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Clinical Pathologic Correlations

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A Novel Source of Enterococcal Endocarditis

ERIC MILBRANDT, M.D.

Department of Internal Medicine, St. Vincent Hospital, Indianapolis, Indiana, USA

Summary: An important element of the evaluation of patients with infective endocarditis is the determination of an infectious source. In approximately 20–45% of cases, no source is identified. Often the specific organism involved implicates the source, as is classically described by the association of *S. bovis* with colonic neoplasia. Other gut organisms have been reported to infect heart valves when colorectal pathology is present, but at far less frequency than *S. bovis*. This report deals with the case of a 75-year-old man with *Enterococcus faecalis* endocarditis of an unusual source—a cecal carcinoma that was causing intermittent appendiceal obstruction and infection. This case adds to previous case reports which suggest that the occurrence of enterococcal endocarditis in the absence of a classic infectious source should lead to a search for occult colorectal pathology.

Key words: enterococcal endocarditis, colonic neoplasm, chronic appendicitis

Case Report

A 75-year-old man was admitted to the hospital with fever, chills, and cough. The patient had been well until 2 weeks prior to presentation when he developed a febrile illness with a nonproductive cough and diffuse myalgias. His physician had treated these complaints with erythromycin and then azithromycin, with no improvement in symptoms. He sought care at the local emergency room.

Upon presentation, the patient complained of fever and appeared acutely ill. He stated that his cough was nonproductive and denied hemoptysis or blood-streaked sputum. He had no known sick contacts and no prior history of respiratory illness. He denied chest pain, palpitations, syncope, orthopnea, or paroxysmal nocturnal dyspnea, as well as nausea, vomiting, diarrhea, abdominal pain, or urinary tract symptoms.

His past medical history included diverticulosis, cholelithiasis, and mitral valve prolapse (MVP) with regurgitation (for which he received appropriate prophylaxis). His medications were lanoxin 0.125 mg p.o. q.d. and dyazide prn swelling. He had had knee surgery several years prior and a tonsillectomy as a child. He denied smoking, drinking, or intravenous (IV) drug use.

Physical examination revealed a well-developed, well-nourished man in mild distress. His temperature was 104.3°, heart rate 103 beats/min, respiratory rate 20/min, and blood pressure 151/72 mmHg. No rash or adenopathy was present. Head and neck examination was unremarkable, including good dentition and normal fundoscopic findings. His neck was supple without lymphadenopathy, bruits, jugular venous distension, or hepatojugular reflux. His lungs were clear with no rales or wheezes. Examination of the heart revealed mild regular tachycardia with a systolic thrill and a III/VI holosystolic murmur located just lateral to the left lower sternal border radiating to the axilla. Abdominal examination was negative for organomegaly, masses, or peritoneal signs. His peripheral pulses were 2+ and symmetric. The was no clubbing, cyanosis, edema, nor were there splinter hemorrhages. Rectal examination was heme negative, with a smooth mildly enlarged prostate and no masses. Neurologic examination was nonfocal.

Laboratory studies were obtained. Hemoglobin was 12.8 g/dl, platelet count 86,000 cells/mm^3, and white blood count 4,200 cells/mm^3 with a normal differential (normals 14–18,

Address for reprints:

Eric Milbrandt, M.D.
St. Vincent Hospital
Department of Internal Medicine
2001 West 86th St.
Indianapolis, IN 46260, USA

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150,000–350,000, and 4,500–11,000, respectively). Electrolytes were within normal limits, but the blood urea nitrogen and creatinine were 21 mg/dl and 1.7 mg/dl, respectively (normals 11–23 and 0.8–1.5). Gamma glutanic transaminase was mildly elevated at 93 mU/dl (normal 8–78), but no other liver enzyme elevations were present. Urinalysis was unremarkable. The chest radiograph was normal, with no infiltrate or evidence of congestive failure. Electrocardiogram revealed sinus arrhythmia, but was otherwise normal.

With the patient's history of MVP, loud murmur, and fever, the diagnosis of infective endocarditis (IE) was considered. Serial blood cultures were obtained and transesophageal echocardiography (TEE) was performed. The TEE revealed a partial flail mitral valve with eccentric mitral regurgitation and a 2 × 3 cm mobile echogenic mass adherent to the posterior mitral valve leaflet, which was suspicious for vegetation. There was normal left ventricular systolic function with an estimated ejection fraction of 50%.

A presumptive diagnosis of IE was made and empiric IV antibiotics (ampicillin and gentamycin) were initiated. Multiple blood cultures from Days 1, 2, and 3 of hospitalization were positive for *Enterococcus faecalis*. Urine culture was sterile.

