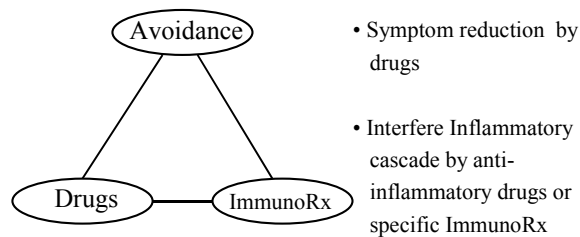


비염과 부비동염의 증례 토의

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동 헌 종

Treatment Strategy of AR



Treatment Options

- H1-antihistamine : oral, intranasal
- Glucocorticosteroid : intranasal, systemic
- Decongestant: oral, intranasal
- Cromones
- Anti-cholinergic
- Anti-leukotrienes
- Immunotherapy
- Surgery

증례 1

- 만성간염을 앓고 있는 48세된 남자가 2주전 부터 시작된 재채기와 맑은 콧물을 주소로 병원을 방문하였다. 증상은 가을철 환절기에 발생하며 생활이 불편할 정도는 아니었다.
- 비내시경소견은 다음과 같았으며 피부반응검사상 ragweed 에 (+++) 보였다. 이 환자의 적절한 치료는?



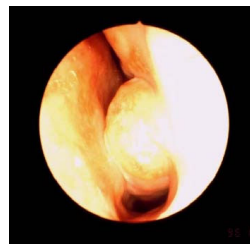
증례 2

- 7세된 아동이 코막힘을 주소로 병원을 방문하였다. 물처럼 맑은 콧물을 흘리고 심한 소양감을 호소하였다. 증상은 매년 봄에 세달간 지속되었다.
- 비내시경소견은 다음과 같았으며 단순방사선검사는 정상소견을 보였다. 피부반응검사상 검사상 grass, tree pollen에 (++++를 보였다. 이 환자의 적절한 치료는?



증례 3

- 24세된 남자환자가 가 2달 이상 지속된 코막힘을 주소로 병원을 방문하였다. 평상시에도 입으로 호흡하는 경우가 많았으며 환절기에 발생하는 천명을 호소하였다. 재채기를 발작적으로 하며 물처럼 맑은 콧물을 불편할 정도로 흘렸다.
- 비내시경소견은 다음과 같았으며 단순방사선검사상 상악동에 일부 혼탁이 관찰되었고 RAST 검사상 Der p(+++), Der f(+++) 보였다. 이 환자의 적절한 치료는?



New Classification of AR: ARIA

(*Allergic Rhinitis and its Impact on Asthma*)

Intermittent

- Less than 4 days a week
- Or for less than 4 weeks

Persistent

- More than 4 days a week
- And for more than 4 weeks

New Classification of AR: Severity-ARIA

Mild

- No troublesome symptoms or disturbance of :
 - Sleep
 - Daily activities, leisure and/or sport
 - School or work activities

Moderate-severe

- There are troublesome symptoms and disturbance of:
 - Sleep
 - Daily activities, leisure and/or sport
 - School or work activities

Mild Intermittent Disease

- Oral or intranasal H1-antiHst
- Intranasal decongestant
 - For less than 10 days, not to be repeated more than twice a month
- Oral decongestant
 - not usually recommended in children

Mild Persistent Disease

- Oral or intranasal H1-antiHst
- Oral antiHst and decongestant
- Intranasal glucocorticoid
- Cromones / Anti-leukotrienes
- Intramuscular/intranasal injection of steroid :not recommended
- Reassessment after 2-4 weeks
 - Sx-free or less Sx: Continue Tx with reduced dosage
 - Mild persistent Sx using antiHst→use topical steroid
 - Moderate-severe Sx: step-up
 - Severe and uncontrolled Sx: consider ImmunoRx

Moderate/Severe Intermittent Disease

- Oral or intranasal H1-antiHst
- Oral antiHst and decongestant
- Intranasal glucocorticoid
 - Efficacy of short and repetitive courses not demonstrated by publication
- Cromones / Anti-leukotrienes
- Intramuscular/intranasal injection of steroid :not recommended

Moderate/Severe Persistent Disease

- Intranasal steroid: first-line Tx
- If severe obstruction:
 - oral steroid, topical decongestant(<10 days)
- Reassessment after 2-4 weeks
 - No improvement: consider reason for failure
 - Itch/sneeze : add H1-blocker
 - Rhinorrhea : add ipratropium
 - Blockage : increase topical steroid
add decongestant or short term oral steroid
 - Structural problem : surgery
 - Improvement: set down to mild persistent disease
 - Tx last for at least 3 months or for the duration of pollen season

