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Fungal Sinusitis: Diagnosis with CT and MR Imaging¹

Of 293 patients who underwent computed tomography (CT), surgery, and pathologic examination for chronic sinusitis, 25 had a diagnosis of fungal sinusitis at pathologic examination. Of these, 22 had foci of increased attenuation at CT (in four patients the mean representative CT number [Hounsfield unit] was 122.2 HU [SD, 8.2 HU]), and three did not. Of the 22, 19 patients (76%) met the CT criterion of this study (there was a 12% false-positive and a 12% false-negative diagnostic rate). Six of the 19 patients and one additional patient underwent magnetic resonance (MR) imaging, and all demonstrated remarkably hypointense signal characteristics on T2-weighted images. The findings at MR imaging therefore appear more characteristic of fungal sinusitis than the findings at CT. Furnace atomic absorption spectrometry showed increased concentrations of iron and manganese in mycetoma compared with their concentrations in bacterially infected mucus. This finding and the presence of calcium in the fungal concretion may explain the hypointense T2-weighted signal on MR images.

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FUNGAL disease affecting the paranasal sinuses is demonstrated radiologically as a nodular mucoperiosteal inflammation leading to homogeneous opacification of the sinus cavity (1-4). At computed tomography (CT) fungal disease has been described as a rim of soft-tissue attenuation of variable thickness along the bone walls of the paranasal sinuses (3). These findings, however, have proved indistinguishable from those of bacterial infection or neoplastic disease (1-4). Stammberger and Kopp et al (5-7) examined 140 patients with paranasal sinus fungal disease with standard radiography and pluridirectional tomography. They found nondescript areas of increased density in 50% of these patients, with well-defined, markedly hyperdense foci in 25%. They attributed such hyperdensity to calcium phosphate and calcium sulfate deposits in necrotic areas of the mycetoma (5,6).

CT, with its inherent high contrast resolution, allows for excellent demonstration of bone architecture, air in the sinuses, and soft-tissue masses in the paranasal sinuses and nasal cavity. CT should thus be superior to standard radiography and pluridirectional tomography in demonstrating fine areas of increased attenuation in soft-tissue masses. In this study we evaluated the premise that foci of increased attenuation can be a guide for diagnosis of fungal sinusitis, evaluated whether CT could allow detection of fungal concretions with greater accuracy than standard radiographic modalities used by previous authors, and examined the role of magnetic resonance (MR) imaging for this diagnosis.

PATIENTS AND METHODS

Study Population

From July 1, 1985, to December 31, 1987, 1,251 patients underwent CT exami-

nations for chronic sinusitis when they failed to respond to medical therapy or when the possibility of complications was entertained. From this population 293 patients were surgically treated. Patients with chronic sinusitis were selected for surgery on the basis of the severity of their symptoms, the potential for intracranial-intraorbital complications, or the demonstration of surgically correctable problems that had resulted in recurrent, acute inflammatory disease. Those patients suspected of having fungal disease at clinical or radiologic examination underwent surgery as part of their initial therapy. The criterion used for the diagnosis of fungal disease was the presence of foci of increased attenuation in a soft-tissue mass on a study unenhanced with contrast material.

All patients with a diagnosis of fungal sinus disease at CT or histopathologic examination of tissues removed at surgery were included in the study. Twenty-two patients were identified at CT. The group included 11 women and 11 men. Their ages ranged from 21 to 79 years (mean, 44 years). During the same period, three additional patients were identified at histopathologic examination. All three had undergone CT for chronic sinusitis and included one man and two women, with ages ranging from 24 to 46 years (Table 1).

CT Examination

The CT examinations were performed on a Somatom DR-3 scanner equipped with version E/F software (Siemens, Iselin, NJ). The scanning values were 4-mm section thickness, 3-mm table incrementation, 5-second scan time, 450 mAs, and 125 kVp. Multiplanar reconstructed images were obtained as necessary to improve demonstration of disease, its extent, and possible complications.

