaired CFTR (cystic fibrosis transmembrane regulator) observed in CF pts, leads to polyp formation (50%)
Polyps as a neoplastic process (fritz 2003):

- **Confirms it**
  - Discovered mamoglobin in polyp epithelium, which is also found in some neoplasms (e.g. breast). It is a steroid binding inflammatory modulator.
  - Gene for glutathione transferase (bladder, lung, ovaries, prostate CA)
De Castro, Chemotherapeutic agents (mitomycin) administered locally, showed good results in nasal polyp tx.

- Low antioxidant levels in nasal polyp pts. (Olzewski)
- Low lysosomal exoglycosidases in nasal polyps (bosmann, Kim)
Polyps as a result of dysfunctional epithelial barriers

- Occludin, zonula occludin 1 protein, E-cadherin are reduced in polyp epithelium
- Allowing more proteases from infective agents to pass
Figure 1: Expression of tight junction molecules in patients with CRSwNP in comparison to healthy people (inferior turbinate): significantly reduced expression leading to weak epithelial barrier in CRSwNP.
Genetics?
- study population consisted of 275 patients with CRSwNP and 338 patients with CRSsNP as well as a series of controls from a publicly available database.

Table 1: List of SNPs that were associated with CRS in former publications and that could be replicated in our investigations. The more those associations are confirmed in other cohort, the more probable is their significance [12].

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNP ID</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>PARS2</td>
<td>rs2873551</td>
<td>0.77 (0.70–0.84)</td>
</tr>
<tr>
<td>TGFB1</td>
<td>rs1800469</td>
<td>0.81 (0.74–0.89)</td>
</tr>
<tr>
<td>NOS1</td>
<td>rs1483757</td>
<td>0.84 (0.77–0.91)</td>
</tr>
<tr>
<td>NOS1AP</td>
<td>rs4657164</td>
<td>0.79 (0.70–0.89)</td>
</tr>
<tr>
<td>IL22RA1</td>
<td>rs11579657</td>
<td>1.21 (1.13–1.30)</td>
</tr>
<tr>
<td>DCBLD2</td>
<td>rs828618</td>
<td>1.18 (1.10–1.25)</td>
</tr>
<tr>
<td>ALOX5AP</td>
<td>rs17238773</td>
<td>0.75 (0.62–0.89)</td>
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No general consensus upon etiology of nasal polyps
Most support is for bioelectric and neoplastic theory
Probably no single homogenous etiology for polyposis (multi co-existing mechanisms)
Asymmetric dimethylarginine levels in allergic rhinitis and nasal polyposis

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Aim: Asymmetric dimethylarginine (ADMA) is the major endogenous inhibitor of nitric oxide synthase. We aimed to investigate the ADMA levels in allergic rhinitis (AR) and nasal polyposis (NP).

Materials and methods: A total of 29 AR patients, 21 NP patients, and 30 healthy subjects to be used as a control group were enrolled in the study. ADMA was measured in the AR, NP, and control groups with enzyme-linked immunosorbent assay. Any patients or control subjects with coronary artery disease, renal failure, diabetes mellitus, or hypertension were excluded from the study.

Results: The mean ADMA serum concentration was 0.52 ± 0.08 μmol/L in the AR group, 0.62 ± 0.10 μmol/L in the NP group, and 0.67 ± 0.09 μmol/L in the control group. The ADMA serum concentration in the AR group was significantly lower than in the control group (P < 0.001). Considered together, the NP and AR groups had ADMA levels that were significantly lower than in the control group (P < 0.001).

Conclusion: In the present study, lower ADMA levels were found in the AR and NP groups.
ADMA (asymmetric dimethylarginine): NOS inh.

29 AR pts, 21 NP pts, 30 healthy

Method: ADMA measured with enzyme linked immunosorbent essay

Conclusion: ADMA is lower in pts with AR & NP than normal population
STUDY OF EOSINOPHIL INFILTRATION IN NASAL POLYP

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ABSTRACT: Polyps of the nasal cavity and paranasal sinuses are hypertrophied, oedematous mucosa. Nasal polyps can be broadly divided into two groups, bilateral nasal polyposis & Ochronal polyp (ACP). They are infiltrated with cells including, eosinophils, mast cells, lymphocytes and plasma cells. The study was aimed to evaluate the varying degree of eosinophil infiltration and to determine the significance of the infiltration of eosinophils. Out of total 50 cases (30 male & 20 female) 38 cases (76%) had bilateral polyposis and 14 cases (28%) had antrochoanal polyps. Infiltration of eosinophil in both types of polyps was found to be statistically significant (p < 0.05). Median value of number of eosinophils/HPF in B/L polyposis was 40 and in ACP it was 11. Difference in number of eosinophils/HPF among B/L polyposis and ACP found to be statistically significant (p = < 0.05). From the above context we can say eosinophil infiltration in local tissue may play an important role in the pathogenesis of bilateral nasal polyposis. So the use of anti-inflammatory agents should logically from the medicine of choice in bilateral nasal polyps.
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Pathophysiology of chronic rhinosinusitis, pharmaceutical therapy options

Claus Bachert*1,2 and Gabrièle Holtappels1

Abstract

Research in immunology has brought great progress in knowledge of inflammatory processes in the last 2 decades, which also has an impact on the upper airways. Our understanding of the pathophysiology of chronic rhinosinusitis developed from a rather mechanistic point of view with a focus on narrow clefts and...
Recurrence after surgery

- Studies showed inc. rate of recurrence in patients whom nasal polyps showed inc. expression of total IgE, SE-IgE, and IL-5 at first surgery
<table>
<thead>
<tr>
<th>Endotype</th>
<th>Clinic</th>
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<tbody>
<tr>
<td>Non-inflammatory endotype</td>
<td>90% of CRSsNP, asthma in &lt;20%</td>
</tr>
<tr>
<td>Neutrophil endotype</td>
<td>70% of CRSsNP, asthma in &lt;20%</td>
</tr>
<tr>
<td>Mainly eosinophilic endotype; increased IL-5, ECP, IgE, and albumin</td>
<td>70% of CRSwNP, asthma in 20–40%</td>
</tr>
<tr>
<td>Clearly eosinophilic/SE-IgE endotype: much increased IL-5, IgE, ECP,</td>
<td>&gt;90% of CRSwNP, asthma in &gt;60%</td>
</tr>
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<td>and albumin with SE-IgE positivity</td>
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Histologic structure of antrochoanal polyps.

Min YG, Chung JW, Shin JS, Chi JG

Abstract
The antrochoanal polyp (ACP) is defined as a maxillary sinus polyp that originates in the maxillary sinus, passes through the sinus ostia, and extends into the choana. The aim of this study was to compare the histologic findings of 40 cases of ACP with those of allergic and non-allergic nasal polyps, and so possibly to elucidate the pathogenesis of ACP. No allergy could be verified in any of the ACP patients. Inflammatory cell infiltration was significantly more severe in the ACP group than in the allergic polyp group. Eosinophilic infiltration was significantly less severe in the ACP group than in the allergic polyp group. Edema was not significantly different between the ACP, allergic, and non-allergic groups. In the ACP group, the presence of submucous glands was significantly less pronounced than in the ordinary nasal polyp groups. The fibrous type was present significantly more often than the infiltrative or granulating type in the ACP group. The histologic findings and clinical features of the ACP indicate that it has little causal relationship with nasal allergy but is all the more intimately associated with inflammatory processes. The paucity of submucous glands suggests that the ACP results from edematous hypertrophy of the respiratory epithelium rather than from distension of the glandular structures.

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THANK YOU