Oral Antihistamines (I)

- Histamine: major mediator involved in development of AR
- Role of histamine : reproduce nasal symptom after provocation with histamine
- Symptom can be reduced by H₁-antagonists
- H₁-receptor antagonists reduce itching, sneezing and rhinorrhea
- Effective in non-nasal symptom: conjunctivitis, urticaria

First-generation Oral Antihistamines

- Phenbenzamine in 1942
- Unwanted effect
 - Sedation
 - Anticholinergic effect
- Short half-life

<div> <div>1.3.2</div> <div>국·내에서 판매되고 있는 1세대 항히스타민제의 보통명과 상품명</div> </div>	
Generic name	Trade name
Brompheniramine	브로 모펜 (장인)
Budione	보지논 (유씨비), 부크진 (대웅)
Chlorpheniramine	클로라민 (대웅), 알레르제인스클로비테라민 (장성) 다오리진 (삼아), 메타도라민 (한미약품), 세르비 (금강) 세라리 (금강), 메타스도라민 (건일), 이레민 (한성) 안티타민 (일성), 알레타민 (대웅), 오로친 (유아), 타오친 (크라운)
Clemastine	클레마스틴 (제), 레카솔 (유아), 클스틴 (대웅) 테베르 (한인), 열풍모프리스클레르스틴 (한일통) 미베 (대웅), 타베콜 (한진), 비타스 (주)
Cyproheptadine	사이프로헵타딘 (제), 사이프로 (본초)
Hydroxyzine	히드록시 (유씨비), 히포크스틴 (대웅), 시드엑스 (유아), 히타드 아디드메진, 헐렉스 (에이치제), 프진 (대웅), 뉴비루메 (셀마)
Megastadine	메가스타민 (한성), 대해메가스타민 (대웅), 메카진 (동구) 프라이마 (주), 히스 (한진), 메카스타민 (제) 아라 (한진), 브리콜 (성진), 코라공 (유아), 크로공 (수도)
Piprinhydrate	파인 (유씨비약품)
Pheniramine maleate	페니라민 (유씨제약),
Promethazine	메라진 (유씨제약),

Newer Antihistamines

1.4 국제에서 사용되고 있는 2세대 항생소분제		
Generic name	Trade name	용량, 용법
Aztreonam	제트렐름 GSO (경)	12세 이상 아동 성량: 1T tid
Azoxime	제프록시름 (경)	Azoxime HD 1mg 1T tid
Cefazolin	세파록시름 (경), 게스톨 (주) 노스판트린 (주), 제비도 (주) 노스판트린 (주), 신대우 (주) 제비도 (주), 제비도 (주), 노리드 (주) 세비도 (주), 제비도 (주) 세비도 (주), 제비도 (주) 제비도 (주), 제비도 (주) 제비도 (주), 제비도 (주)	Cefazolin 10-12mg 6세 이상 아동 및 성인 1T tid 구토: 4회까지
Ebastine	에바스티름 (경)	Ebastine 10 mg 성량 12세 이상 6-14T 1T tid
Emedastine	에메다스틴 (경)	Emedastine 1mg 12-14T tid
Ebastine	에바스티름 (경)	Ebastine 10 mg 12-14T tid
Fexofenadine	페코펜 (경)	Fexofenadine 120mg 12세 이상 아동 성량: 1T tid
Fexofenadine	페코펜 (경)	Fexofenadine 120mg 12세 이상 아동 성량: 1T tid
Fexofenadine	페코펜 (경)	Fexofenadine 120mg 12세 이상 아동 성량: 1T tid

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Efficacy of Oral Antihistamines

Newer antihistamine

- Acrivastine, (astemizole*), azelastine, cetirizine, ebastine, fexofenadine, loratadine, mizolastine, (terfenadine*)
- Effective in reducing itching, sneezing, discharge
- Less effective on nasal blockage
- Rapid onset(1~2hr), long duration(24h)
- Anti-allergic effect

Safety of Oral Antihistamines

CNS side effect

- Sedation, CNS depression
- Potentiated by alcohol
- Greater risk in elderly patients
- New generation antiHst
 - Decreased lipophilicity
 - Reduced affinity for CNS histamine receptors