To evaluate the presence and appearance of hyperattenuated foci in fungal concretions, all examinations were performed initially without administration of contrast material. In nine patients who had or were suspected of having intracranial or intraorbital extension, contrast medium was administered intravenously. The CT scans were analyzed for the presence and extent of soft-tissue masses in

the nasal cavity and paranasal sinuses, areas of increased attenuation in the soft-tissue masses, and the presence and extent of bone erosion and intraorbital or intracranial invasion. For optimal evaluation of paranasal sinus soft-tissue masses and simultaneous demonstration of ethmoid sinus air passages, a window width of approximately 2000 and a level of -200 were used (8). The attenuation of paranasal sinus soft-tissue masses are similar to those of the orbital rectae muscles. Fungal concretions were suspected when areas of increased attenuation in these sinus masses appeared denser than the intraorbital musculature and were closer in attenuation to the regional cartilage and fine bone architecture. When these areas of increased attenuation were present, the windows were changed to maximally enhance the contrast between the increased attenuation, the suspected fungal concretion, and the surrounding inflammatory tissue (usually a window width of 300 and a level of 30) (Figs 1c-1e; 2b). Attenuation values of the focal areas of high attenuation in soft-tissue sinus masses were determined in four patients (Fig 1c-1e).

Six of the patients with proved fungal sinusitis were also examined with MR imaging with a Signa (General Electric, Milwaukee) 1.5-T or Technicare (Cleveland) 0.6-T unit and a head coil. The T1-weighted images were obtained with a short repetition time (TR) (600-800 msec) and a short echo time (TE) (20-40 msec) (TR/TE 600-800/20-40). The T2-weighted images were obtained with a long TR and a long TE (2,000-3,000/60-80). Images were reconstructed with a 256 × 128 data matrix acquired with either two or four excitations. The section thickness was 5 mm with an intersection gap of 1-2 mm. The signal intensities of the nasal cavity and paranasal sinus masses on T1- and T2-weighted images were compared with those of the normal turbinate mucosa. In addition, ten patients (seven with chronic bacterial sinusitis free of fungal disease and three with maxillary sinus squamous cell carcinoma) were used as preliminary controls to compare their MR imaging findings with those in patients with known fungal disease.

Pathologic Examination

Pathologists (J.I.E., L.C.H.) examined the surgical specimens, specifically searching for the presence of organisms (bacterial and fungal) and the presence of calcifications. Von Kossa stain and the Dahl method for calcium analysis were used to verify the presence of calcium in the mycetomas. The presence of hemorrhage was formally evaluated with Prussian blue stain to identify areas of hemosiderin deposition.

In addition, specimens of fungal concretion from two of the patients examined with MR imaging were evaluated with furnace atomic absorption spectrometry for the presence of iron, magnesium, and manganese. These values were compared with those from similar tests per-

