study is required to determine the change in expression of these cytokines and the FcεR1 receptor in the middle ear mucosa.

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Practical guideline for management of acute rhinosinusitis in Japan

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1. Introduction

Recently high prevalence of antimicrobial resistant bacteria has made rhinosinusitis refractory resulting in frequent prescription of antimicrobial agents at the usual clinical setting. Despite the high incidence and economical impact of sinusitis, considerable practice variations exist across and within multiple disciplines involved in managing the condition.

This guideline provides evidence-based recommendations on managing acute rhinosinusitis. The targeted patients for the guideline are children aged 15 years or less and adults aged 16 years or above with no symptoms of acute rhinosinusitis 1 month before the onset, those with no craniofacial anomalies, and those with no immunodeficiency. The guideline is not intended to apply to patients with acute exacerbation of chronic sinusitis or those with odontogenic maxillary sinusitis.

2. Definition of acute rhinosinusitis

Acute rhinosinusitis is defined as symptomatic inflammation of the nose and paranasal sinuses with an acute onset that presents with respiratory symptoms, such as nasal obstruction, rhinorrhea, postnasal discharge, and coughing, accompanied by headaches, cheek pain, and a sensation of facial compression.

Acute rhinosinusitis is defined as inflammation persisting 4 weeks [1], and this definition was also employed in this guideline. Also, the guideline does not apply to the acute exacerbation of chronic sinusitis because its pathological features differ from those of acute rhinosinusitis.

3. Bacteriology in acute rhinosinusitis

The drug susceptibility of *Streptococcus (St.) pneumoniae* has been defined on the basis of the minimal inhibitory concentration (MIC) of penicillin G according to the criteria of the National Committee for Clinical Laboratory Standards (NCCLS) revised in 1998 [2]. *St. pneumoniae* has been classified as follows on the basis of its susceptibility to penicillin G: penicillin susceptible *St. pneumoniae* (PSSP): MIC $\leq$ 0.06 μg/mL, penicillin intermediately resistant *St. pneumoniae* (PISP): MIC = 0.125–1.0 μg/mL and penicillin resistant *St. pneumoniae* (PRSP): MIC $\geq$ 2 μg/mL.

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Some resistant strains of *Haemophilus (H.) influenzae* show resistance to ampicillin (ABPC) without producing β-lactamase, and are called β-lactamase non-producing ampicillin-resistant (BLNAR) strains. In BLNAR strains, there are mutations in the gene encoding peptidoglycan synthetase PBP3, formed in the division of *H. influenzae* and involved in septal formation, and mutations affecting resistance have been reported at least at 3 loci. The resistance level is low in strains with a mutation at 1 locus but increases in those with mutations at 2 loci. The former are called low BLNAR and the latter high BLNAR (or simply BLNAR). In this guideline, an MIC of 4 μg/mL or higher and 2 μg/mL or higher are regarded as criteria for BLNAR and low BLNAR, respectively. Strains that produce β-lactamase and are resistant to ampicillin are called β-lactamase-producing ampicillin resistant (BLPAR) *H. influenzae*.

Of the 415 strains detected from patients with acute rhinosinusitis, *St. pneumoniae* accounted for 22.4%, *H. influenzae* for 19.5%, *Staphylococcus (Stap.) aureus* for 17.8%, and *Moraxella (M.) catarrhalis* for 9.9% in the 2nd National Surveillance of Clinical Isolates from Patients with Infectious Diseases in Otolaryngology (November 1998–March 1999) [3]. According to the categories of the MIC breakpoint announced by the NCCLS (presently CLSI), the susceptibility of the 93 strains of *St. pneumoniae* was PSSP in 43.0%, PISP in 33.3%, and PRSP in 23.7%. The susceptibility of the 81 strains of *H. influenzae* was BLNAS in 74.1%, BLNAR in 22.2%, and BLPAR in 3.7%.

Of the 303 strains detected from patients with acute rhinosinusitis, *St. pneumoniae* accounted for 29.4%, *H. influenzae* for 21.5%, *Stap. aureus* for 8.6%, and *M. catarrhalis* for 7.6% in the 3rd National Surveillance of Clinical Isolates from Patients with Infectious Diseases in Otolaryngology (January 2003–May 2003) [4]. In particular, *St. pneumoniae* accounted for 29.2%, *H. influenzae* for 37.5%, *Stap. aureus* for 10.4%, and *M. catarrhalis* for 18.8% in those aged 5 years or less. According to the categories of the MIC breakpoint announced by the NCCLS (presently CLSI) [2], the susceptibility of the 89 strains of *St. pneumoniae* was PSSP in 41.6%, PISP in 39.3%, and PRSP in 19.1%. The susceptibility of the 55 strains of *H. influenzae* was BLNAS in 50.8%, BLNAR in 44.6%, and BLPAR in 4.6%.

