CLINICAL PRACTICE

Acute Bacterial Sinusitis

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 43-year-old man has a two-week history of nasal congestion, postnasal drip, and fatigue. He has used an over-the-counter nasal decongestant and acetaminophen, without relief. During the past few days, facial pain and pressure have developed and have not responded to decongestants. In addition, his nasal discharge has turned from clear to yellow. How should he be treated?

THE CLINICAL PROBLEM

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Acute bacterial sinusitis is an infection of the paranasal sinuses with inflammation of the nose. On the basis of national population surveys and insurance-reimbursement claims, sinusitis is one of the most common health problems in the United States.[1] Acute bacterial sinusitis most commonly develops as a complication of a viral infection of the upper respiratory tract. Approximately 0.5 to 2 percent of cases of viral rhinosinusitis develop into bacterial infections.[2-4] Symptoms include nasal congestion, purulent nasal discharge, maxillary tooth discomfort, hyposmia or anosmia, cough, facial pain or pressure that is made worse by bending forward, headache, fever, and malaise. Physical findings include nasal turbinate edema, nasal crusts, purulence of the nasal cavity and posterior pharynx, and failure of transillumination of the maxillary sinuses.[5] Transillumination is performed in a completely darkened room by placing a flashlight against the skin overlying the infraorbital rim and directing the light inferiorly (Fig. 1). The patient then opens his or her mouth, and the hard palate is examined. The possible results are a palate that appears opaque or dull and a normal palate. However, the value of this procedure is limited; since it is not easy to perform, the clinician cannot differentiate viral from bacterial sinusitis, and results vary depending on the skill of the clinician.

A particularly challenging task is to distinguish viral from bacterial sinusitis. In most patients, rhinoviral illness improves in 7 to 10 days[6]; therefore, a diagnosis of acute bacterial sinusitis requires the persistence of symptoms for longer than 10 days or a worsening of symptoms after 5 to 7 days. Symptoms of viral sinusitis, including fever, mimic those of bacterial sinusitis, although the color and quality of nasal discharge — classically, clear and thin during viral sinusitis and yellow-green and thick during bacterial sinusitis — may help to differentiate the two.

Studies over the past two decades have indicated that *Streptococcus pneumoniae* and *Haemophilus influenzae* are the major bacterial pathogens in adults with sinusitis.[7] Other species (including β-hemolytic and α-hemolytic streptococci, *Staphylococcus aureus*, and anaerobes) have also been cultured from adults with sinusitis but are much less frequent.[8-11]

Potential complications of bacterial sinusitis include local extension (e.g., osteitis of the sinus bones, infection of the intracranial cavity, and orbital cellulitis) and the spread of bacteria to the central nervous system (which can result in meningitis, brain

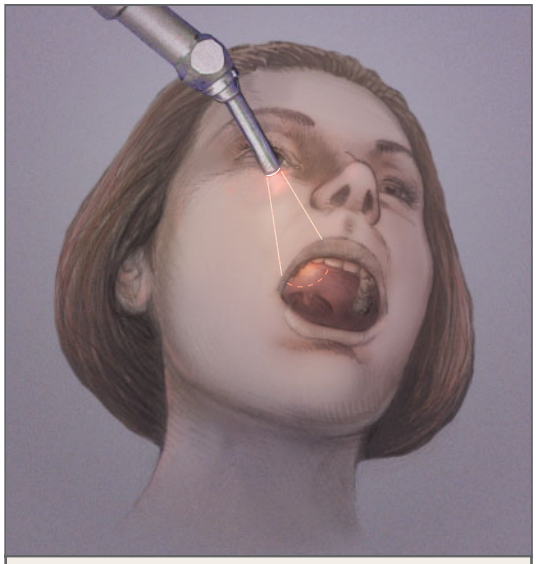

Figure 1. Transillumination of the Maxillary Sinus.
A light source is placed along the infraorbital rim, and the hard palate is inspected.