Table 1
Findings in 22 Patients with Fungal Sinusitis

Age	Sex	History	Focal Hyperintensity at CT	Marked Signal at T2 MR Imaging	Presence of Hemosiderin	Abnormality
46	F	Allergies	MS	NA	+	Hemorrhage, thrombi, heavy <i>Pseudomonas</i> , <i>E coli</i> , <i>Streptococcus</i> spp
24	F	Asthma, allergies	MS	NA	+	Heavy <i>Streptococcus</i> spp pneumoniae
33	F	Allergies	SS	+	-	<i>Aspergillus</i> spp
45	F	Hypothyroidism, frontal craniotomy	FS	+	-	<i>Dreschlera</i> spp
21	M	No abnormality	MS, ES, SS	NA	-	<i>Dreschlera</i> spp
47	M	Asthma, allergies	SS	NA	NA	<i>Aspergillus</i> spp
45	F	Headaches	FS, ES	+	NA	<i>Aspergillus</i> spp
38	M	Nasal polyposis	MS, ES, SS	+	NA	<i>Aspergillus</i> spp
48	M	No abnormality	MS, ES, SS	+	+	<i>Aspergillus</i> spp
33	F	Allergies	MS, ES	NA	+	<i>Aspergillus</i> spp
79	F	Diabetes	SS	NA	NA	<i>Mucormycosis</i>
30	M	Diabetes, nasal polyposis	MS, SS (Figs 4, 5)	+	-	<i>Aspergillus</i> spp
61	M	Allergies	MS (Fig 3)	NA	+	<i>Aspergillus</i> spp
36	F	Nasal polyposis	SS	NA	NA	<i>Aspergillus</i> spp
37	M	Asthma	SS	NA	+	<i>Staphylococcus aureus</i> , <i>Pseudomonas</i> spp
57	M	No abnormality	MS	NA	-	<i>Aspergillus</i> spp
34	F	No abnormality	MS	NA	+	<i>Aspergillus</i> spp
57	F	Pansinusitis & hypopituitarism	MS (Fig 2)	NA	-	<i>Aspergillus</i> spp
54	F	Chronic sinusitis	SS	NA	-	<i>Aspergillus</i> spp
49	M	Chronic sinusitis	MS, FS, ES	+	+	<i>Dreschlera</i> spp
34	M	Nasal polyps	MS, ES	NA	+	<i>Aspergillus</i> spp
21	M	Nasal polyps	MS (Fig 1)	NA	NA	<i>Aspergillus</i> spp

Note.—MS = maxillary sinus, SS = sphenoid sinus, FS = frontal sinus, ES = ethmoid sinus, NA = not available, (+) = positive, (-) = negative.

formed on bacterially infected mucus from four patients.

RESULTS

Fungal sinusitis was diagnosed in the surgical specimens of 25 of 293 patients. Nineteen of these patients demonstrated focal hyperattenuation in the soft-tissue sinus masses (Figs 1c-1e; 2) on the CT examination. Three patients were incorrectly suspected of having fungal sinusitis (false positive). At pathologic examination, two of these patients demonstrated very thick bacterial pus, and one demonstrated a bacterial infection with hemorrhage. In addition, three patients were not diagnosed with CT (false negative) and were only identified as having fungal sinusitis after histopathologic findings proved positive. Thus in this group of 25 patients with a pathologic diagnosis of fungal sinusitis with or without suspicion at CT 19 (76%) were correctly diagnosed, with three (12%) false-positive and three (12%) false-negative diagnoses.

The age, sex, medical history, and CT and MR imaging findings of each patient are listed in Table 1. The CT

evaluation revealed hyperattenuated foci in the maxillary sinus in 14 patients, in the sphenoid sinus in ten patients, in the ethmoid sinus in seven patients, and in the frontal sinus in three patients. The lowest representative CT number was 89.0 HU (SD, 7.84 H); the highest was 211.4 HU (SD, 7.25 HU); and the mean was 122.2 HU (SD, 8.1 H). Areas of focal hyperattenuation varied in size (Fig 1c, 1d). The smallest area measured 4 mm in diameter; the largest nearly formed a cast of the maxillary sinus and measured 2.5 cm at its greatest width (Figs 1c-1e; 2b; 3). Furthermore, CT revealed invasion intracranially in four patients, intranasally in three, and intraorbitally and in the infratemporal fossa in one patient each. On plain radiographs the mycetomas appeared as either a homogeneous soft-tissue mass or in some cases as a well-defined attenuation similar to that seen with calcium or bone (Figs 1a, 1b; 2a).

Of the six patients who also underwent MR imaging, the short TR/TE images demonstrated that the fungal mass was iso- to hypointense compared with the normal mucosa surrounding the turbinates (Figs 4a; 5a).