Of the 134 strains detected from patients with acute rhinosinusitis, *St. pneumoniae* accounted for 23.9%, *H. influenzae* for 13.5%, *Stap. aureus* for 8.2%, and *M. catarrhalis* for 6.0% in the 4th National Surveillance of Clinical Isolates from Patients with Infectious Diseases in Otolaryngology (January 2007–June 2007) [5]. In particular, *St. pneumoniae* accounted for 33.3%, *H. influenzae* for 33.3%, *Stap. aureus* for 0%, and *M. catarrhalis* for 20.8% in those aged 5 years or less. The susceptibility of the 78 strains of *St. pneumoniae* was PSSP in 53.9%, PISP in 33.3%, and PRSP in 12.8%. The susceptibility of the 63 strains of *H. influenzae* was BLNAS in 41.3%, BLNAR in 52.5%, and BLPAR in 6.2%.

4. General methods and literature search

In creating this guideline the Japanese Rhinologic Society selected a panel representing the fields of infectious diseases, allergy, otolaryngology-head and neck surgery, nutrition, and medical informatics. Several members in this multidisciplinary panel had significant prior experience in developing clinical practice guideline.

5. Collection of evidence

In preparing the guideline, clinical questions were prepared regarding (1) the diagnosis, (2) clinical examination, (3) treatments, and (4) complications, and relevant existing literature searches were performed through December 20, 2009.

PubMed, Cochrane Library, and Japana Centro Revuo Medicina Web version 4 were searched as literature database.

The relevant literature published between 2000 and 2009 was reviewed for the search period. Priority was given to systematic reviews of randomized controlled trials and reports on individual randomized controlled studies. If such were absent, reports of observational studies, such as cohort studies and case-control studies, were adopted. If the literature was still deficient, the range of the search was extended to case series.

6. Classification of and recommendation of evidence-based statements

In preparing this guideline, evidence levels were indicated by the following notational system proposed by the Japan Stroke Society.

Evidence levels were determined as follows: Ia, meta-analysis (with homogeneity) of randomized controlled trials; Ib, at least one randomized controlled trial; IIa, at least one well designed, controlled study without randomization; IIb, at least one well designed, quasi-experimental study; III, at least one well designed, non-experimental descriptive study (e.g., comparative studies, correlation studies, and cases studies); and IV, expert committee reports, opinions, and/or experiences of respected authorities.

Evidence-based statements reflect both the quality of evidence and the balance of benefit and harm that is anticipated when the statement is followed. For this, the following recommendation grades of the Medical Information Network Distribution Service (MINDS) were used: A, there is strong scientific evidence and implementing the treatment is strongly recommended; B, there is scientific evidence and implementing the treatment is recommended; C1, there is no scientific evidence, but implementing the treatment is recommended; C2, there is no scientific evidence and not implementing the treatment is recommended; and D, there is evidence suggesting ineffectiveness or harm, and not implementing the treatment is recommended.

Clinical Question (CQ)-1: Is the bacteriological examination useful for the diagnosis of acute rhinosinusitis?

Acute rhinosinusitis often originates from a viral infection but transitions to a bacterial infection within a few days [6]. The major causative microorganisms are *St. pneumoniae* and *H. influenzae*, followed in the frequency of isolation by *M. catarrhalis* [5,7–9].

Acute rhinosinusitis frequently occurs as part of inflammation involving the entire upper airway during the course of a cold. The disease is often initiated by an infection with viruses, such as rhinovirus, parainfluenza virus, and influenza virus [10–12], but the condition often transitions to a bacterial infection within a few days. It is not practical to exhaustively examine all of the many causative viruses. Regarding bacteria, whether pathogenic bacteria detected in nasal secretions can be regarded as microorganisms responsible for the disease is controversial. However, it is considered reasonable to suspect isolates from fluid collected from the maxillary sinus, which is normally aseptic, as the microorganisms responsible for the susceptibility to antimicrobial agents, and the results obtained from these surveillances have sufficient value as references [5,7,13,14].

Pneumococcal Antigen Rapid Detection Kit (Rapiran-HS®) has been placed into the Japan health insurance list since November 2011. The kit is a detection tool for pneumococci in middle ear effusion, ear discharge or nasopharyngeal secretion, while it is not used for other body samples including serum and urine [15]. The efficiency of the kit was evaluated in clinical experiments based on the microbiological culture results. True positivity was 76.8% (169/220), true negativity was 83.3% (260/312) and rate of concordance was 80.6% (429/532) in middle ear effusions and nasopharyngeal

secretions. The concordance rates with microbiological culture results in both types of samples were favorable. Based on those results, the kit is considered to be efficient for the diagnosis of pneumococcal infection of upper respiratory tract including otitis media and rhinosinusitis [16,17].

ANSWER: Bacteriological examination should be considered in patients showing persisted symptoms.

Evidence level: Ib

Recommendation grade: B

CQ-2: Is the drug susceptibility of bacteria from patients with acute rhinosinusitis useful for the antimicrobial selection?

In children, amoxicillin (AMPC) and cefditoren-pivoxil (CDTR-PI), cefcapene-pivoxil (CFPN-PI), and cefteram-pivoxil (CFTM-PI) among the cephem antibiotics have high antibacterial activity against *St. pneumoniae*. Regarding *H. influenzae*, BLNAR strains are increasing, and susceptibility to penicillin is decreasing, but CDTR-PI, among the oral cephems, has high antibacterial activity. CVA/AMPC has excellent antibacterial activity against BLPAR and β-lactamase-producing *M. catarrhalis* [4,5,18]. In adults, the respiratory quinolones levofloxacin (LVFX), garenoxacin (GRNX), moxifloxacin (MFLX), and sitafloxacin (STFX) are effective against the above 3 bacterial species, and GRNX and STFX also have excellent antibacterial potency against *St. pneumoniae* [4,5,18].