Figure 2. Plain Radiograph of the Sinuses.
The right maxillary sinus shows mucosal thickening (arrow).

abscess, or infection of the intracranial venous sinuses, including the cavernous sinus). Today, when antimicrobial treatment is routinely given, these complications are exceedingly rare, with an estimated frequency of 1 per 10,000 cases of sinusitis.[12]

STRATEGIES AND EVIDENCE

DIAGNOSIS

The clinical diagnosis of acute bacterial sinusitis is made primarily on the basis of the medical history, symptoms, and physical findings. The prevalence of acute bacterial sinusitis among adults presenting to a general medical clinic with symptoms of sinusitis may be 50 percent[13-16]; among patients presenting to otolaryngology practices, the prevalence can be as high as 80 percent.[17]

Acute sinusitis is defined radiologically by the presence of complete sinus opacity, by the air–fluid level, or by marked mucosal thickening (Fig. 2)[18-21]; however, radiography cannot be used to differentiate viral from bacterial sinusitis.[22] In a meta-analysis that compared the results of sinus radiography with those of sinus puncture,[23] radiography had moderate sensitivity (76 percent) and specificity (79 percent) for the identification of bacterial sinusitis.

Several studies have suggested that symptoms and signs are only moderately useful in the identification of patients who have sinusitis, as determined by the results of sinus aspiration after puncture[24,25] or by evidence of sinusitis on a sinus radiograph.[13,21] The sensitivity, specificity, and predictive values of common symptoms and signs are shown in Table 1.

Images obtained by computed tomography (CT) provide a detailed view of the paranasal sinuses (Fig. 3), but this technique is not routinely indicated in the evaluation of uncomplicated sinusitis. Its limitations include the lack of a correlation between the location of sinus symptoms and CT findings,[26] the fact that CT cannot be used to differentiate viral from bacterial sinusitis,[22] and the high frequency of abnormal scans in asymptomatic persons.[27,28]

THERAPY

Symptomatic Therapy

There have been few rigorous studies of the effect of over-the-counter treatments on the symptoms of sinusitis. Available evidence[29] suggests that the effect of these treatments is minimal. The goal of general treatment is to establish a more normal nasal environment through moisturization, humidification, and a reduction in the viscosity of mucus and in local swelling. The use of topical decongestants for more than five days will lead to rebound symptoms and should be avoided.

Table 1. Various Signs and Symptoms Used to Predict the Presence of Sinusitis.

Method of Diagnosis of Sinusitis and Measure of Performance	Purulent Nasal Discharge	Pain on Bending Forward	Maxillary Toothache	Symptoms after Upper Respiratory Infection	Nasal Obstruction	Pain with Chewing
Bacterial sinusitis on the basis of sinus puncture and aspiration[24,25]						
Sensitivity (%)	35	75	66	89	60	—
Specificity (%)	78	77	49	79	22	—
Positive predictive value (%)	62	78	59	83	53	—
Negative predictive value (%)	78	73	56	87	15	—
Sinusitis on the basis of plain sinus radiography[13,21]						
Sensitivity (%)	61	—	18	70	—	17
Specificity (%)	71	—	93	53	—	86
Positive predictive value (%)	66	—	63	58	—	54
Negative predictive value (%)	66	—	64	54	—	53

Uncomplicated Sinusitis

Antibiotics are indicated for the treatment of acute bacterial sinusitis. The goals of antibiotic therapy are to decrease the severity and duration of symptoms and to preclude the development of complications. Studies of the effectiveness of antimicrobial therapy are often compromised by methodologic limitations[30] — for instance, the inclusion of patients with viral sinusitis, the lack of demonstration of bacteriologic cure by nasal-aspirate culture, the high spontaneous-cure rate of acute sinusitis, and inadequate follow-up to detect chronic sinusitis among patients with persistent symptoms. Since the apparent success of antibiotics depends on the percentage of enrolled patients who have bacterial as opposed to viral sinusitis, the method of diagnostic assessment is important. Studies that use less objective diagnostic criteria and enroll patients who have had symptoms for seven days or fewer will tend to show less benefit of antibiotics.[31] In the discussion that follows, the studies cited are grouped according to the method of diagnosis and the inclusion or absence of a placebo group.

Randomized, placebo-controlled trials[32,33] that have assessed the effects of antibiotic therapy among patients with a clinical diagnosis of acute sinusitis, without the use of objective criteria for the diagnosis, have yielded conflicting results. Although one such study demonstrated the superiority of cyclacillin over placebo,[32] another study[33] showed no difference in outcomes between patients who had been randomly assigned to receive doxycycline and those who had been assigned to placebo groups; the patients who received doxycycline had a greater number of adverse events.