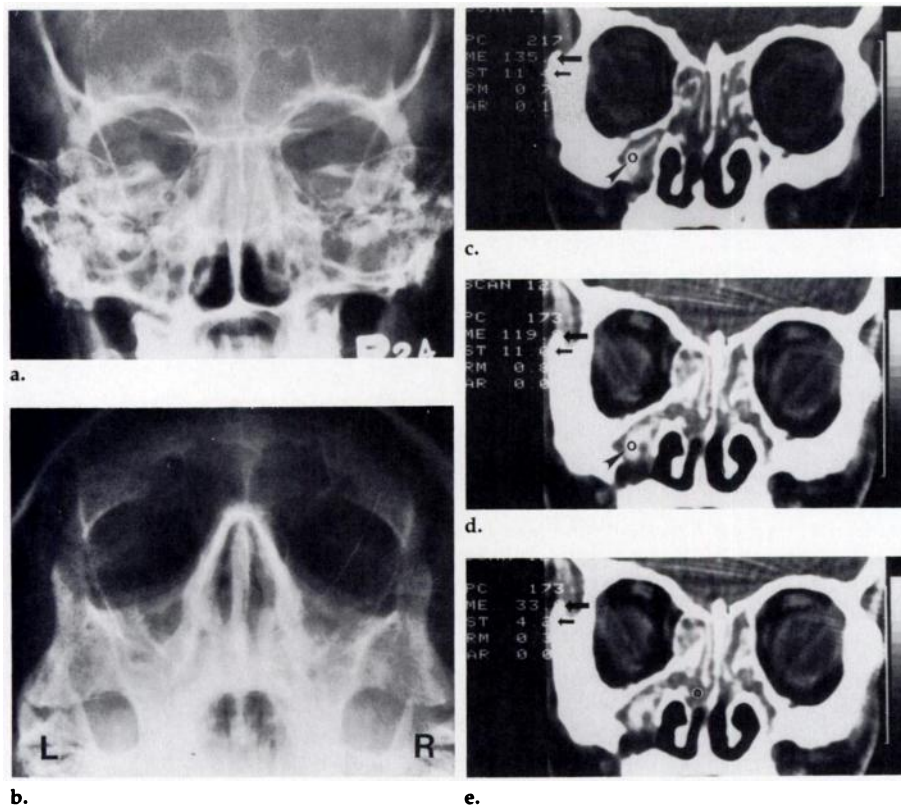
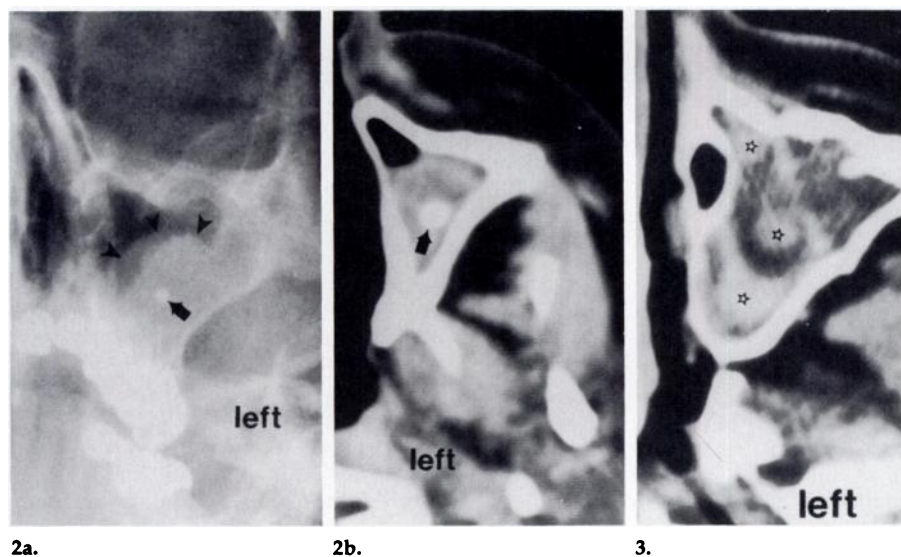


Figure 1. Standard radiographic and CT views of a patient with fungal sinusitis. (a, b) Caldwell and Waters views reveal mild mucosal thickening in the frontal sinus, moderate ethmoid opacification, and a diffuse opacity superimposed on the maxillary sinuses. L = left; R = right. (c-e) Coronal noncontrast CT scans through the anterior ethmoid and maxillary sinuses reveal a well-defined region of increased attenuation in the left maxillary sinus (arrowhead). Note the mean attenuation (ME, large arrow) and standard deviation (ST, small arrow) delimited by a round cursor (o) over the area of increased attenuation in c and d and over a soft-tissue density in the left middle meatus (e).



