Marantic Endocarditis in Children and Young Adults: Clinical and Pathological Findings

Richard S. K. Young, M.D. and Edwin L. Zalneraitis, M.D.

SUMMARY The clinical and pathologic findings of 7 children and young adults with marantic endocarditis are reviewed. Cerebral embolic infarction attributable to the marantic vegetations occurred in 3 patients. The most common neurologic findings were altered mental status, seizures, and hemiplegia. Five of the 7 patients had had cardiac catheterization. Sepsis, pneumonia, hypoxia, disorders of coagulation, and renal failure were frequently present in these seriously ill patients. In each instance, the diagnosis of marantic endocarditis was unsuspected and established only at autopsy.

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Marantic Endocarditis (ME) is an uncommon disorder in children. Although marantic endocarditis is included in the differential diagnosis of embolic stroke in childhood, we were unable to find a documented case complicated by cerebral embolization in our literature review.

We examined the clinical and pathologic findings of patients with ME at the Massachusetts General Hospital between the years 1962-1979. A diagnosis of marantic endocarditis was accepted when the vegetation was composed primarily of an amorphous mixture of platelets and fibrin on a valve leaflet free of inflammation, ulceration, fungi or bacteria.

There were 7 young patients aged 5 days to 34 years. All of the patients had neurologic findings; 5 of the 6 brains examined had neuropathologic lesions. Cerebral embolic infarction occurred in 4 patients, and could be directly attributed to the cardiac vegetations in 3. Their clinical and neuropathologic findings are reviewed.

Report of Patients

Patient 1: An 11-year-old boy developed cervical lymphadenopathy, cough, and respiratory distress due to a mediastinal mass and pleural effusion. Biopsy revealed lymphoblastic lymphoma. After mediastinal radiation and chemotherapy, he improved and was discharged. Two months later, he was readmitted.
because of severe interstitial pneumonia. Respiratory failure required mechanical ventilation. On 100% oxygen, the arterial pH was 7.4, the Po2 41 and the PCO2 40 mm Hg. Broad spectrum antibiotics were given; blood cultures yielded no growth. Laboratory evidence of a coagulopathy included: platelets 12,000/cu mm, prothrombin time 16.5/11.4 seconds, partial thromboplastin time > 100 seconds, and fibrinogen 100 mg%.

On the sixth hospital day, he became lethargic and had a dilated and unreactive right pupil and left hemiplegia. A computerized tomographic (CT) brain scan showed an extensive low density in the territory of the right middle cerebral artery with mass effect. Despite therapy for cerebral edema he became comatose and died 2 days later.

At autopsy, multiple reddish-yellow friable vegetations were found on the free surface of the tricuspid and mitral valves. The lungs showed an acute interstitial pneumonitis without organisms. There were multiple pulmonary infaracts and focal papillary muscle infarction, both embolic in origin. Neuropathologic examination disclosed a swollen brain (1600 g) with subfalcial and uncal herniation. An amorphous fibrin platelet embolus occluded the stem of the right middle cerebral artery. There was a fresh hemorrhagic infarct in the territory of the right middle cerebral artery (fig. 1).

Patient 2. An 18-year-old boy suffered a traumatic rupture of the left mainstem bronchus in a motor vehicle accident and became hypoxic (pH 7.3, Po2 44, and PCO2 44 mm Hg on 100% O2). CT brain scan on admission was normal. Following operative repair of his bronchus, he was awake and able to follow commands. Refractory hypoxemia persisted, and he became progressively obtunded. Selective catheterization of the pulmonary artery showed increased vascular resistance. Blood cultures grew a bacillus species. A coagulopathy developed: platelet count 15,000/cu mm; prothrombin time 12.9/11.0 seconds; partial thromboplastin time 29.0 seconds; fibrin split products 1/512. Renal failure ensued, and he died on the fifth post-operative day.