Several randomized trials that have compared antibiotics with placebo among patients with radiographically confirmed sinusitis have also produced variable results. In one study,[14] which involved 214 patients who were randomly assigned to receive either amoxicillin or a placebo for seven days, 83 percent of the patients treated with amoxicillin and 77 percent of those treated with the placebo had greatly decreased symptoms after two weeks ($P=0.20$). Side effects were reported more commonly in the group that received amoxicillin (28 percent vs. 9 percent, $P<0.01$). In another study,[34] which was conducted in a primary care setting, 130 patients received penicillin, amoxicillin, or a placebo. The median duration of illness reported by the patients in the three groups was 11, 9, and 17 days, respectively (duration was significantly shorter in each of the groups receiving antibiotics than in the group receiving the placebo). By day 10, 86 percent of patients who received antibiotics considered themselves to be recovered or much better, as compared with 57 percent of patients who received the placebo ($P<0.001$). However, half of the patients who received the placebo felt recovered or much better after 10 days, and more than half of the patients who received antibiotics reported side effects. A third study[35] included 156 patients who were randomly assigned to receive nasal decongestants, nasal decongestants plus irrigation, penicillin, or

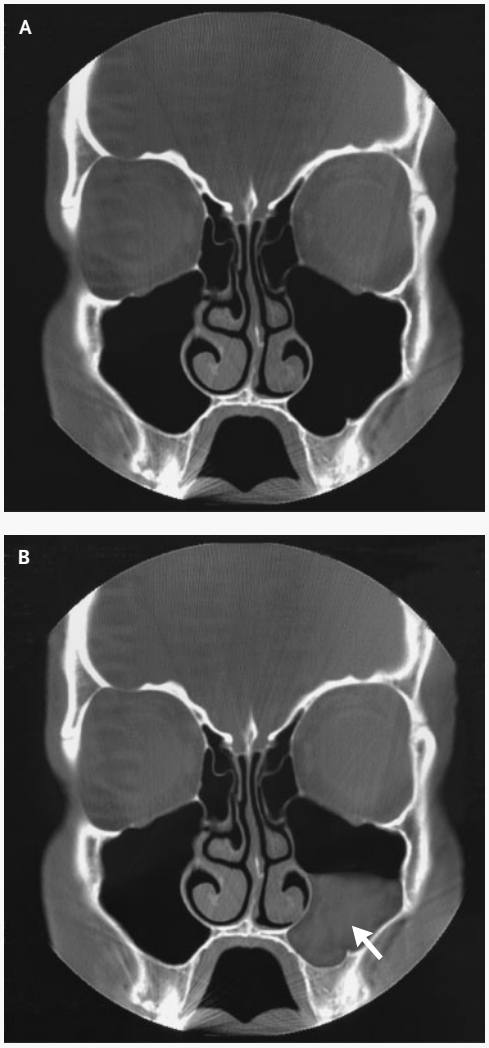

Figure 3. CT Scans of the Paranasal Sinuses.
Panel A shows normal sinuses. In Panel B, the air–fluid level in the left maxillary sinus (arrow) suggests the presence of acute sinusitis.

lincomycin. At day 10, the rates of resolution or improvement did not differ significantly among the groups (72 percent, 80 percent, 83 percent, and 85 percent, respectively). No serious side effects were noted in any of the groups.

In an analysis of a large pharmaceutical database,[36] 29,102 patients were identified with a billing diagnosis of acute sinusitis and a related prescription for an antimicrobial agent. Clinical success was defined as the absence of an additional prescription for an antimicrobial agent within 28 days after the initial prescription. The success rate was 90.1 percent for the patients who received older antimicrobial agents (e.g., amoxicillin, trimethoprim–sulfamethoxazole, and erythromycin) and 90.8 percent for the patients who received newer drugs (e.g., clarithromycin, azithromycin, and amoxicillin–clavulanate). Serious complications (such as brain abscess and meningitis) occurred in one patient in each group. The average pharmaceutical charge was $18 for patients receiving older antimicrobial agents and $81 for those receiving newer antimicrobial agents.