Safety of Oral Antihistamines

Cardiac side effect

- Metabolized by cytochrome P450 in liver
- Antifungal agent, Macrolide antibiotics
- Grapefruit juice
- Interfere with cardiac repolarization cycle→QT prolongation, serious cardiac arrhythmia
- Acrivastine, astemizole, ebastine, loratadine, terfenadine
- Fexofenadine, cetirizine, mizolastine: poorly metabolized in liver

Safety of Oral Antihistamines

Other side effect

- Anti-cholinergic effect: older compound
- Cyproheptadine, ketotifen, astemizole: appetite stimulation and weight gain
- Adrenergic effect by α -adrenergic receptor blocking: promethazine
- GI disturbance: some of ethylenediamine class
- Antihistamine plus decongestants
 - cause insomnia and nervousness
 - esp, children and elderly persons

Oral Antihistamines

Recommendations (A)

- Second generation antihistamines can be considered first-choice treatment for intermittent or mild persistent AR
- Long-term use is preferable to “on demand” regimen, especially in persistent disease d/t anti-allergic activities
- Once daily are preferred, recommended dosages should not be exceeded
- Troublesome nasal blockage in PAR : intranasal steroid should be added

Topical Antihistamines



Topical Antihistamines (I)

- Limited to the target organ
- Do not show any significant side effect
- Effective and highly specific H₁-receptor antagonist
- Prompt relief for itching and sneezing(15 minutes)
- When BID regularly, prevent onset of symptom
- In DB-PC studies, effective in SAR and PAR

Topical Antihistamines

- Effective in children
- Long-term continuous treatment is more effective than “on demand” regimen
- More rapidly effective than beclomethasone, but less potent
- Effective on nasal obstruction to less extent than intranasal steroid
- Short-lasting perversion of taste: azelastine

Topical Antihistamines

Recommendations (A)

- Rapid onset of action(<15min) at low drug dosage
- Act only on treated organ
- Usually require BID to maintain satisfactory clinical effect
- Recommended for mild organ-limited disease, as “on demand” medication in conjunction with continuous one

Intranasal Decongestants(I)

Efficacy

- In short term, very effective for nasal obstruction in allergic & non allergic rhinitis
- Local vasoconstriction occurs within 10 minutes
- Last for less than 1 hr for epinephrine
- Long-lasting effect of oxymetazoline, xylometazoline
- No improvement of itching, sneezing, rhinorrhea
- Prophylaxis before air traveling

Intranasal Decongestants(I)

Safety

- Nasal burning, stinging, dryness, mucosal ulceration, septal perforation may occur
- Prolonged use(>10days) induces tachyphylaxis
 - Rebound swelling, rhinitis medicamentosa(RM)
 - Functional and morphological alteration
 - Oxy- and xylometazoline : less small risk of RM
 - Tx: (avoid topical decongestant) + (topical steroid)
- Intranasal S/E from benzalkonium chloride

Oral Decongestants(I)

Efficacy

- Ephedrine, phenylephrine, pseudoephedrine
- Weaker effect on obstruction than topical decongestant
- No rebound vasodilatation
- No effect on other rhinitis symptoms
- Effect occurs within 30 minutes, last for 6 hrs(8-24 hrs with sustained release formulation)

Oral Decongestants(I)

Safety

- Less effective than sprays: no rhinitis medicamentosa
- Commonly irritability, dizziness, headaches, tremor, insomnia
- Tachycardia, esp in pregnant women
- Hypertension may occur
- In pregnant, transfer to fetus via systemic circulation
- Usually avoided in:
children < 1 year, pregnancy, hypertension, cardiopathy, prostatism, glaucoma, hyperthyroidism

Decongestants

Recommendation(A)

- Limited duration(<10 days)
- Short course of topical decongestant: prompt reduce severe blockage
- Narrow range between Rxtic and toxic doses
- Advised not to prescribe to elderly person, pregnant women, cardiovascular disease, hyperthyroidism, BPH, glaucoma, psychiatric disorder, β -blocker or MAO inhibitor users

Topical Corticosteroids

- Suppress many stages of allergic inflammatory process
- Strong anti-inflammatory capacity in reducing cytokine, chemokine release
- Decrease cellular infiltration of antigen-presenting cells, T cells, eosinophils within the nasal mucosa (lesser reduce mast cells)

표 1 국내에서 시판되는 대표적인 국소 스테로이드제 (스프레이)