ANSWER: Examination of the drug susceptibility of bacteria is useful for antimicrobial selection on the treatment of patients with acute rhinosinusitis.

Evidence level: Ib

Recommendation grade: B

CQ-3: What are points of interviews for diagnosis of acute rhinosinusitis in children?

Interviewing is important for diagnosis and subsequent treatments. In particular, following inquiries are essential: (1) how long the patient has had symptoms, (2) whether the patient is attending a nursery school, (3) whether the patient has complications including immunodeficiency, (4) age of 5 years or below, and (5) whether the patient had been prescribed antibiotics within 1 month [9].

In children exhibiting symptoms of rhinosinusitis, clarification of influential circumstances of the disease, such as catching a cold, specific symptoms, and the duration of symptoms, is important for diagnosing that the patient suffers acute rhinitis or complicated by sinusitis, has a viral infection alone or complicated by a bacterial infection. Also, the patient's present and past history may serve as indices for predicting prolongation or recurrence of the disease.

ANSWER: Interviewing is important for diagnosis and subsequent treatments of acute rhinosinusitis in children.

Evidence level: III

Recommendation grade: B

CQ-4: What are points of interviews for diagnosis of acute rhinosinusitis in adults?

Acute rhinosinusitis in adults can be diagnosed to an extent by inquiries about symptoms, such as nasal obstruction, rhinorrhea, postnasal discharge, cheek pain, and headache; the differentiation of acute rhinosinusitis from diseases such as odontogenic maxillary sinusitis and barosinusitis is necessary. Also, rhinosinusitis is often made refractory or recurrent if it is complicated by diabetes and lower airway disorders, such as asthma. Whether inquiries about symptoms, the differentiation of these disorders, and the clarification of complications such as diabetes and lower airway disorders (asthma, diffuse panbronchiolitis, and chronic obstructive pulmonary disease; COPD) by inquiries are useful for diagnosis, treatment, and outcomes was valuated.

The patients who showed fluid retention by puncture of the maxillary sinus were diagnosed with acute rhinosinusitis, and the usefulness of medical interviews and radiography of the paranasal sinuses was evaluated by meta-analysis. As a result, 49–83% of the patients complained of nasal symptoms such as unilateral or bilateral purulent rhinorrhea and unilaterally dominant cheek pain, and most patients also showed findings on radiography of the paranasal sinus.

ANSWER: Inquiries about nasal symptoms are important for diagnosis acute rhinosinusitis in adults.

Evidence level: III

Recommendation grade: B

CQ-5: How should the score of acute rhinosinusitis and the severity based on this score be evaluated? (Table 1).

It is appropriate to grade the severity of acute rhinosinusitis as mild, moderate, or severe according to nasal findings and clinical symptoms. In this guideline, the severity of nasal findings and clinical symptoms was expressed as a score, and the severity of the disease was evaluated as the sum of the scores.

Acute rhinosinusitis is defined as infections of nose and paranasal sinuses within a 30-day duration with sustained or severe symptoms. Sustained symptoms mean symptoms persisting for at least 10–14 days and within 30 days and include rhinorrhea or postnasal discharge and/or a daytime cough (often exacerbated during the nighttime). In children, severe symptoms mean a fever of 39 °C or higher and purulent rhinorrhea persisting for at least 3–4 days [19–21]. Postnasal discharge is a symptom characteristic of acute rhinosinusitis. In particular, purulent

Table 1
Scoring system and severity grading of acute rhinosinusitis.

		None	Mild/small amount	Moderate or more severe
Adults				
Clinical symptoms	Rhinorrhea	0	1	2
	Facial pain/frontal headache	0	1	2
Nasal findings	Nasal secretions/postnasal discharge	0 (serous)	2 (mucopurulent/ small amount)	4 (intermediate or larger amount)
Children				
Clinical symptoms	Rhinorrhea	0	1	2
	Bad temper/a wet cough	0	1	2
Nasal findings	Nasal secretions/postnasal discharge	0 (serous)	2 (mucopurulent/ small amount)	4 (intermediate or larger amount)

Mild: 1–3; Moderate: 4–6; Severe: 7–8. *Supplementary note*: If sustained fever (38.5 °C or higher), facial swelling/reddening, and signs of inflammation (blood test) are observed, imaging examinations are necessary with the complications of acute rhinosinusitis in mind. *Explanatory note*: The severity of a wet cough is graded as follows: 0: No cough; 1: Cough observed; 2: Cough interfering with sleep.

rhinorrhea/postnasal discharge reflects the course of treatment and is the most important index of the therapeutic effect [18,22,23].