Figures 2, 3. Fungal sinusitis. (2) (a) Waters view demonstrates a polypoid mass in the left maxillary sinus (arrowheads), with a well-defined calcific hyperattenuation near its center (arrow). (b) Axial CT scan better defines the mass with its well-circumscribed calcific density (arrow). (3) Unenhanced axial CT scan shows left maxillary sinus occupied by a somewhat hypoattenuated mass in which patchy zones of hyperattenuation (stars) are shown. At pathologic examination *Aspergillus flavus* containing calcium was found.

On the long TR/TE images the fungal mass in the involved sinus had a greater decrease in intensity in the in-

volved sinus (the intensity being similar to that of air in the normal sinus), while the intensity of adjacent

soft-tissue sinus masses and brain increased markedly (Figs 4b; 5b). Table 2 summarizes the appearances at MR imaging seen in our control patients with mucoperiosteal inflammation and squamous cell carcinoma, and in one patient with concurrent neoplasm, hemorrhage, and bacterial inflammation (Fig 6). All patients with bacterial mucoperiosteal inflammation demonstrated a high T2 signal. The neoplasms had a lower signal intensity than bacterially infected mucosa, which had intermediate signal intensity. The subacute hemorrhage present in one patient (Fig 6) had a low T2 signal.

The results of the Prussian blue staining of the pathologic specimens to identify hemosiderin deposits are listed in Table 1. Of the 22 specimens, six were unavailable for evaluation. The patients with a false-positive CT diagnosis of fungal sinusitis all had positive findings for hemosiderin. In the remaining 14 specimens with CT and pathologic diagnoses of fungal sinusitis, half were positive and half were negative for hemosiderin.

The use of von Kóssa stain and the Dahl method for calcium analysis revealed the presence of calcium in each of the fungal specimens. Furnace atomic absorption spectrometry was performed to establish the presence of metal (iron, magnesium, manganese) in fungal concretions of two patients with proved *Aspergillus* sinusitis. The findings were compared with those at the metal analysis performed in four patients with proved bacterially infected mucus and no evidence of fungal infection. Iron and manganese, both electromagnetic elements, were found in larger quantities in the fungal concretions than in the bacterial mucus (Table 3).

DISCUSSION

Clinical Background

Fungal sinus disease may first be seen as a slowly progressing extramucosal fungus ball, a slowly invasive disease, or, in immunologically compromised patients, a fulminant infection with vascular invasion. Fulminant disease has more typically been attributed to mucormycosis, and benign extramucosal disease to *Aspergillus* species. A review of the literature, however, shows that appraisal of the aggressiveness of the disease on the basis of the organism alone is incomplete and invalid (9-16).

Extramucosal fungal sinusitis develops as a saprophytic growth in retained secretions in a sinus cavity. The disorder is usually benign and is rarely associated with mucosal invasion. The disease appears to be more frequent than previously recognized (5). This may be related to increased recognition of the problem. Since the disease usually requires surgical intervention, accurate radiologic diagnosis is important for the clinician. Typically, the disease is first seen as a chronic sinusitis that does not resolve with antibiotic therapy or maxillary sinus irrigation. Typically, however, the true identity of the disorder is not recognized until surgery or even until the subsequent pathologic evaluation. The treatment of extramucosal fungal disease entails removal of the fungal mucus, the restoration of mucociliary drainage, and sinus ventilation. A biopsy should be performed on the mucosa at the time of surgery to exclude mucosal invasion (5).

Radiologic Diagnosis

At plain radiography and pluridirectional tomography of the sinuses, fungal disease is described as having nodular mucoperiosteal thickening, absence of air fluid levels, clouding of ethmoid sinuses, sinus wall destruction (1-3), and focal increased attenuation (5-7). These characteristics, however, are sufficiently non-specific that distinction between chronic sinusitis and neoplasm remains difficult (1-4).

