The adenoid cystic carcinoma may originate from the major or minor salivary glands in the oral cavity, and from the mucus glands of the upper respiratory airways. It intermittently grows slowly and aggressively over periods of five to 20 years. It spreads to the surrounding tissue, and despite repeated and wide resections, it keeps recurring. Its typical perineural spread causes pain and invasion of the base of the skull along the cranial nerves. Regional lymph node invasion is frequent. Also, distant metastases occur early and predominantly in the lungs, less frequently in bone, liver and brain. The ultimate prognosis is poor. Radiotherapy may induce temporary regression, but does not cure the disease. The results of chemotherapy do not seem to be promising either.

We have presented two cases of classic cribriform adenoid cystic carcinoma of the salivary glands in whom the lung metastases have regressed spontaneously. The lung lesions were detected five and ten years after the first resection of the original tumor. We have no clear explanation for these spontaneous regressions. Yet, the multiple resections of the primary tumor may have had a favorable effect by reducing tumor volume. Interestingly, the first patient, who was moribund when the lung metastases were detected, displayed progressive improvement in his general condition and regression of the lung metastases after starting a very severe diet.

**DISCUSSION**

The adenoid cystic carcinoma may originate from the

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Two-dimensional echocardiography has been shown to be a reliable diagnostic procedure in patients with valvular lesions due to fungal endocarditis. We describe a patient with four-chamber Aspergillus endocarditis localized to the nonvalvular endocardium. In this case, two-dimensional echocardiography failed to demonstrate cardiac abnormalities despite the presence of extensive endomyocardial disease at autopsy. The case emphasizes the diagnostic limitations of two-dimensional echocardiography in the absence of valvular vegetations.

Fungal endocarditis is a rare disease that occurs primarily in patients with prosthetic cardiac valves, chronic illnesses, and malignant neoplasms. Candida species are most commonly involved, while Aspergillus is seen infrequently. The antemortem diagnosis of Aspergillus endocarditis is rarely made, since classic signs of endocarditis are often absent, and blood cultures are usually negative. Therefore, early treatment of this disease has been extremely difficult.

Two-dimensional echocardiography has been shown to be a reliable diagnostic procedure in patients with endocarditis. Recently, this technique has been used to demonstrate vegetations of Aspergillus fumigatus on a "normal" cardiac valve. We describe a patient with A nidus endocarditis and myocarditis who had a normal echocardiogram despite the presence of extensive nonvalvular cardiac disease at autopsy. Our case emphasizes the diagnostic limitations of two-dimensional echocardiography in the absence of valvular vegetations.

Case Report

A 36-year-old Hispanic man had a one-year history of refractory anemia, perioral ulcerations, and erythema nodosum. He had received intermittent antibiotics and low-dose steroids, and bone marrow examination reportedly showed severe myelodysplasia. The patient was admitted to a local hospital on March 16, 1982, with fever, cough, and fatigue. Because of the possibility of evolving acute leukemia, he was transferred to University of California San Francisco Medical Center on March 19.

On admission, physical examination revealed a thin man in mild respiratory distress. The fundi were normal, and no oral lesions were seen. The neck was supple. Rales were heard at both pulmonary bases, and cardiac examination disclosed a grade 1/6 systolic ejection murmur. The abdomen was normal without hepatosplenomegaly. The findings from neurologic examination were unremarkable.

A 3 × 3-cm ulcer was noted on the right foot, and a 4 × 4-cm crusting lesion was seen on the left ankle. No Osler's nodes or splinter hemorrhages were found.

Laboratory values on admission were as follows: white blood cell count, 10,400/cu mm; platelet count, 9,000/cu mm; hematocrit, 32.8 percent; and hemoglobin, 11.2 g/100 ml. The peripheral blood smear showed 10 percent blast cells. Fine bibasilar pulmonary infiltrates were observed on the chest x-ray film. Initial blood cultures were negative for bacteria and fungi. Biopsy of the ulcer on the right foot showed a mononuclear perivascular infiltrate without bacterial or fungal organisms. A bone marrow examination showed severe myelodysplasia with 5 percent peroxidase-positive blast forms. The patient demonstrated cutaneous anergy to mumps, tuberculin, Trichophyton, and coccidioidin.

On March 24, Roth's spots were noted in both fundi; no change was detected in the patient's cardiac murmur. A two-dimensional echocardiogram showed normal left ventricular function and normal mitral, aortic, tricuspid, and pulmonic valves. The sizes of the cardiac chambers were normal. In particular, no bulky valvular vegetation was demonstrated (Fig 1).

The patient remained febrile to a maximum of 39.7°C over the next few days. Bronchoscopy revealed only nonspecific inflammatory changes, and cultures of bronchial washings were negative. Therapy with amphotericin B, ticarcillin, and tobramycin was begun, but a repeat chest x-ray film showed no resolution of the pulmonary infiltrates; antibiotics (including amphotericin B) were discontinued.
Valve up to 1 cm in diameter. Note that tricuspid valve is normal, with no evidence of fungal colonization.

On March 30, the patient became refractory to platelet transfusions, and the platelet count fell to 5,000/cu mm. On April 1, therapy with prednisone (120 mg daily) was begun. The patient’s fever abated, and his platelet count rose to 40,000/cu mm to 70,000/cu mm.