While fever is an important finding for evaluating the severity of infections in children, it was excluded because it is not specific to acute rhinosinusitis and is not closely correlated with the severity of the disease. For nasal findings, the amount of nasal secretions or postnasal discharge was graded using the 3-point scale of small, large, and intermediate (between small and large) because it is difficult to check nasal findings by rhinoscopy in small children or by nasal endoscopy in all small children.

A viral infection is often accompanied by other systemic symptoms such as headache and myalgia at an early stage of the disease. Generally, these symptoms are alleviated within the first 48 h, and respiratory symptoms become dominant; however, in viral infection, purulent rhinorrhea does not appear in the first few days [24]. Therefore, if a high fever and purulent nasal secretions persist simultaneously over at least 3–4 days, acute bacterial rhinosinusitis is suspected. Facial pain is not a common complaint in children, and facial tenderness is a rare finding in small children. They also cannot be reliable indications of acute bacterial rhinosinusitis in older children and adolescents [24].

ANSWER: Acute rhinosinusitis is scored by the following clinical findings; rhinorrhea, facial pain/frontal headache, and properties/amount of nasal secretions or postnasal discharge in adults and rhinorrhea, bad temper/a wet cough, and properties/amount of nasal secretions or postnasal discharge in children.

Evidence level: III

Recommendation grade: B

CQ-6: Is the no-administration of antibiotics appropriate for mild acute rhinosinusitis?

Since acute rhinosinusitis occurs secondary to upper airway inflammation [25], and since viral infection is considered to be core to the early stage of the disease, antibiotics are expected to be not effective in mild cases. It has been reported that most patients with acute rhinosinusitis have a viral infection and that antibiotic treatment is unnecessary unless the patient exhibits purulent nasal secretions that persist for 5 days or longer [26]. A previous report showed that acute rhinosinusitis is difficult to diagnose accurately, particularly in children, that the grounds for diagnosis are uncertain, and that antibiotic treatment is better than placebo treatment; however, this indication is inaccurate [27]. If there is an exacerbation of symptoms during an observation of the natural course, and if the condition is aggravated to moderate or severe rhinosinusitis, an antibiotic treatment should be initiated. Excessive use of antibiotics leads to an increase in resistant microorganisms, and appropriate judgment of whether antibiotics should be used or not is important.

ANSWER: Observation of the natural course without the administration of antimicrobial agents is recommended only in mild cases.

Evidence level: Ia

Recommendation grade: B

CQ-7: Are β-lactam antibiotics effective for the treatment of acute rhinosinusitis?

St. pneumoniae and *H. influenzae* are 2 major pathogenic microorganisms of acute rhinosinusitis, but the resistance rates of these 2 species are high in Japan. Of the β-lactam antibiotics, penicillin antibiotic in particular, are effective for the elimination of even resistant *St. pneumoniae* if used at a high dose [5,28]. Cephem antibiotics such as CCL (cefaclor), CFDN (cefdinir), CPDX-PR (cefpodoxime proxetil), CDTR-PI (cefditoren pivoxil), CFPN-PI (cefcapene pivoxil), and CFTM-PI (cefteram pivoxil) have also been reported to be effective. In consideration of the high resistance rates of *St. pneumoniae* and *H. influenzae* in Japan, CDTR-PI, CFPN-PI, and CFTM-PI (high dose) are expected to be effective, and CDTR-PI also shows a low MIC and is expected to be effective against resistant *H. influenzae* [34].

In August 2009, the world's first oral carbapenem antibiotic (tebipenem pivoxil, TBPM-PI) was marketed in Japan. In clinical trials, the drug showed a nearly comparable clinical effect and high bacterial elimination rate against acute rhinosinusitis in children caused by *St. pneumoniae* or *H. influenzae* to that with conventional oral antibiotics. It is considered to be an effective antibiotic with the high resistance rates of the 2 major pathogenic microorganisms in Japan in mind [29–31]. It is expected to be a useful alternative for severe cases or infants with refractory rhinosinusitis not responding to other drugs.

It is necessary to use such oral antibiotics with high antibacterial activity appropriately according to strict rules. If such a drug is used clinically in large amounts, the development of resistance to injection preparations of carbapenem antibiotics may be accelerated, leading to an increase in infections difficult to treat even with carbapenem injections, which are presently a trump card in antibiotic treatment.

ANSWER: AMPC is administered as the first choice, and, if no clinical or bacterial effect is observed, cephem antibiotics should be selected.

Evidence level: IIb

Recommendation grade: A

CQ-8: Are respiratory quinolone antibiotics effective for the treatment of acute rhinosinusitis?

Evidence is scarce, and this treatment is not recommended at present in children. In adult patients with acute rhinosinusitis, respiratory quinolones are used as the second choice for patients with moderate acute rhinosinusitis not responding to treatment with a high dose of AMPC or a high dose of a third-generation oral cephem antibiotic, or as one of the first choices for patients with severe acute rhinosinusitis [18,22]. To achieve high antibacterial activity on the basis of PK/PD theories, it is desirable to select a preparation that is effective by a once-a-day administration protocol and administer it over 5–7 days [18,22,23].

No significant difference was observed in efficacy between respiratory quinolones and β-lactams [32,33], but bacteriological efficacy was higher in respiratory quinolones than β-lactams [34]. Therefore, respiratory quinolones are considered to be useful for adults with acute sinusitis in whom early bacteriological responses are expected.