After several days, the patient defervesced and his cough subsided. Blood cultures obtained on Day 4 and subsequent hospital days were sterile. Cardiac catheterization revealed minimal coronary artery disease and normal systolic function. The patient was transferred to our facility for further evaluation for possible mitral valve repair or replacement.

It was determined that the patient would a good candidate for surgical intervention, but there was concern regarding the repair of the infected valve without prior identification of the source of infection. Plans were made to continue antibiotics for an additional week prior to valve replacement to allow for sterilization of the site and for further search for the source of the enterococcal organism.

Enterococci are frequently encountered in urinary, biliary, and gastrointestinal tract infections.[1] With no history of urinary tract infection (UTI) and a negative urinalysis and culture, a urinary source was considered unlikely. The patient did have a history of cholelithiasis that had been symptomatic a few years prior, but he was currently asymptomatic and had never had an episode of acute cholecystitis. An abdominal ultrasound was obtained that verified the presence of cholelithiasis, but was negative for acute cholecystitis or choledolcolithiasis. A gastrointestinal consult was obtained to evaluate for other possible gastrointestinal sources, and a colonoscopy was performed.

The colonoscopy was initially unremarkable, revealing only noninflamed diverticuli. Upon advancement to the ce-

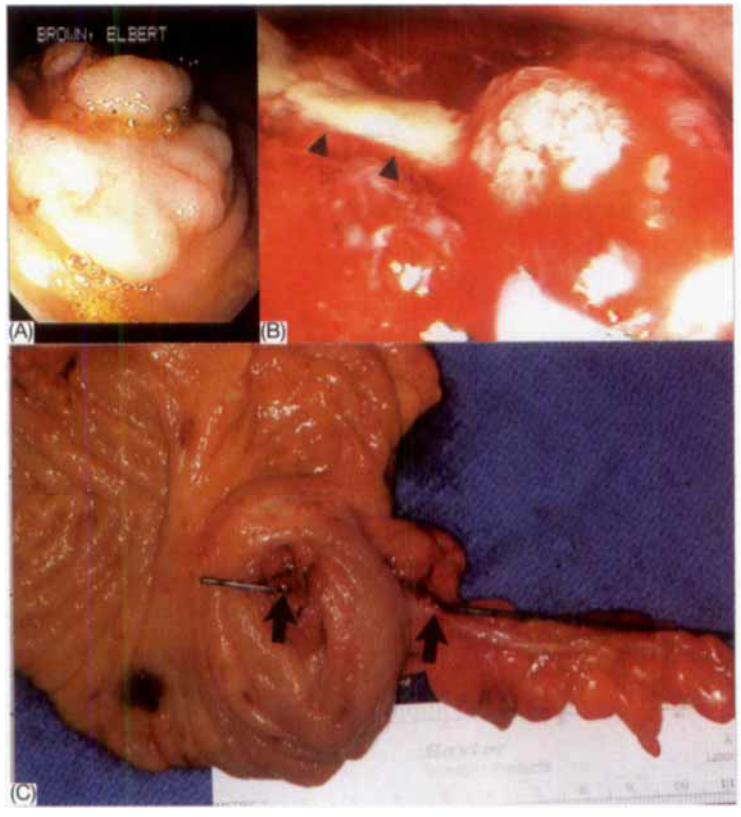

FIG. 1 (A) View through the colonoscope of the cecal polyp covering the appendiceal orifice (not visible). (B) The base of the polyp after partial endoscopic removal. Pus is seen emanating from the center of the lesion (see arrowheads). (C) Probe advanced proximally from the appendiceal lumen through the orifice and surrounding polyp tissue into the cecum (see arrows).