On April 11, a left pleural effusion developed, and the pulmonary infiltrates worsened. Therapy with ticarcillin and tobramycin was restarted. Thoracocentesis yielded nondiagnostic pleural fluid that was culture-negative. Chemotherapy was begun on April 12 with cytarabine (3 gm/sq m twice daily for six days), followed by m-AMSA (150 mg/sq m for three days). Chemotherapy-induced leukopenia ensued, and fever developed. Roth’s spots were again noted in both fundi. An open lung biopsy was performed on April 16. Microscopic examination showed mild fibrosing alveolitis without fungal or bacterial organisms, and multiple cultures of pulmonary tissue were negative. Fever persisted; blood cultures obtained on April 26 grew Staphylococcus epidermidis, and therapy with vancomycin was begun. The patient was subjectively improved but continued to have episodes of fever reaching 38.5°C.

On May 10, the patient complained of acute loss of vision. Neuroophthalmologic evaluation disclosed cortical blindness, and several new retinal hemorrhages were also noted. No other neurologic localizing signs or symptoms were found. A computerized tomographic brain scan showed bilateral parieto-occipital abnormalities consistent with infarcts. The patient regained his vision over the next three days. His fever abated, and antibiotics were discontinued on May 14, when the leukocyte count returned to normal; however, abdominal pain and distention developed, and tests of hepatic function became abnormal. On May 25, the patient became febrile and hypotensive. A chest x-ray film revealed a new left upper lobe cavitary lesion with a “fungus ball,” and therapy with amphotericin was restarted; however, on May 27, the patient became lethargic and unresponsive. He died on the following day.

Postmortem examination revealed four-chamber endocarditis and myocarditis with additional abscesses in the brain and lungs. Fungi consistent with Aspergillus were seen on microscopic section, and A nidus was cultured from pulmonary and cardiac tissues. The foramen ovale was probe-patent, and there was no colonization of the cardiac valves by fungi. Large vegetations (10 to 25 mm) were present in the atria and ventricles (Fig 2 and 3), with underlying colonization of the myocardium by fungal hyphae. Chronic atrophic pancreatitis was also present. The bone marrow was cellular without evidence of residual leukemia.

**DISCUSSION**

Fungal infection of the heart is a rare disease, accounting for less than 1 percent of all reported cases of endocarditis. Candida species are the most common etiologic agents, and these fungi can often be cultured from the blood. In contrast, Aspergillus is an unusual causative organism that is rarely cultured from the bloodstream. In most cases of fungal endocarditis, classic signs and symptoms such as fever, cardiac murmur, Roth’s spots, and large-vessel embolization may be absent, and only 60 percent of patients have elevated leukocyte counts. Thus, a high index of suspicion is important for the early detection of fungal endocarditis.

Most cases of Aspergillus endocarditis occur in patients with prosthetic cardiac valves. Natural valvular endocarditis due to Aspergillus has been reported in only 15 patients, most of whom had underlying chronic diseases or neoplasms. Aspergillus fumigatus is the most commonly isolated species, and the disease is uniformly fatal when therapy is instituted late in the course, even with successful early therapy, relapse can occur as long as two years after the initial infection. In patients with prosthetic valvular endocarditis due to Aspergillus, resistance to amphotericin B and 5-flucytosine is common, and early surgical excision of the infected valve remains the treatment of choice. Thus, early diagnosis of this disease is essential if therapy is to be effective.

Two-dimensional echocardiography provides a rapid noninvasive means of detecting valvular vegetations larger than 5 mm. In a recent case report, the procedure was found useful for the initial diagnosis of Aspergillus endocarditis on a natural valve, as well as for detection of recurrent vegetations on a valvular prosthesis, however, according to that report, the presence of fungal endocarditis was strongly suggested by large-vessel embolization and a new cardiac murmur, and the valvular vegetations were large, making the diagnosis by two-dimensional echocardiography relatively easy.

In contrast, our patient had a complicated course that tended to obscure the signs of endocarditis, even though some of these (Roth’s spots; cardiac murmur) were present. In this setting, two-dimensional echocardiography could have been particularly useful. Unfortunately, the lesions in our case were entirely nonvalvular, although the disease was quite extensive. Consequently, two-dimensional echocardiography failed to establish an early diagnosis of endocarditis, and adequate antifungal therapy was not given. Although it is possible that the echocardiogram was performed before the patient’s cardiac lesions developed, the presence of embolic phenomena and the extent of disease at autopsy make this possibility unlikely. By the time Aspergillus infection finally became evident on the chest x-ray films, a repeat echocardiography was performed before the patient’s cardiac lesions developed, the presence of embolic phenomena and the extent of disease at autopsy make this possibility unlikely. By the time Aspergillus infection finally became evident on the chest x-ray films, a repeat echocardiography was performed before the patient’s cardiac lesions developed, the presence of embolic phenomena and the extent of disease at autopsy make this possibility unlikely.

**FIGURE 2.** Right atrium and ventricle of heart showing vegetations (arrows) up to 1 cm in diameter. Note that tricuspid valve is normal, with no evidence of fungal colonization.

**FIGURE 3.** Large vegetation (2.5 cm) in left ventricle below mitral valve (arrows). No valvular vegetations are present.
gram might have demonstrated the large cardiac vegetations seen at autopsy; however, at this late stage in the disease, effective therapy would have been virtually impossible.

In summary, the usefulness of two-dimensional echocardiography in evaluating fungal heart disease must be qualified. Patients with large valvular lesions who are at risk for fungal endocarditis are amenable to early diagnosis by this technique; however, in patients such as ours with extensive nonvalvular disease but without valvular vegetations, early detection by two-dimensional echocardiography may be extremely difficult. We recommend serial evaluations in these patients and particular attention to the subvalvular endocardium. These steps may improve the diagnostic accuracy of two-dimensional echocardiography in fungal endocarditis.

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