ANSWER: Respiratory quinolones are recommended as the second choice for moderate cases of acute rhinosinusitis not responding to AMPC and as one of the first choices for severe cases. This treatment is not recommended at present in children.

Evidence level: IIb

Recommendation grade: B for adults and C2 for children

CQ-9: Are macrolide antibiotics effective for the treatment of acute rhinosinusitis?

Since major pathogens, *St. pneumoniae* and *H. influenzae*, have been highly resistant to 14-membered macrolides such as CAM, EM, or RXM, these macrolides are unlikely to become the first choice for antibiotic treatment for acute rhinosinusitis [5,23,35]. AZM (azithromycin, 15-membered macrolide), which can be administered once at a high dose, is expected to be effective against acute rhinosinusitis [35–37].

Since low-dose long-term administration of macrolide antibiotics was reported to be effective for the treatment of diffuse

panbronchiolitis (DPB), attention has been directed to the effectiveness of macrolides for the treatment of chronic sinusitis showing similar pathologic features to DPB. However, the development of resistance of *St. pneumoniae* and *H. influenzae*, which cause acute rhinosinusitis, to macrolides has recently emerged as a problem, and caution is needed for the frequent use of macrolides [38].

Azithromycin (AZM), which shows a low MIC against *H. influenzae* and is expected to have antibacterial potency, should be used for *H. influenzae* infection [35]. In adults, the administration of AZM once at a high dose (2 g) is expected to be effective [35–37].

ANSWER: Macrolides except for azithromycin are unlikely to become the first choice for antimicrobial treatment for acute rhinosinusitis.

Evidence level: Ib

Recommendation grade: C1

6.1. Treatment algorithm for acute rhinosinusitis

The fundamental issue in determining appropriate treatment for acute rhinosinusitis is identifying cases warranting antimicrobial agents. The key features for evaluating antibiotic appropriateness should be severity and duration of the disease. Treatment algorithm is developed based on the severity of disease judged by scores of symptoms and nasal/postnasal discharges. The severity of acute rhinosinusitis is graded into mild, moderate and severe by the total score, 1–3, 4–6, and 7–8, respectively. Nasal treatments for symptomatic relief such as enlargement of the natural opening of the paranasal sinuses following the administration of corticosteroids by nebulizer are generally recommended initially for all cases as "good clinical practice".

Watchful waiting for 5 days and symptomatic relief by nasal treatments such as enlargement of the natural opening of the paranasal sinuses following the administration of corticosteroids by nebulizer are generally recommended initially for mild cases (Figs. 1 and 4). In cases of no improvement within 5 days of watchful waiting or in moderate cases (Figs. 2 and 5), a usual dose of AMPC for children or a usual dose of AMPC or cephem antibiotics

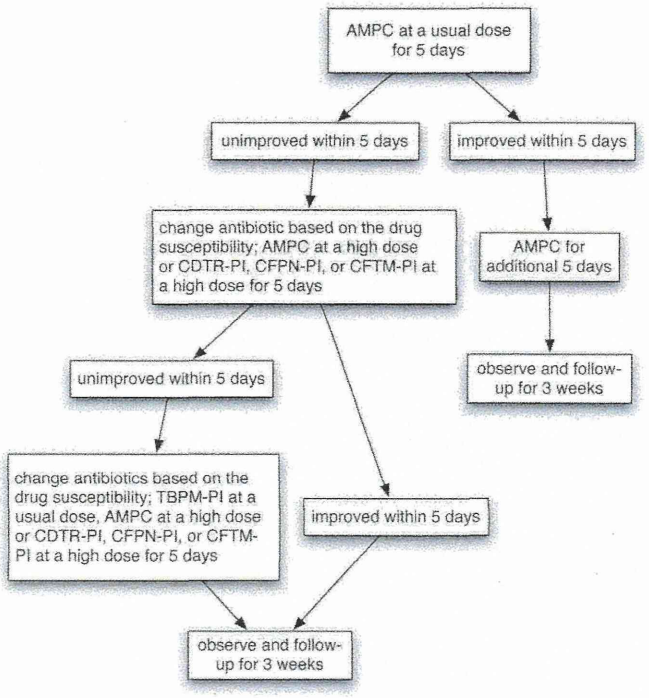

Fig. 2. Treatment algorithm for acute rhinosinusitis (children, moderate case).

