avoided in this patient because of possible adverse effects on the fetus.[29] Biotype I of *H influenzae* identified from patient 1 has been described as more common than other biotypes in respiratory tract infections, although ampicillin resistance was not common in one study of biotype I organisms.[30]

An important complication of pericarditis is cardiac tamponade. Timely drainage either by surgical intervention or by means of repeated pericardiocentesis or catheter drainage is usually required for *H influenzae* pericarditis. Anterior interphrenic pericardiectomy has recently been recommended for drainage and prevention of constrictive pericarditis.[31] The patient in case 1 underwent pericardiectomy and had pronounced hemodynamic improvement following the procedure. Remarkably, our second patient and two previously reported patients had an uneventful recovery from their illness without drainage. None of these cases, however, had cultural confirmation of *H influenzae* purulent pericarditis. Aggressive diagnostic techniques and a drainage procedure are still recommended.

Although *H influenzae* is a rare cause of pericarditis in adults, it should be particularly considered in any patient presenting with an antecedent history of upper respiratory tract symptoms and a concurrent pneumonia, particularly with an associated empyema. Gram's stain of the sputum, pleural fluid or pericardial fluid (or all three) will often provide the diagnosis before culture confirmation; the use of counterimmunoelectrophoresis is another consideration. The prognosis is good with a combined approach of appropriate antimicrobial therapy that initially takes into account the prospect of bacterial resistance and adequate surgical drainage.

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Treatment of Cranial Osteomyelitis From Disseminated Coccidioidomycosis

RITCHIE GILLESPIE, MD
Reno, Nevada

COCCIDIOIDOMYCOSIS has been recognized for less than 100 years with as many as 100,000 cases occurring yearly in the United States. The fungus is acquired by the respiratory route and usually causes only asymptomatic infection found by skin test conversion. It is estimated to account for 70 deaths annually.[1]

The fungus is endemic to areas of the southwestern United States and Central and South America. Within the past four decades studies have suggested the incidence and severity of infection is related to race,[2,3] immune competence,[4] pregnancy[5] and age.[3] Blacks and Filipinos, patients with defects of immune competence, pregnant women and persons at either extreme of age seem more likely to have development of the infection and complications associated with dissemination.

Report of a Case

This 13-month-old black male child was in good health until 10 months of age when a slowly enlarging subcutaneous mass developed in the right maxillary region and in the right foot. The child was a military dependent whose family had recently been stationed in the San Joaquin area of California.

(Gillespie R: Treatment of cranial osteomyelitis from disseminated coccidioidomycosis. West J Med 1986 Nov; 145:694-697)

From the Department of Neurology, University of Nevada School of Medicine, and Veterans Administration Medical Center, Reno.

Reprint requests to Ritchie Gillespie, MD, Veterans Administration Medical Center, 654/151, 1000 Locust St, Reno, NV 89520.

There was no history of respiratory problems, skin rash or other systemic complaints. The child's growth and development were normal.

On physical examination on admission August 1983, he had a low-grade fever; a nontender, firm, 2- by 2-cm subcutaneous mass just inferior and lateral to the right orbit (Figure 1), and a diffuse, nontender, nonerythematous swelling in the right first metatarsal region.

Initial laboratory studies showed a leukocyte count of 30,000 per μl with a hematocrit of 29% and Westergren sedimentation rate of 140 mm per hour. A chest x-ray film and results of a urinalysis were normal. Coccidioidin and spherulin skin tests were negative, as were purified protein derivative, *Trichophyton* and *Candida* skin tests. A serum coccidioidal complement-fixation antibody titer was 1:256. A bone scan showed areas of diffuse uptake throughout the calvarium and the right first metatarsal. Skull x-ray films and a computed tomographic scan showed the soft tissue mass lateral to the right orbit and several confluent lytic lesions in the calvarium in both frontoparietal regions (Figures 1 and 2). Radiographs of the right foot showed changes consistent with osteomyelitis (Figure 3).

A biopsy specimen of the maxillary mass showed granuloma with spherules consistent with coccidioidomycosis. A regimen of amphotericin B was started that was administered for a total dose of 1 gram. Following institution of amphotericin therapy, more severe fevers developed that may have been related to use of the medication. Despite amphotericin therapy, the disease continued its relentless progression with worsening of the lesions seen on skull x-ray films, increased soft tissue swelling around the right orbit and right foot and new swelling in both frontoparietal regions.

Because of the lack of response to medication and persistence of the patient's anergic state, neurologic and orthopedic surgeons were asked to consider debriding the focal areas of bony involvement. On December 8, 1983, the child underwent debridement of the right foot lesion and a bifrontal approach to the cranial lesions.