Stammler and Kopp et al (5-7) stated that the focal hyperattenuation seen on plain radiographs represents calcium phosphate and calcium sulfate deposits within necrotic areas of the mycelium. They reported that at plain radiography and pluridirectional tomography an increased attenuation was present 50% of the time. In half of these patients the increased attenuation was similar to that of a soft-tissue inflammatory mass, and in the other half, discrete, very dense areas were observed. These areas of hyperattenuation on plain radiographs have been attributed by some authors to zinc oxide from overfilled teeth (16,17).

The combination of metal ions and calcium salts in fungal masses should be more readily detected at CT. The presence of areas of increased attenuation in the paranasal sinus masses did indeed correlate well with fungal sinusitis in our population. However, since only 75% of the patients were

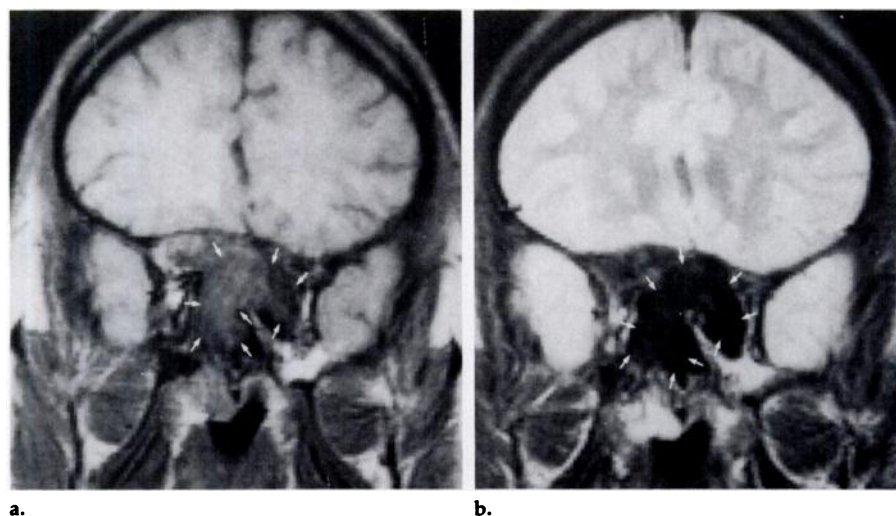


Figure 4. Sphenoid fungal sinusitis. (a) Coronal T1-weighted MR image through the sphenoid sinus reveals hypointense signal from a mass (arrows). (b) T2-weighted image shows an even lower intensity signal (arrows) than on the T1-weighted image.