At autopsy, multiple pink-tan friable vegetations were present on the leaflet edges of the tricuspid and pulmonic valves (fig. 2). There were multiple recent (non-adherent) pulmonary emboli in the small and large arterioles. Multiple fibrin thrombi were present in the kidney. Neuropathologic examination showed diffuse cerebral edema (brain weight = 1480 g), and small hemorrhages in the corpus callosum and cerebellum. Microscopically, there were multiple areas of cerebral and cerebellar ischemic necrosis due to microembolic occlusion by fibrin material identical in appearance to the marantic vegetations (fig. 3).

Patient 3. A young woman with presumed collagen vascular disease was well until age 21 when she suddenly became quadriparetic. Cerebral arteriography failed to demonstrate vascular occlusion. Multiple laboratory investigations were normal except for a false positive serology. Over the next 18 months she gradually regained full motor function, but then developed generalized seizures. Her joints became painful and swollen. She had some improvement on corticosteroids.

At age 28, she was evaluated for severe headaches...
FIGURE 3. An organized embolus occludes the lumen of a meningeal vessel. The elastica of the artery is distended and smooth.

and vomiting. A diagnosis of pseudotumor cerebri was made (CSF pressure, 600 mm H\textsubscript{2}O). Subsequently, she developed renal failure, hypertension, and congestive heart failure. The sedimentation rate was elevated (84 mm/hr). Tests for lupus erythematosus cells and antinuclear antibody were negative. She was admitted for the final time because of progressive obtundation, renal failure, and digital gangrene. The only neurologic deficit was dysphasia. The platelet count was 40,000 cu mm. She died of progressive cardiac and renal failure.

Autopsy disclosed emboli in the pulmonary artery branches, pulmonary infarction, bronchopneumonia, and empyema. Red-yellow granular material was present on the mitral valve. The kidneys were atrophic with many petechiae. There was no fibrinoid necrosis or vasculitis in any of the organs. Examination of the brain showed twenty small cerebral cortical and cerebellar infarcts of varying age (fig. 4). On microscopic examination, many of the arterioles in these infarcted regions were occluded by embolic material. Some of the arterioles had recanalized.

FIGURE 4. A cavitated cortical infarct is present.

Discussion

Marantic endocarditis, non-bacterial thrombotic endocarditis, and verrucous endocarditis are synonymous terms which refer to the presence of sterile vegetations on the heart valves. These vegetations are composed of an amorphous mixture of platelets and fibrin. Hammer first described these vegetations in a patient who had suffered embolic occlusion of the coronary arteries: "The aortic valves were not thickened, but smooth and shiny . . . there were fresh, soft whitish endocarditic excrescences which looked like little pillows that formed a network of granulation tissue resembling a condyloma." For many years these vegetations were considered to be only incidental pathologic changes in terminally ill patients.

In the past 2 decades, the potential of these cardiac vegetations to embolize to the pulmonary and systemic circulations has become well recognized. The most common sites of embolization in the adults with marantic endocarditis are spleen, kidney, brain, and coronary arteries. In children, emboli to the lungs and coronary arteries predominate. 4, 5 Embolic infarcts in the spleen, liver, kidney, and iliac arteries are less common. The rarity of cerebral embolization in children with marantic endocarditis remains unexplained. Paradoxical embolization has been previously noted, i.e. pulmonary infarcts have been reported in children with only mitral and aortic valve involvement. Similarly, systemic embolization may occur in patients with no intraventricular communication and with vegetations only on the pulmonary and tricuspid valves (see patient 2). These paradoxical emboli may arise from mural thrombi in the ventricles. 4

Patients with marantic endocarditis frequently have serious underlying diseases. Early reports focused on the association of ME with neoplasms, particularly mucin-producing adenocarcinomas. Hematologic malignancies are the next most common tumor associated with ME. Disseminated intravascular coagulopathy (DIC) is frequently present in patients with ME and is associated with an increased number of embolic events. Four of our patients had hematologic abnormalities consistent with DIC, while the other 3 had coagulopathies which were less well defined.