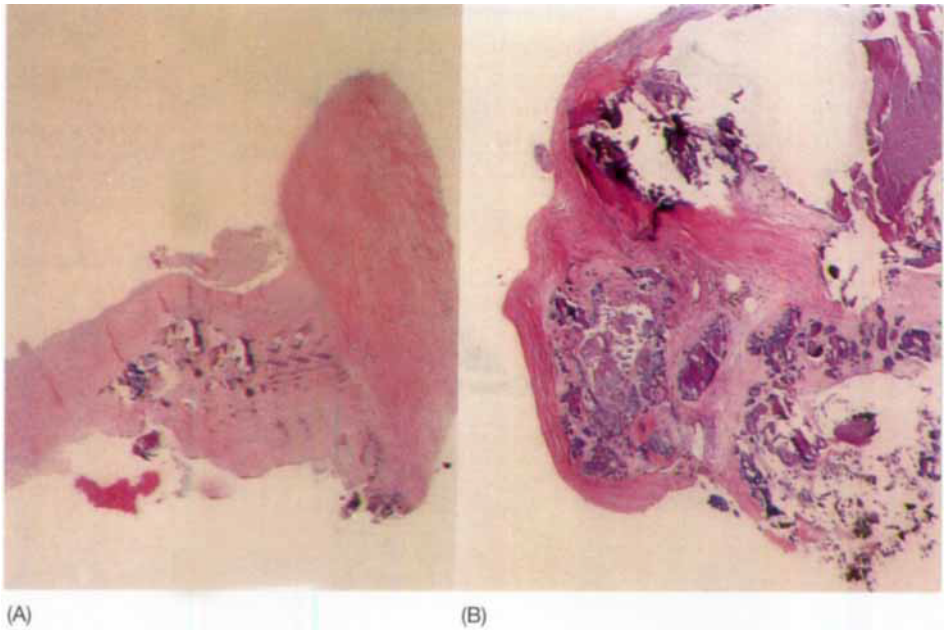

FIG. 2 Low (A) and high power (B) photomicrographs of the posterior mitral valve leaflet revealing fibrosis with areas of acute and chronic inflammatory cell infiltrates and nodular calcification.

cum, a 2.5 cm sessile polyp was encountered that covered the appendiceal orifice (Fig. 1A). The polyp was removed in a piecemeal fashion until about 30% of the polyp remained. Further removal was attempted using a saline injection technique to raise the base of the polyp. With subsequent probing, copious amounts of pus began emanating from the center of the lesion where the appendiceal orifice was located (Fig. 1B). In light of this obvious infection and the likely need for surgical resection, further attempts at polyp removal were abandoned.

Three days later the patient underwent laprotomy with right colectomy and cholecystectomy. An intraoperative cholangiogram showed no evidence of cystic duct obstruction, while pathologic examination of the gall bladder revealed cholelithiasis and fibrosis without signs of acute infection. Gross examination of the cecum revealed a 2.5 × 2.0 × 0.4 cm sessile polyp extending around the appendiceal orifice. Clear identification of the orifice was only possible by opening the appendix distally and advancing a small probe proximally (Fig. 1C). Passage of the probe through the orifice was somewhat difficult due the presence of the polyp. Sectioning of the appendix revealed a fibrotic wall and a pinpoint lumen. There was no evidence of acute infection. Microscopic examination of the polyp revealed adenocarcinoma in situ ($T_{is}N_0M_0$) without evidence of metastasis.

The patient tolerated the surgery well. After finishing a 6-week course of IV antibiotics, he underwent surgical repair of his mitral valve. Pathologic examination of the resected tissue revealed considerable fibrosis with areas of acute and chronic inflammatory cell infiltrates and nodular calcification (Fig. 2).

Discussion

Colonic neoplasms have been reported as the source of many infections, including endocarditis, meningitis, septic arthritis, and various visceral abscesses.[2] *S. bovis* is classically described as the organism responsible for colonic neoplasm-associated IE, but enterococci, *E. coli, Listeria, Clostridia, and Gemella spp* have also been implicated.[3–5]

Enterococci cause 5–20% of cases of native-valve IE and 6–7% of cases of prosthetic valve IE in the absence of IV drug abuse.[1] These infections involve both normal and previously damaged valves. As is the case in IE in general, no source of infection is identified in 19–47% of cases of enterococcal IE. When a source is identified, the genitourinary tract is the most prevalent, but biliary and gastrointestinal sources are also common.

This patient had no evidence for UTI, acute cholecystitis, or acute appendicitis. He did, however, have a cecal carcinoma overgrowing the appendiceal orifice that appeared to have restricted drainage of the appendiceal contents. It has been reported that occasionally a carcinoma in the cecum will lead to chronic intermittent obstruction of the appendiceal lumen, usually causing chronic recurrent symptoms that mimic appendicitis.[6] While this patient had no signs or symptoms of acute appendicitis, it appears that by intermittently obstructing the appendiceal orifice the neoplasm caused a subacute or chronic infection of the appendix which subsequently served as a source of infection. A review of the medical literature reveals at least four cases of colonic neoplasm-associated enterococcal endocarditis, with an additional four cases associated with noncancerous polyps.[2, 3] There were, however, no previ-

ously reported cases (enterococcal or otherwise) in which neoplasm-associated chronic appendicitis was the implicated source. Thus, this case represents a novel source of infective mitral valve endocarditis and adds to previous case reports that suggest that the occurrence of enterococcal endocarditis in the absence of a classic infectious source should lead to a search for occult colorectal pathology.

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