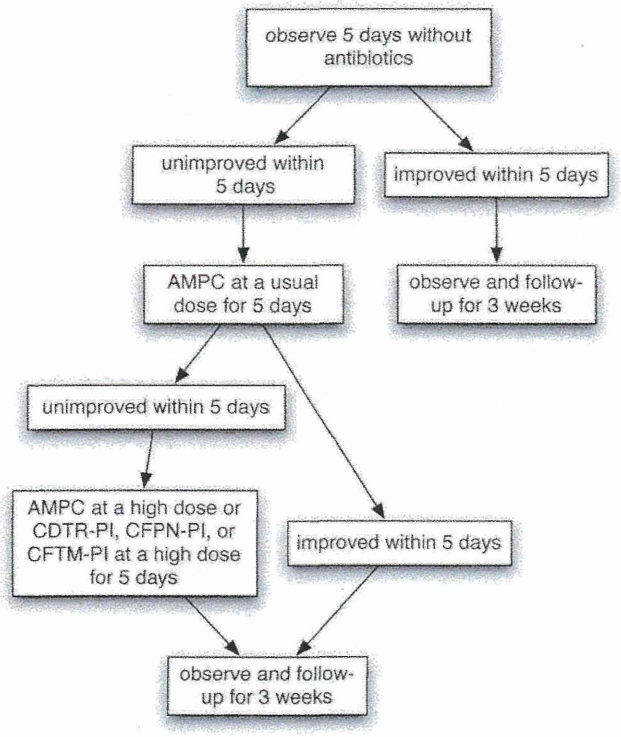

Fig. 1. Treatment algorithm for acute rhinosinusitis (children, mild case).

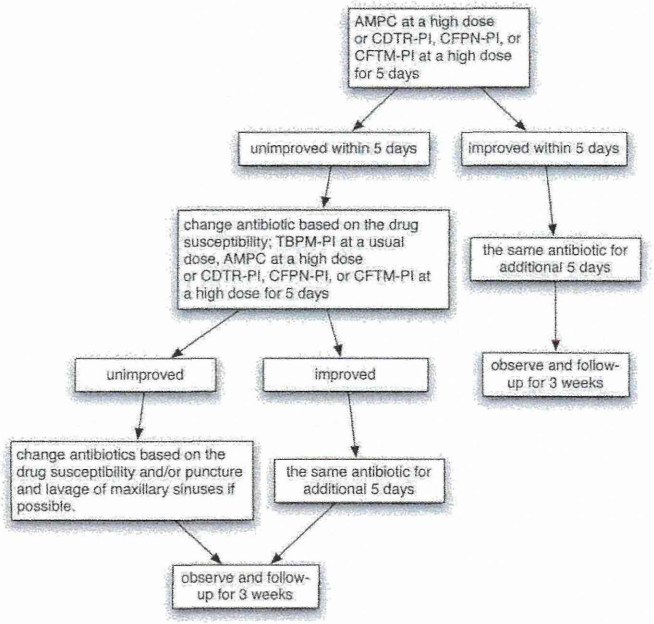

Fig. 3. Treatment algorithm for acute rhinosinusitis (children, severe case). 1. Nasal treatments such as aspiration of nasal discharge and opening of the middle nasal meatus should be of the first management priority. 2. If the patient has fever at 38.5 °C or higher, consider acetaminophen at 10 mg/kg (single dose). 3. Bacterial examinations (bacterial culture or Pneumococcal antigen rapid detection kit) of nasal secretion are recommended. 4. Butyric acid bacterium or antibiotic-resistant lactobacillus preparations should be added in oral antibiotic therapy. 5. Antibiotic doses must not exceed the largest dose for adults. 6. The dose of AMPC must not exceed 1500 mg. 7. The observation period is 3 weeks after the initial examination.

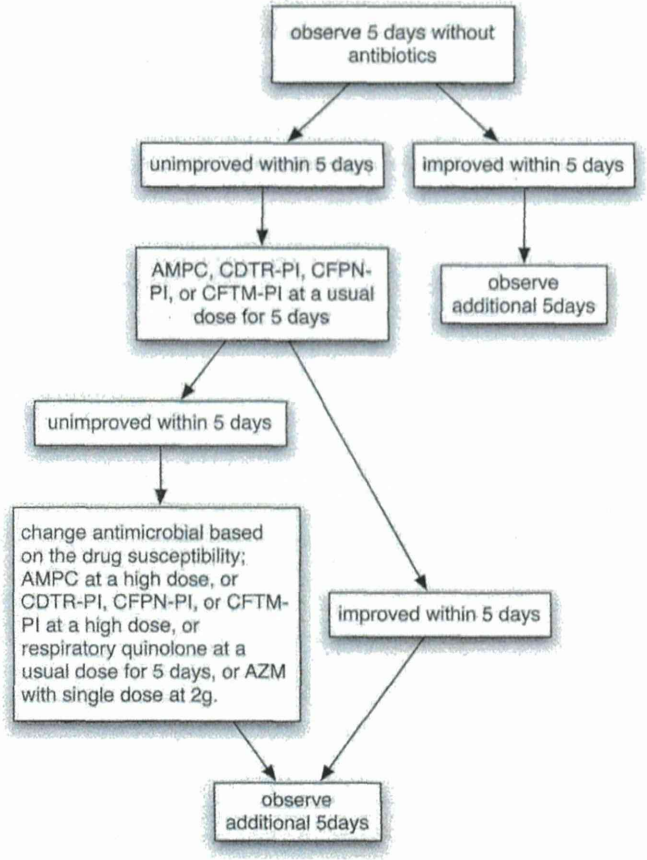

Fig. 4. Treatment algorithm for acute rhinosinusitis (adults, mild case). 1. Nasal treatments such as aspiration of nasal discharge and opening of the middle nasal meatus should be of the first management priority. 2. Bacterial examinations (bacterial culture or Pneumococcal antigen rapid detection kit) of secretions from middle nasal meatuses are recommended.