약물명	상표명 및 회사명	의약품상 용량	사용량
Betamethasone dipropionate	비코나아제 코약 (글락소스미스클라인) Deconase nasal spray	42 μ g	12세 이상 소아: 비강강 1분부, 1일 2회
Flunisolide hemihydrate	나살라이드 비분무제 (한국보신) Nasalide	25 μ g	6~14세: 비강강 1분부, 1일 2회 또는 비강강 2분부, 1일 2회
Budesonide	몰비코프 비약 (한국아스트로제네카) 올콕무네스비어드 비약 (온코제카) Budecortid nasal spray	50 μ g	6~12세: 비강강 1분부, 1일 2회 또는 비강강 2분부, 1일 1회 12세 이상: 비강강 2분부, 1일 2회 또는 비강강 1분부, 1일 1회 12세 이하 소아: 비강강 1분부, 1일 2회 또는 비강강 2분부, 1일 1회
Desonase	데소나비약 (한일제약) Desono nasal spray	50 μ g	12세 이상: 비강강 2분부, 1일 2회 또는 비강강 1분부, 1일 1회 12세 이하 소아: 비강강 1분부, 1일 2회 또는 비강강 2분부, 1일 1회
Nasacort	나사코트 점비약 (산신당제약) Narta nasal spray	50 μ g	12세 이상: 비강강 2분부, 1일 2회 또는 비강강 1분부, 1일 1회 12세 이하 소아: 비강강 1분부, 1일 2회 또는 비강강 2분부, 1일 1회
Fluticasone propionate	푸릭소나제 코약 (글락소스미스클라인) Fluonase nasal spray	50 μ g	12세 이상: 비강강 2분부, 1일 1회 4~11세: 비강강 1분부, 1일 1회
Triamcinolone acetonide	나사코트 점비약 (한일제약) Nasacort nasal inhaler Nasacort AQ	55 μ g	12세 이상: 비강강 2분부, 1일 1회 (5~11세: 비강강 1분부) 5~11세: 비강강 2분부, 1일 1회 12세 이상: 비강강 2분부, 1일 1회
Mometasone furoate	나코프루스나장스프레이 (유한양행 Schering-Plough) Nasonex nasal spray	50 μ g	12세 이상: 비강강 2분부, 1일 1회 3~11세: 비강강 1분부, 1일 1회

Topical Corticosteroids(I)

- First-line Rx for adults in moderate to severe cases of SAR and PAR
- Most potent medication for Rx of AR and non-AR
- Regular prophylactic use is effective in reducing nasal blockage, rhinorrhea, sneezing, itching in adults and in children
- More effective than systemic antiHst, topical antiHst, topical cromoglycate
- Slower onset of action than H1-antiHst (<12 hrs)
- Maximum efficacy (>days and weeks)
- OD is sufficient

Safety of Topical Corticosteroid(I)

Local side effect

- From freon-propelled aerosol to mechanical aqueous pump or dry powder
- Well tolerated and used on a long-term basis without mucosal atrophy
- Occasionally crusting, dryness, minor epistaxis
- More rarely: septal perforation d/t prolonged use
 - Greatest during first 12 months, esp. young women

Safety of Topical Corticosteroid

Systemic side effect

- Swallowed portion(80-90% of inhaled dose) is deactivated in liver before reaching systemic circulation
- No effect on HPA axis except dexamethasone spray and beclomethasone drops
- Adverse effect on children's growth by beclomethasone in one study
- Inhaled route: skin thinning, cataract formation, glaucoma, metabolic change, behavioral abnormalities
 - However, absent these S/E in intranasal route only

Topical Corticosteroid

Failure to respond

- Inadequate compliance
- Nasal obstruction preventing drug delivery
- Additional nasal pathology (sinusitis, polyps)
- Heavy persistent allergen exposure
- Patient (or doctor) misunderstanding the dose and frequency of administration
- Wrong diagnosis



Topical Corticosteroid

Recommendations(A)

- Highly effective first-line treatment in AR with moderate to severe and/or persistent symptoms
- Effect on nasal blockage and anti-inflammatory properties is better than other treatments
- Relatively slow onset of action (12h), maximum efficacy over days and weeks

Systemic Corticosteroid

- Not the first line of treatment for AR
- Relatively few scientific data available
- Lack of comparative studies on the dosage, route of administration, dose-response relationship
 - oral (pd 20-40mg/day), depot injection (methylpd 40-80mg/injection)
- Effective on most symptoms of rhinitis
 - esp. obstruction and smell dysfunction