Clinical conditions not previously associated with ME, but present in our patients, were hypoxia and renal failure (table 1). Of our 6 patients with hypoxia, 4 had severe pneumonia, one had fat embolization, and the remaining patient had a bronchial tear. Renal failure, present in 4 of our patients, appeared to be secondary to hypotension in 2 patients, collagen vascular disease in one patient, and fat emboli in another patient.

Several recent reports have called attention to the increased incidence of marantic vegetations in patients who had catheterization of the pulmonary artery. 10, 11 Experimental insertion of a polyethylene catheter in the hearts of rabbits consistently established sterile vegetations on the heart valves within 3 days. 12 Five of our patients had either pulmonary artery catheteriza-
TABLE 1  Clinical Findings in Children and Young Adults with Marantic Endocarditis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Infection</th>
<th>Duration Final Illness</th>
<th>Coagn. Defect</th>
<th>Renal Failure</th>
<th>Hypoxia</th>
<th>Pulm Artery Cath</th>
<th>Hospital Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11 y</td>
<td>M</td>
<td>Lymphoblastic lymphoma</td>
<td>Acute interstitial pneumonia</td>
<td>8d</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Severely hypoxic; sudden left hemiplegia; massive cerebral swelling; coma.</td>
</tr>
<tr>
<td>2</td>
<td>18 y</td>
<td>M</td>
<td>Motor vehicle accident</td>
<td>Septicemia (Bacillus species)</td>
<td>5d</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Progressive hypoxemia; obtundation and coma; renal failure.</td>
</tr>
<tr>
<td>3</td>
<td>32 y</td>
<td>F</td>
<td>Collagen vascular disease</td>
<td>Broncho-pneumonia, pulmonary abscess</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Initially comatose; later fluctuating level of consciousness and dysphasia; progressive renal failure and multi-system deterioration.</td>
</tr>
<tr>
<td>4</td>
<td>5d</td>
<td>M</td>
<td>Pulmonic stenosis</td>
<td>Tricuspid regurg. Atrial septal defect</td>
<td>4d</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Severe hypoxia postoperatively; recurrent seizures; refractory hypotension.</td>
</tr>
<tr>
<td>5</td>
<td>8 y</td>
<td>F</td>
<td>Tetralogy of Fallot</td>
<td>Acute broncho-pneumonia</td>
<td>6d</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Severe hypoxia on 5th postoperative day; mechanical ventilation necessary; renal failure; coma.</td>
</tr>
<tr>
<td>6</td>
<td>19 y</td>
<td>F</td>
<td>Goodpasture's Syndrome</td>
<td>Pneumonia and septicemia, pseudomonas</td>
<td>3d</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Initially obtunded; severe hypoxemia led to trial of extracorporeal membrane oxygenation; refractory hypotension.</td>
</tr>
<tr>
<td>7</td>
<td>24 y</td>
<td>M</td>
<td>Motor vehicle accident</td>
<td>Septicemia (Enterobacter)</td>
<td>27d</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Initially alert, but level of consciousness fluctuated; followed commands inconsistently on day 16; hypoxemia led to trial of extracorporeal membrane oxygenation; progressive renal failure and unremitting sepsis.</td>
</tr>
</tbody>
</table>


tion or surgical manipulation of their cardiac valves within 2-21 days of death. Mechanical injury of the valve and presence of congenital heart disease may, in part, account for the larger proportion of younger patients in our series. As in other pediatric patients with ME, the right heart valves in our patients were more often affected than the left (table 2).

Lesions were present in 5 of the 6 brains examined, with evidence of embolic infarction from the marantic vegetations in 3. In 2 remaining patients, the brain lesions could have resulted from some other underlying condition. In one, the tentorial hemorrhage may have occurred after hypoxia. In the other, the multiple petechial hemorrhages might be attributed solely to fat emboli.