A Cochrane Review[37] analyzed the results of 49 different antibiotic trials involving 13,660 participants. The methods — including whether sinus puncture or radiography was used for diagnostic confirmation — varied among studies. The comparisons included antibiotic with placebo, newer, nonpenicillin antibiotics with simple penicillin, nontetracycline antibiotics with tetracycline, amoxicillin–clavulanate with other broad-spectrum antibiotics, and miscellaneous others. The duration of treatment was generally short, ranging from 3 to 15 days, with 39 of the 49 studies reporting treatment that lasted for 10 days or less. Among the 10 trials that compared newer, nonpenicillin antibiotics (e.g., cephalosporins, macrolides, and minocycline) with penicillin or related antibiotics (e.g., amoxicillin), the rates of cure or clinical improvement were not different (84 percent for each). Relapse rates did not differ between the groups, and there was no trend toward reduced efficacy of amoxicillin over time as resistant bacteria became more prevalent. Similarly, of the 16 trials that compared newer, nonpenicillin antibiotics with amoxicillin–clavulanate, the rates of cure or improvement and the relapse rates were the same for both groups; the number of patients who dropped out because of adverse effects was significantly smaller in the group receiving the newer, nonpenicillin antibiotic (1.9 percent) than in the group receiving amoxicillin–clavulanate (4.4 percent).

A study published after the most recent Cochrane Review update compared 3- and 6-day regimens of azithromycin with a 10-day regimen of amoxicillin–clavulanate.[38] Self-reported cure or improvement rates were similar in the three groups at 28 days — 72 percent, 73 percent, and 71 percent, respectively. However, treatment-related side effects were significantly more frequent in patients who received amoxicillin–clavulanate (51 percent) than in patients who received either the three-day course of azithromycin (31 percent) or the five-day course (38 percent).

A cost-effectiveness analysis performed by the Agency for Health Care Policy and Research[39] underscores the benefit in many cases of waiting for spontaneous resolution of symptoms before prescribing antibiotics. Four different treatment strategies were compared: the use of sinus radiography and initiation of antibiotic therapy if there were signs of sinusitis; the use of clinical criteria (including the presence of suggestive symptoms, such as local pain over the maxillary sinuses, and the findings on physical examination, such as purulent rhinorrhea) to guide treatment; the initial treatment of symptoms with the use of decongestants, nasal saline, steam inhalation, and mild analgesics; and the routine empirical use of antibiotics, either amoxicillin or trimethoprim–sulfamethoxazole. The authors emphasized that about two thirds of patients with acute bacterial rhinosinusitis improve or are cured without antibiotics. Treatment with any antibiotic, regardless of type, reduces the rate of clinical failure by about half. In terms of the duration of symptoms, empirical treatment, treatment directed by radiography, and treatment guided by clinical criteria were all about equal. With the usual prevalence of acute bacterial sinusitis in most primary care settings (up to 38 percent), the evidence indicates that a strategy of either initial symptomatic treatment or the use of clinical criteria to guide treatment would be a cost-effective approach for uncomplicated cases. The authors go on to suggest that a 7-to-10-day course of watchful waiting before antibiotics are prescribed would be reasonable, since symptoms in most patients resolve without the use of antibiotics and serious complications are rare. For the large number of patients with uncomplicated acute bacterial rhinosinusitis, a course of inexpensive antibiotics is probably an adequate first-line treatment if antibiotics are to be given.

The antibiotics commonly prescribed for sinusitis and the dosage, duration of treatment, cost, and contraindications associated with them are shown in Table 2.

Complicated or Severe Sinusitis

The results of the studies of antibiotics cited above do not pertain to patients with clinically significant coexisting illnesses or with more potentially serious disease, such as frontal or sphenoidal sinusitis. Patients with intense periorbital swelling, erythema, and facial pain or with changes in mental status may have complications, and they should be treated more aggressively than those with uncomplicated sinusitis. A more aggressive approach includes the use of CT scanning to assess the extent of disease and the use of antibiotics such as azithromycin, the fluoroquinolones (e.g., gatifloxacin, levofloxacin, and moxifloxacin), ceftriaxone, or amoxicillin–clavulanate. Such patients should be reassessed for a response to therapy after 72 hours, and the absence of a response should prompt a change in therapy.