Safety of Systemic Corticosteroid

- Risk of S/E depends on duration of Tx
- Intranasal depot injection into turbinates or polyps should be avoided
- Continuous release of injected depot will suppress HPAA more
- ContraIx
 - Glaucoma, DM, herpes keratitis, psychological instability, osteoporosis, severe HT, Tbc, chronic infection

Systemic Corticosteroid

Recommendations

- Not used as first-choice treatment
- Severe symptoms refractory to other treatment
- Short course(<3weeks) can be prescribed
- Can be repeated every 3 months
- Pd tablets in the morning during troublesome periods following pollen count
- Avoid in children, pregnant women, patients with known contraindications

Leukotriene Receptor Antagonist

- Cysteinyl leukotrienes (LTC₄, LTD₄, LTE₄)
 - Important mediator of nasal allergic reaction induces nasal obstruction
- Pranlukast, Montelukast, Zafirlukast
- Ineffective alone
- May have additive effect with antihistamines
- May be effective in aspirin-induced rhinitis and asthma

Cromones

- Disodium cromoglycate, Sodium nedocromil
- Inhibit nasal connective tissue mast cell
 - Blockage of Cl^- channels on mast cell membrane
 - Phosphodiesterase inhibition
 - Blockage oxidative phosphorylation
- DSCG inhibit IL-4 induced IgE synthesis

Efficacy of Cromones(I)

- DSCG 4 times daily(DB-PC): effective in Tx & prophylaxis in SAR and PAR in some but not all studies
- Sneezing, rhinorrhea, itching >> obstruction
- Ineffective in non-allergic, non-infectious rhinitis
- Less effective than oral or intranasal antiHst or intranasal glucocorticosteroid in adults and children
- Combined Rx of nedocromil+astemizole: more effective than H1-antiHst alone
- Rapid efficacy of nedocromil

Safety of Cromones

- Not absorbed through nasal surfaces
- Swallowed portion is poorly absorbed from GI tract and excreted in feces
- No teratogenic effect in animal study

Cromones

Recommendations(A)

- Not a major Rx option in adults AR
- Valuable one for Tx of allergic conjunctivitis
- Recommended in children, pregnant women
- DSCG 4 times daily: effective in AR and conjunctivitis, although less effective than H1-antiHst or topical steroid
- Nedocromil BID also effective in AR and conjunctivitis

Topical anti-Cholinergics

- Ipratropium bromide
- Parasympathetic stimulation cause watery secretion via acetylcholine, vasodilatation of vessels serving glands
- Recommended daily dose (120-320µg) in 3 to 6 administration
- Poorly absorbed by nasal mucosa
- Do not cross BBB

Topical anti-Cholinergics

Efficacy

- Effective in watery rhinorrhea in allergic and non-allergic rhinitis
- Not affect sneezing, obstruction
- Effective in common cold, gustatory rhinitis, rhinitis in elderly person
- Fast onset (15-30 min)
- No tolerance develop
- Combination with terfenadine is more effective than terfenadine alone

Topical anti-Cholinergics

Safety

- Topical S/E is uncommon
- Usually dose-dependant
- Nasal dryness, irritation, burning, followed by stuffy nose, dry mouth, HA,
- Do not affect ciliary beat, olfaction, and clinical appearance of nasal mucosa
- Systemic bioavailability of ipratropium: 10%
- Systemic S/E: rare until 400µg/day

Topical anti-Cholinergics

Recommendation

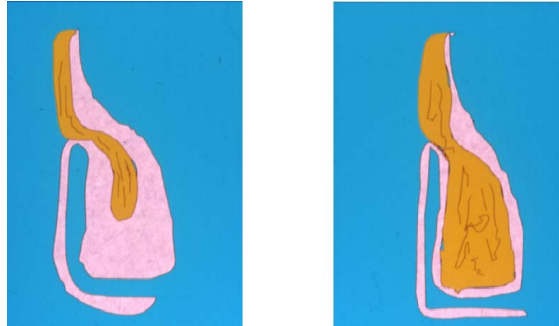
- Only improve nasal hypersecretion
 - When rhinorrhea is the primary symptom
 - In elderly person with isolated rhinorrhea
- No data available for SAR
- Other drugs are preferable as first-line agent to ipratropium in most cases of AR
- Combination with H1-antiHst, or topical steroid in patients where rhinorrhea is predominant or not fully response to other Rx

증례 4

- 19세된 여자환자가 1년이상 달 이상 지속된 코막힘을 주소로 병원을 방문하였다. 때때로 재채기나 코가 가려운 증상이 있었으며 콧물은 호소하지 않았다.
- 비내시경소견은 다음과 같았으며 피부반응검사는 모두 음성이었다.