At the operation the scalp flap was greatly swollen due to diffuse fungal cellulitis. Focal areas of calvarial erosion and granuloma formation were debrided with resection of bone extending into the right sphenoid wing and lateral orbital wall.

Figure 1.—A computed tomographic scan shows coccidioidal granuloma in the right periorbital region **(arrow)** with rarefaction of the sphenoid.

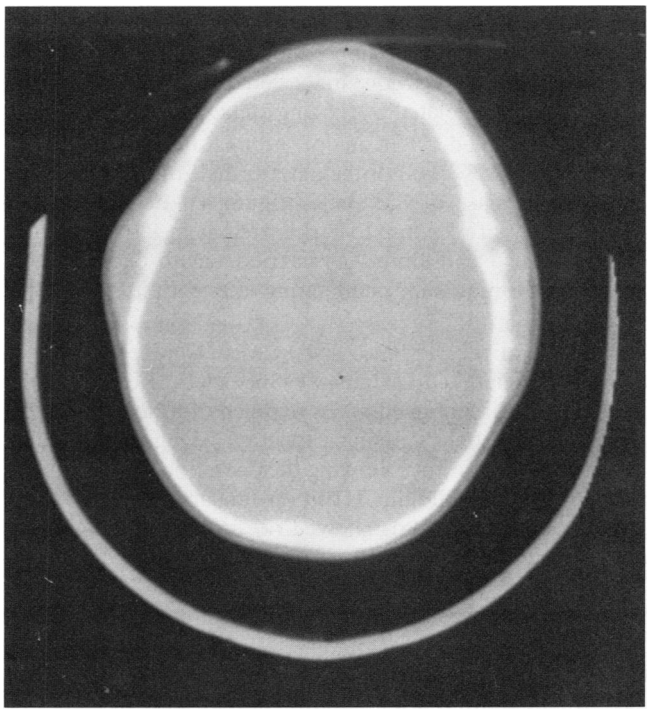

Figure 2.—A computed tomographic scan shows bilateral frontoparietal bone erosion and soft tissue swelling.

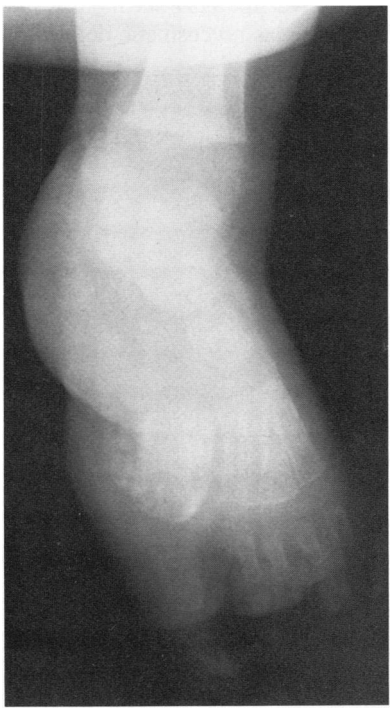

Figure 3.—Erosion and lytic and hypertrophic changes are noted in the right first metatarsal.

The patient's condition worsened postoperatively. Oral administration of ketoconazole, 100 mg, was begun in early January with gradually increased dosage to 200 mg a day. Skull and foot x-ray films showed progression of the bony involvement, and debridement of the right foot lesion was repeated. The most prominent area of involvement still appeared to be the calvarium, with skull x-ray films now showing evidence of total calvarial involvement with pronounced soft tissue swelling and edema of the entire scalp. Repeat skin tests remained negative and the serum complement-fixation antibody titer fell to 1:16. This fall in titer was unexpected and suggests suppression of the humoral immune system as this titer was done in the context of clinical deterioration usually associated with rising titers.

The patient underwent an operation on January 20, 1984, with a radical resection of the anterior half of the calvarium down to the base of the skull (Figure 4). In view of the patient's lack of response to earlier treatment, as thorough a debridement as possible was carried out to decrease the number of organisms challenging the patient's immune system.

Postoperatively a plastic helmet was fashioned to protect the areas where calvarium was resected. Ketoconazole therapy was discontinued and a regimen of itraconazole was started. The patient's immune function began to show evidence of improvement following the operation, with skin test reactivity to coccidioidin 1:100 on January 30, 1984. Follow-up skull x-ray films showed no further progression of bony erosion and the swelling of the scalp resolved. Antifungal therapy with itraconazole was continued and the patient was discharged.