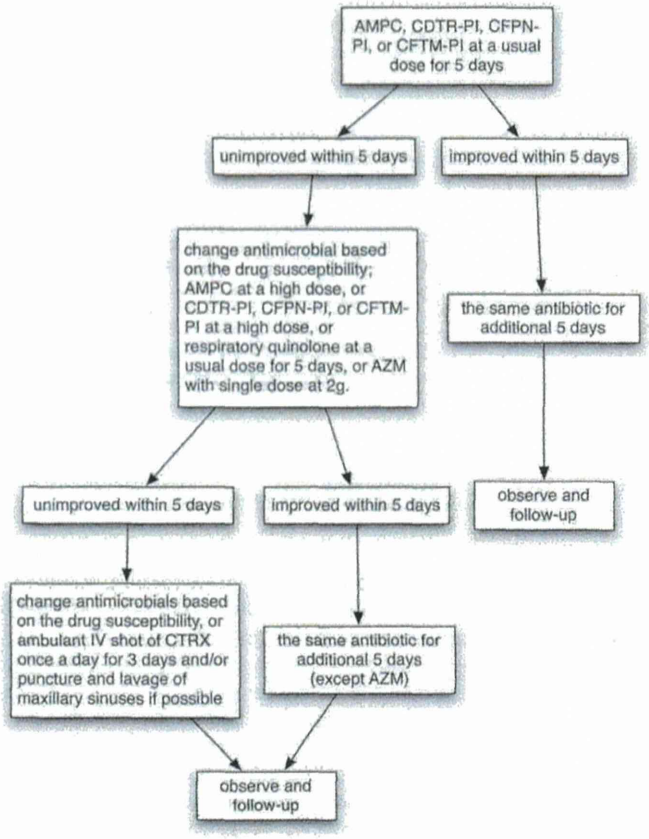

Fig. 5. Treatment algorithm for acute rhinosinusitis (adults, moderate case).

such as CDTR-PI, CFPN-PI, and CFTM-PI for adults are recommended for the treatment of choice. In principle, when a decision is made to treat acute rhinosinusitis with antimicrobial agents, the clinician should prescribe amoxicillin that is efficacious, cost-effective, and results in minimal side effects.

For improved cases within 5 day-treatment the treatment should be continued with additional 5-day administration of the same antimicrobial agent, and for unimproved cases bacterial examination such as bacterial culture or Pneumococcal antigen rapid detection kit is recommended to select an appropriate antimicrobial to be used. A high dose of AMPC or a high dose of any one of CDTR-PI, CFPN-PI, or CFTM-PI for 5 days administration is recommended for unimproved cases. Since drug-resistant microbes are highly prevalent in children and adults with refractory rhinosinusitis, a treatment with a high dose of antimicrobials has been mandatory.

In cases with severe grade (Figs. 3 and 6), bacterial examinations such as bacterial culture or Pneumococcal antigen rapid detection kit is strongly recommended to infer refractoriness of the disease. A high dose AMPC or cape antibiotic is recommended as the first-line therapy for children of severe grade and as the second-line therapy for moderate grade. As the second-line therapy in severe cases, TBPM-PI for children and respiratory quinolones such as LVFX, GRNX, MFLX, STFX or AZM of single-dose at 2 g for adults are recommended as well as a high dose of AMPC or cipher antibiotics.

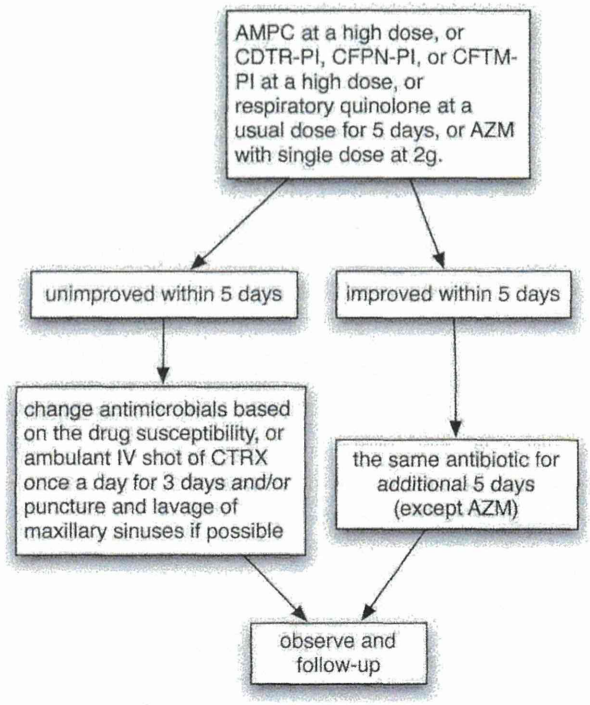

Fig. 6. Treatment algorithm for acute rhinosinusitis (adults, severe case). 1. Nasal treatments such as aspiration of nasal discharge and opening of the middle nasal meatus should be of the first management priority. 2. Bacterial examinations (bacterial culture or Pneumococcal antigen rapid detection kit) of secretions from middle nasal meatuses are recommended. 3. Patients with complications should be hospitalized for proper treatments.