Patients with Allergic Rhinitis

Antihistamines are often recommended for patients with an underlying allergy.[42] In a multicenter, randomized, double-blind, placebo-controlled study[43] 139 patients with chronic allergic rhinitis (as defined by the results of skin tests, a radioallergosorbent test, and medical history) were followed. All of the patients had acute exacerbation of sinusitis and were already receiving amoxicillin and oral corticosteroids. As compared with a placebo, loratadine significantly reduced rhinorrhea after 14 days and nasal obstruction after 28 days. Other symptoms, such as sneezing, nasal itching, and cough, were similar in the two groups.

It remains uncertain whether topical nasal steroid sprays ameliorate symptoms in acute uncomplicated sinusitis. In one randomized, double-blind study[44] of patients with acute or chronic sinusitis, most of whom had allergic rhinitis, the addition of an intranasal flunisolide spray to oral antibiotic therapy significantly reduced symptoms of turbinate swelling and obstruction and improved the overall rating of the treatment response. However, patients with acute and chronic sinusitis were not analyzed separately. In another study of adults with a history of recurrent sinusitis or chronic rhinitis who had evidence of superimposed acute sinusitis,[45] the addition of an intranasal corticosteroid to antibiotic therapy significantly shortened the time to resolution of symptoms (median, 6.0 vs. 9.5 days) and increased the rate of complete resolution at 21 days (94 percent vs. 74 percent). In nonallergic patients, there is no evidence that antihistamines, decongestants, or intranasal steroids are prophylactic or therapeutic for acute sinusitis.

AREAS OF UNCERTAINTY

The true incidence of bacterial sinusitis after viral respiratory infection, the incidence of complications after acute sinusitis, the factors that mediate a transition from acute to chronic sinusitis, and

Table 2. Common Antimicrobial Agents for the Treatment of Sinusitis.

Antimicrobial Agent	Adult Dose	Duration	Cost*	Contraindications and Warnings†
		days	*$*	
Penicillins				
Amoxicillin‡	500 mg every 8 hr 875 mg every 8 hr	7	8.61 19.74	
Amoxicillin–clavulanic acid (Augmentin)§	500 mg/125 mg every 8 hr	7	85.05	Previous history of cholestatic jaundice or hepatic dysfunction associated with treatment with amoxicillin–clavulanic acid
Amoxicillin–clavulanic acid (Augmentin XR)§	2000 mg/125 mg every 12 hr	10	55.00	Gastrointestinal upset
Tetracycline				
Doxycycline	100 mg every 12 hr on day 1, then 50 mg every 12 hr thereafter	10	9.04	Photosensitivity; neutropenia
Macrolides				
Erythromycin–sulfisoxazole	200 mg erythromycin ethylsuccinate and 600 mg sulfisoxazole fixed dose based on weight four times per day	10	4.00	Gastrointestinal distress; prescribe with caution for patients with arrhythmias; for concomitant use with medications metabolized by P-450 enzymes; for patients with liver disease
Azithromycin (Zithromax)§	500 mg once per day	3	45.69	Prescribe with caution if liver function is impaired; serious allergic reactions such as angioedema and anaphylaxis may occur
Clarithromycin (Biaxin)§	500 mg every 12 hr	14	117.60	Prescribe with caution if liver or renal function is impaired; potential for significant drug interactions; toxicity increases with concomitant administration of other medications
Ketolides				
Telithromycin (Ketek)¶	Every day	5		
Folate inhibitors				
Trimethoprim (160 mg)–sulfamethoxazole (800 mg)	One tablet every 12 hr	10 3[41]	12.20 3.66	Hypersensitivity to sulfonamides; megaloblastic anemia due to folate deficiency; pregnancy In Stevens–Johnson syndrome, fatalities due to severe adverse reactions may occur

the effectiveness of the treatment of symptoms with medications other than antibiotics are all unknown. Since most therapeutic studies assign treatment with antibiotics for 7 to 10 days, the data are limited for studies that use a shorter duration of such treatment. More research is needed to understand how the increasing rates of bacterial resistance may affect the choice of antibiotics to be used for treatment. Also, the potential effect that the decreased use of antibiotics for the treatment of uncomplicated bacterial sinusitis may have on the development of serious complications needs to be monitored and evaluated.

GUIDELINES

The Clinical Practice Guidelines of the American College of Physicians[40,46] (www.annals.org/cgi/content/full/134/6/495), which have been endorsed by the Centers for Disease Control and Prevention, the American Academy of Family Physicians, the American College of Physicians–American Society

Table 2. (Continued.)