Each of the 3 patients with cerebral emboli had a different clinical presentation. Sudden hemiplegia developed in patient 1 due to embolic occlusion of the middle cerebral artery. This type of catastrophic presentation is commonly seen in the adult with ME. Adams has stressed the fact that unexplained hemiplegia in the setting of malignancy should suggest ME. A second type of clinical presentation is that of subtle and progressive neurologic decline as occurred in patient 2. Examination of this brain disclosed multiple occlusions of small arterioles by embolic fragments. This extensive small vessel disease may be related to a hypercoagulable state. In the third patient marantic endocarditis may have caused multiple, focal transient neurologic deficits. Eliakim states that ME may be a chronic process.

Marantic endocarditis is often diagnosed only at postmortem examination since the embolic events may be silent. Hematuria may signal the presence of renal emboli. Cardiac coronary emboli may be accompanied by chest pain or transient elevations of cardiac enzymes. The presence of a new heart murmur may also alert the clinician to the presence of ME. Neurologic events are the most dramatic manifestation of ME, but may be incorrectly ascribed to other processes. None of the 7 patients in this series was suspected of having ME. In patient 1, the sudden
hemiparesis was initially believed to be due to intracranial hemorrhage. In patient 2, his coma was attributed to preceding head injury. In patient 3, focal neurologic deficits were presumed to be due to "vasculitis."

Diagnosis of ME during life by echocardiography and treatment by valvular resection has been reported. No proven guidelines for prevention or management exist, but experimental data would suggest that pulmonary artery catheters may contribute to the development of ME and should be withdrawn as soon as possible. Early correction of coagulopathies, renal failure, and hypoxia may also benefit the patient with marantic endocarditis.

Acknowledgment

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References


Arch Path Lab Med 103: 76-78, 1979

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Table 2

<table>
<thead>
<tr>
<th>Case</th>
<th>Heart</th>
<th>Lung</th>
<th>Other</th>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Marantic endocarditis, mitral and tricuspid v.</td>
<td>Acute bilateral pneumonia</td>
<td>Multiple pulmonary infarcts with thromboembolism</td>
<td>Acute embolic occlusion of R. mid-cerebral artery with infarction</td>
</tr>
<tr>
<td>2</td>
<td>Marantic endocarditis, tricuspid and pulmonic v.</td>
<td>Multiple pulmonary emboli</td>
<td>Pulmonary hemorrhage Left bronchial tear</td>
<td>Multiple occlusions of cerebral and cerebellar arterioles by marantic emboli with infarction</td>
</tr>
<tr>
<td>3</td>
<td>Marantic endocarditis, mitral valve</td>
<td>Pulmonary emboli Bronchopneumonia</td>
<td>Renal petechiae Gangrenous changes in digits</td>
<td>Multiple small cortical infarcts due to embolic occlusion, recent and old with areas of cavitation</td>
</tr>
<tr>
<td>4</td>
<td>Marantic endocarditis, pulmonic valve</td>
<td>Acute patchy alveolar hemorrhage</td>
<td>Bilateral adrenal hemorrhage Acute hepatic infarct</td>
<td>Multiple, confluent tentorial hemorrhages</td>
</tr>
<tr>
<td>5</td>
<td>Marantic endocarditis, mitral and tricuspid v.</td>
<td>Acute severe bronchopneumonia Pulmonary edema</td>
<td>Focal, hemorrhagic glomerulonephritis</td>
<td>Not examined</td>
</tr>
<tr>
<td>6</td>
<td>Marantic endocarditis, tricuspid and pulmonic v.</td>
<td>Acute hemorrhagic bronchopneumonia</td>
<td>Renal hemorrhage and necrosis Fat emboli in kidney</td>
<td>No abnormalities noted</td>
</tr>
<tr>
<td>7</td>
<td>Marantic endocarditis, mitral and tricuspid v.</td>
<td>Severe pulmonary fibrosis</td>
<td>Diffuse, cerebral petechial hemorrhages due to fat emboli</td>
<td></td>
</tr>
</tbody>
</table>
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