7. Conclusion

This is the position paper for Clinical Practice Guideline for Acute Rhino sinusitis in Children and Adults in Japan. The panel employed scoring systems in line with the severity of clinical symptoms and rhinorrhea/nasal discharge. Recommendations and answers for 9 clinical questions were developed and the treatment algorithm for acute rhinosinusitis was proposed.

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Ⅵ．好酸球性中耳炎

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難知性中耳炎の１つである好酸球性中耳炎は，喘息に合併する慢性気道炎症の１つであり，“one airway, one disease”として認知されている。気管支喘息や好酸球性副鼻腔炎の発症後，10年以上経過してから発症する。ほとんどの症例は副腎皮質ステロイドの鼓室内注入にて安定した状態を維持することができるが，現在の治療ではコントロールが難しい重症例が存在する。重症化を防ぐためには，早期に診断を行い，治療を開始することが必要である。

好酸球性中耳炎／耳管／気管支喘息

はじめに

好酸球性中耳炎は，1992年富岡らによって気管支喘息に合併する難治性中耳炎として発表され[1,2]，2011年に診断基準（**表1**）が提唱された比較的新しい疾患であり[3]，現在では慢性気道炎症の1つ“one airway, one disease”として認知されている[4,5]。2004年の耳科学会による全国疫学調査の中で[6]，この難治性中耳炎の特徴として，副鼻腔炎を合併する症例が多く鼻内視鏡手術後に発症する場合もあるが[7,8]，手術自体は骨導悪化の原因にはなっていないこと，聾の割合は鼓室形成術を受けた群で有意に高く，主に鼓室形成術後骨導悪化が原因となっていることなどが述べられている。その後約10年が経過し，現在好酸球性中耳炎について明らかになっている点を，合併する副鼻腔炎との関係も含めて述べる。また我々が治療の際に用いる重症度スコアについても解説する。

Ⅰ．検査・診断[9]

好酸球性中耳炎の特徴は，非常に粘稠な中耳貯留液で半固形状，ニカワ状を呈する。診断基準では，鼓膜穿孔があるタイプとないタイプで滲出性中耳炎型，慢性中耳炎型の２つに大別されている。我々は中耳粘膜Grade分類を作成し，外来診察の際にはこちらを用いて，治療経過を記載している（**表2，図1，2**）[10,11]。当院外来通院患者の内訳を**図3**に示す。滲出性中耳炎型は，鼓膜切開をして貯留液を吸引すると多くはGrade 1（G1）である。慢性中耳炎型でも中耳粘膜肥厚がほとんどみられない症例はG1，肥厚が中耳腔内に限局する場合はG2とし，過剰な肥厚で肉芽を形成

表１　好酸球性中耳炎診断基準

大項目
好酸球優位な中耳貯留液が存在する滲出性中耳炎 / 慢性中耳炎
小項目
1）膠（ニカワ）状の中耳貯留液
2）中耳炎に対する従来の治療に抵抗
3）気管支喘息の合併
4）鼻茸の合併

確実例：大項目の他に，2つ以上の小項目を満たすもの
除外診断：Churg-Straus 症候群
好酸球増多症候群（hypereosinophilic syndrome）

2011 年に提唱された好酸球性中耳炎の診断基準を示す．
（文献３より）

表２　中耳粘膜 Grade 分類

Grade 1　中耳粘膜の肥厚がほとんどみられない
2　〃　がみられるが中鼓室内に限局している
3　〃　が鼓膜を越え外耳道側へ張り出している

筆者らは中耳粘膜 Grade 分類を作成し，外来診療の際，こちらを用いて治療経過を記載している．
（文献 10 より）

し，鼓膜を越えて外耳道側へ伸展する症例は G3 に分類している。

好酸球性中耳炎の診断の際には，中耳貯留液の好酸球浸潤を確認する（**図４**）。スメアとして細胞診として提出する場合や，粘稠度が強い場合には，そのままホルマリン固定し病理検査へ提出する。感染がある場合には，好中球優位となり診断がつかないことがあり，洗浄や抗菌薬投与により状態を落ち着かせてから，再提出する必要がある[12]。特に G3 に至る症例は感染のコントロールがついていないケースが多く，この状態で肉芽を鉗除してもやはり好中球優位で診断には至らない。急性感音難聴を併発している場合には，入院の上，連日生理食塩水による耳洗浄，抗菌薬点滴，ステロイド内服投与を行い，状態をみながら診断・治療を兼ねて，粘性貯留液と肉芽組織を（載除鉗子などを用いて切除し）病理学的検査へ提出する。この G3 症例にみられる肉芽の存在は重症化した好酸球性中耳炎に特異的な所見であり，炎症を繰り返すうちに線維化組織となる。厚く覆われた耳小骨周囲の肉芽は，機械的に除去することは困難である。気管支喘息をはじめとする慢性好酸球性炎症性疾患の中に粘膜自体が肥厚するものはなく，この機序についてはまだ分かっていない。

G1 (Grade 1)