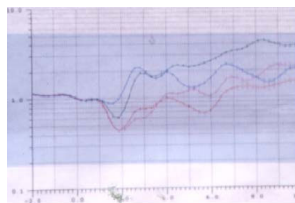


Chronic Hypertrophy : Is It Same?

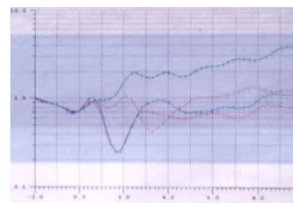


Acoustic Rhinometry

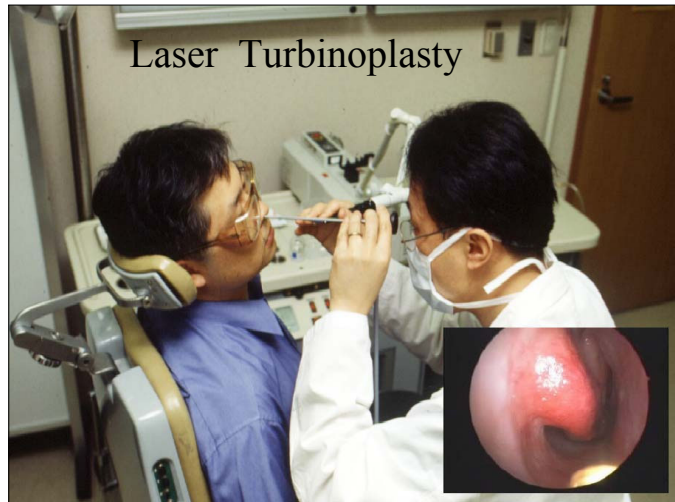
- Preop. planning & postop. tracking
- Non-invasive
- Rapid
- Reproducible
- Reliable
- Easy



Mucosal factor

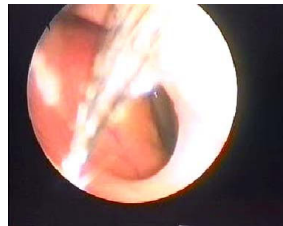


Structural factor



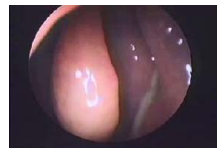
증례 5

- 27세된 남자환자가 6달 이상 지속된 코막힘을 주소로 병원을 방문하였다. 환자는 중학교 때 코에 외상을 입은 과거력이 있었으며 재채기나 콧물은 호소하지 않았다.
- 비내시경소견은 다음과 같았다.



증례 6

- 32세된 여자환자가 3달 전부터 코가 뒤로 넘어가고 두통이 있다고 병원을 방문하였다. 코막힘이나 재채기, 코의 가려움증은 호소하지 않았다.
- 비내시경소견은 다음과 같았다.



Medical Tx of Rhinosinusitis

- Antibiotics
- Corticosteroids
- Decongestants
- Antihistamines
- Mucolytics
- Others
 - Mast cell stabilizer, Leukotriene antagonist, Immunotherapy
- Supportive care

Medical Tx of Rhinosinusitis



Common Pathogens of Rhinosinusitis

- Acute rhinosinusitis
 - *Streptococcus pneumoniae*
 - *Hemophilus influenzae*
 - *Moraxella catarrhalis*
- Chronic rhinosinusitis
 - Mixture of various anaerobe/aerobe
 - *Staphylococcus aureus*

Criteria of Selecting an Antibiotic for Empiric Therapy of Sinus Infection

1. Excellent pneumococcal activity
2. Good gram-negative activity (*H. influenzae*, *M. catarrhalis*)
3. Adequate staphylococcal coverage
4. Adequate anaerobic coverage
5. Acceptable formulation and dosage regimen

증례 7

- 56세된 여자환자가 4달 전부터 코가 막히고 냄새가 둔하여 왔다고 병원을 방문하였다. 때로 재채기나 맑은 콧물이 났으며 목뒤로 누런 가래가 넘어간다고 하였다.
- 비내시경소견은 다음과 같았다.