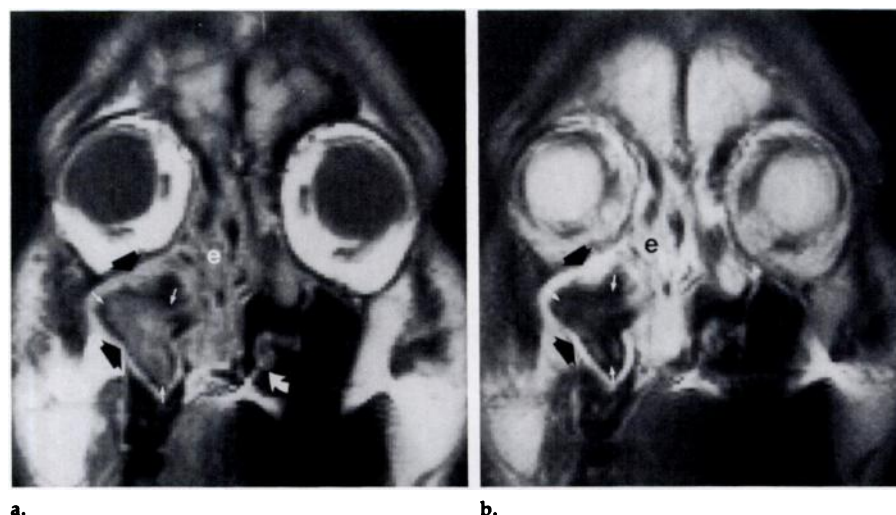


Figure 5. Fungal maxillary sinusitis compounding chronic pansinusitis. (a) Coronal T1-weighted MR image through the anterior ethmoid sinus depicts a soft-tissue mass in the anterior ethmoid sinus (e) isointense with contralateral inferior turbinate mucosa (curved arrow). Mucoperiosteal thickening (black arrows) along the bone wall of the right maxillary sinus has a similar isointensity. A soft-tissue hypointense mass (white arrows) occupies the center of the right maxillary sinus. (b) Coronal T2-weighted MR image demonstrates characteristic increased signal intensity of ethmoid sinus inflammation (e) with similar hyperintensity in the mucoperiosteal thickening (black arrows) of the maxillary sinus. The soft-tissue mass (white arrows) located centrally in the maxillary sinus has a much lower signal intensity than demonstrated on the T1-weighted image. Surgical-pathologic finding: aspergilloma.

diagnosed with this criterion, CT findings alone are not conclusive. It appears that thick pus or thrombus can on occasion exhibit similar findings. In addition, the findings in three patients did not meet our CT criterion. The amount of fungal disease in these cases, however, was very small. Other differential diagnostic entities include invasive carcinoma and sarcoma, meningo-sarcoma, ossifying esthesioneuroblastoma, osteoblastoma, and osteoma sur-

rounded by an inflammatory soft-tissue mass.

The MR imaging findings proved more specific than those at CT. Even though a smaller number of patients were examined with this modality, the outcome was identical in all cases. Several factors might decrease the signal intensity in a T2-weighted image, including the presence of calcium, air, or ferromagnetic elements (18). All of the fungal concretions in this study stained positively for calci-