Antimicrobial Agent	Adult Dose	Duration	Cost*	Contraindications and Warnings†
		days	*$*	
Cephalosporins				
Cefpodoxime proxetil (Vantin)§	200 mg every 12 hr	10	105.40	Adjust dose in cases of severe renal insufficiency
Cefprozil (Cefzil)§	250 mg every 12 hr 500 mg every 12 hr	10 10	20.80 169.60	Adjust dose in cases of severe renal insufficiency
Cefuroxime axetil (generic)§	250 mg twice a day 500 mg twice a day	10 10	75.60 135.20	Adjust dose in cases of severe renal insufficiency
Cefdinir (Omnicef)§	300 mg twice a day	10	87.00	Adjust dose in cases of severe renal insufficiency
Loracarbef (Lorabid)§	400 mg every 12 hr	10	120.80	
Fluoroquinolones				
Ciprofloxacin (Cipro)§	500 mg every 12 hr 500 mg every 12 hr	10 10	24.20 109.40	Concomitant use of theophylline
Gatifloxacin (Tequin)§	400 mg every day	10	91.50	Prolongation of QTc interval; hypokalemia; patients taking class IA or class III antiarrhythmic agents; significant potential for drug interaction
Levofloxacin (Levaquin)§	500 mg every day	10	99.50	Prolongation of QTc interval; hypokalemia; patients taking class IA or class III antiarrhythmic agents; significant potential for drug interaction
Moxifloxacin (Avelox)§	400 mg every day	10	93.80	Prolongation of QTc interval; hypokalemia; patients taking class IA or class III antiarrhythmic agents; significant potential for drug interaction

* The cost shown is the average cost of a unit of therapy in 2003, from Verispan's Source Prescription Audit (www.verispan.com).
† General warnings also apply to all antibiotics: avoid prescribing antibiotics for patients with known sensitivity to an antibiotic or antibiotics in the same class (i.e., cross-reactivity); prescribe with caution for pregnant women or nursing mothers; be aware of the potential for severe diarrhea due to pseudomembranous colitis (as caused by *Clostridium difficile*).
‡ On the basis of recommendations from the American College of Physicians,[40] this agent is the usual first-line agent. Amoxicillin is the preferred drug for use during pregnancy; erythromycin is a good choice for pregnant patients who are allergic to penicillin; other macrolides and cephalosporins are also acceptable choices.
§ This agent has been approved by the Food and Drug Administration (FDA) for the treatment of acute sinusitis.
¶ Approved for use in Europe, Latin America, and Japan. Awaiting final FDA approval for use in the United States.

of Internal Medicine, and the Infectious Diseases Society of America, conclude that most cases of acute sinusitis in ambulatory practice are caused by uncomplicated viral infection, and they do not recommend sinus radiography or antibiotic treatment. Instead, treatment of symptoms (e.g., with analgesics, antipyretics, and decongestants) and reassurance are recommended as the preferred initial strategy for management. For patients who have "severe or persistent moderate" symptoms (these terms are not defined in the guidelines but are generally considered sufficient to result potentially in lost workdays) and in whom there are specific findings of bacterial sinusitis, amoxicillin, doxycycline, or trimethoprim–sulfamethoxazole should be prescribed as reasonable first-line therapy. The use of CT should be reserved for patients who present with dramatic symptoms of severe unilateral maxillary pain, facial swelling, and fever or for patients who have not responded to antibiotic therapy.

CONCLUSIONS AND RECOMMENDATIONS

Acute bacterial sinusitis is suspected in the presence of facial pain and pressure, purulent nasal drainage, and symptoms lasting longer than seven days that do not respond to over-the-counter nasal

decongestants and acetaminophen. For the case described in the vignette, on the basis of the persistence of the symptoms, I would recommend treatment with amoxicillin, 500 mg three times daily for 10 days, and the continued use of nasal saline and decongestant therapy; the use of doxycycline or trimethoprim–sulfamethoxazole would also be a reasonable first-line choice. I would not recommend sinus radiography. If the patient's symptoms did not improve after 72 hours, I would switch to a different antibiotic, such as azithromycin, levofloxacin, or high-dose amoxicillin–clavulanate.

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