Skull x-ray films on outpatient follow-up six months later showed substantial reconstitution of the previously resected calvarium with resolution of radiographic evidence of osteomyelitis in the nonresected bone. The coccidioidin skin test remained positive and coccidioidal complement-fixation antibody titers remained at 1:16. Over the next six months the skull reformed (Figure 5), there was no cosmetic deformity noted and the patient was asymptomatic. Outpatient therapy with itraconazole is continued on a long-term basis.

Discussion

Symptomatic persons with coccidioidomycosis usually present with cough, fever, malaise and pleuritic chest pains. Erythema nodosum occurs in 15% as a reflection of hypersensitivity to *Coccidioides immitis* and may be associated with a lower incidence of disseminated disease.[4] Failure of immune defenses to control the disease can lead to chronic pneumonia, miliary pulmonary coccidioidomycosis, pulmonary cavitation and extrapulmonary dissemination to skin, meninges, gastrointestinal and genitourinary tract, joints, liver and bone.

A diagnosis in asymptomatic patients often depends on positive coccidioidin and spherulin skin tests. In patients with disseminated disease, skin test reactivity often is absent, and, most commonly, complement-fixation titers increase with progression of the disease. In our patient clinical deterioration postoperatively was associated with a fall in titer, which is an unexpected occurrence. This may be related to the patient's young age or a suppressive effect of the large number of organisms on the patient's humoral immune system (or both). After the second more radical surgical debridement, evidence of a cellular immune response returned with the positive skin test reactivity. The persistence of a low complement-fixation titer at 1:16 would be consistent with the patient's clinical improvement.

Disseminated coccidioidomycosis may not be associated with pulmonary symptoms or changes on x-ray films. The diagnosis then rests on finding the fungus in specimens of urine, blood, biopsy or aspirate and an environmental history of exposure to an endemic area.

The role of host immunity in controlling the infection is becoming better defined,[6] and in our patient the disease progressed relentlessly until host immunity was reestablished.

In a recent series of 112 cases of coccidioidal osteomy-

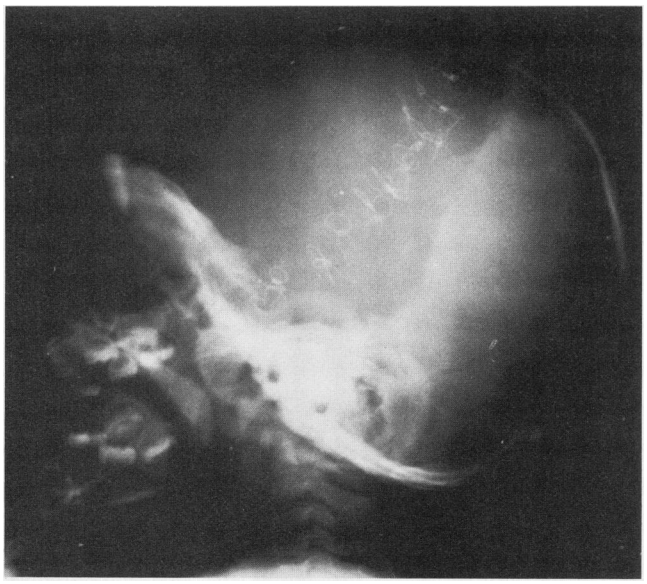

Figure 4.—A postoperative skull x-ray film shows the large area of infected bone removed at operation.

Figure 5.—A skull x-ray film shows reconstitution of resected calvarium and resolution of radiographic signs of osteomyelitis.

elitis, the skull was found to be involved in 13% of cases.[7] This involvement usually takes the form of small cystic areas of bone destruction and poses a significant risk of meningeal spread, which is found in as many as 50% of patients with disseminated disease, often as the only manifestation of coccidioidal infection.[8,9]

The possibility that an infection may overwhelm the host immune system with resulting immunologic nonreactivity to the infecting organism is suggested by the return of an immune response in our patient after decreasing the antigen load by extensive debridement. Recent trials using levamisole hydrochloride are also directed at influencing the host-parasite immunologic interaction by dynamically influencing host defenses.[10] We were prepared to start this treatment if our patient's immune response did not improve following the second debridement.

The improvement of cell-mediated immune responses with treatment has been noted by others.[4,11] In our patient the rapid regrowth of calvarium in the infected area and control of the infection coincided with the return of cellular immune competence as evidenced by positive skin tests. This suggests that the immune defect may be due to the infecting organism itself and offers theoretic justification for aggressively debriding infected areas and administering chemotherapy as a means of improving a patient's immune status by reducing the antigen load.

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