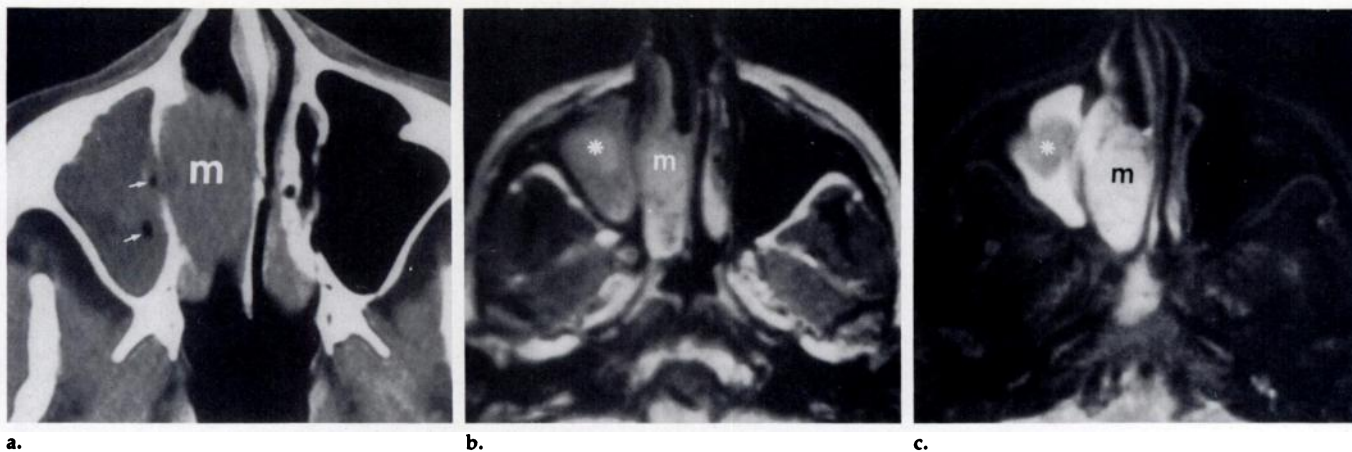


Figure 6. Subacute hemorrhage, mucoperiosteal reaction, and neoplasm in the nasal cavity and maxillary sinus. (a) Enhanced axial CT scan reveals nonenhancing soft-tissue mass (*m*) in the nasal cavity with a similarly attenuated mass occupying the adjacent maxillary sinus. Air density within the maxillary sinus (arrows) may be related to a recent biopsy. R = right; L = left. (b) Axial T1-weighted MR image through the maxillary sinus shows a mass with heterogeneous intensity in the maxillary sinus with a nearly round, larger anterior component (*) of higher intensity than its surroundings but similar in signal intensity to the mass in the nasal cavity (*m*). (c) Axial T2-weighted MR image shows that the larger anterior maxillary component (*) has a low signal intensity compared with the remaining mass in the maxillary sinus. This low signal intensity area proved to be subacute hemorrhage in an infected maxillary sinus. Nasal soft-tissue mass (*m*) is intermediately hyperintense; this proved to be a squamous cell carcinoma.

Table 2
Signal Intensity Characteristics of Paranasal Sinus Abnormality

Abnormality	On T1-Weighted Images	On T2-Weighted Images
Fungal infection	Isointense-decreased	Very decreased
Bacterial infection	Isointense-decreased	Increased
Polyps	Isointense-decreased	Increased
Acute hemorrhage	Decreased	Decreased
Subacute hemorrhage	Increased	Increased-decreased
Neoplasm	Isointense-decreased	Increased

Note.—Isointense = signal similar to noncongested nasal cavity mucosa; increased = higher signal than noncongested nasal cavity mucosa; decreased = lower signal intensity than noncongested nasal cavity mucosa.

Table 3
Furnace Atomic Absorption Spectrometry

	Patient	Magnesium	Manganese ($\mu\text{g/g}$)	Iron
Nonfungal sinusitis	1	62.0	0.19	2.1
	2	78.0	0.06	33.0
	3	148.0	0.03	5.4
	4	58.0	0.01	34.0
Fungal sinusitis	1	100.0	1.50	93.0
	2	50.0	0.96	448.0

um. Moreover, the presence of iron and manganese in quantities significantly greater than those seen in bacterially infected mucus might even better explain the sharp decrease in signal activity seen on T2-weighted MR images of fungal concretions. Iron, magnesium, and manganese were chosen for analysis because these elements are known to be essential in fungal amino acid metabolism (19,20). A test for the presence of iron was undertaken because the

presence of this ferromagnetic element could explain the decrease in signal intensity seen on the T1- and T2-weighted MR images. The mechanism of metal uptake by the mycelia is not clearly understood. An in-depth analysis of the elements present in fungal concretions is currently under way.

Preliminary evaluation of T1- and T2-weighted MR images therefore shows a significant difference between the appearance of fungal sinus

disease and that of hemorrhage (Fig 6, Table 2) (21). The T2 signal intensities of mycetomas, bacterial infection, and squamous cell carcinoma are also shown to vary (Figs 4–6, Table 2) (22). In addition to six of our patients examined with MR imaging, a patient clinically suspected of having nasal papillomatosis (examined by H.D. Curtin, MD, in Pittsburgh) manifested hypointense T1- and very hypointense T2-weighting on MR images; this suggested the diagnosis of fungal sinusitis, which was confirmed at pathologic examination after surgery. Additional studies will be required to see if these observations at MR imaging remain constant.

CONCLUSION

The demonstration of focal or diffuse areas of increased attenuation in paranasal sinus soft-tissue masses on unenhanced CT scans strongly suggests fungal involvement. CT is more sensitive than standard radiography or pluridirectional tomography in depicting the calcium or metal components of fungus infection. MR imaging was even more sensitive than CT in identifying a fungal concretion in a limited number of patients. On the basis of preliminary studies, decreased signal intensity on T1- and very decreased signal intensity on T2-weighted MR images seem to be characteristic of mycetomas. This may be due to the presence of ferromagnetic elements within fungal concretions. ■

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