Letters to the Editor

Cautious Interpretation of Data Regarding Myopericarditis Associated With Smallpox Vaccination

We congratulate Cassimatis et al. (1) for their excellent review of myopericarditis associated with smallpox vaccination. We suggest a different interpretation of the data regarding some important issues.

First, the true incidence of myopericarditis secondary to smallpox vaccination with Dryvax (NYBOH strain) vaccine remains unknown and it is likely higher than the quoted rates of one case per 9,360 (1), 10,000 (2), or 12,819 (3) vaccinations, which represent the recognition of overt, symptomatic myopericarditis in a highly selected, very fit military population. We suspect myopericarditis is underdiagnosed in this population because of the wide spectrum of presenting clinical symptoms and signs that confound accurate diagnosis, the potential for minimal or no-symptom cases that could lead to missed cases, and the characteristics of young, volunteer, military personnel who could conceivably overlook or minimize symptoms that do not limit their service duties. A higher rate of myopericarditis is supported by the 2% to 3% incidence of electrocardiographic changes after smallpox vaccination in Swedish military personnel in the 1960s (4,5). Importantly, a higher incidence of myopericarditis would likely be recognized if mass smallpox vaccination were applied to the general population with higher prevalence rates of cardiovascular and immunologic disease, in an attempt to protect citizens against smallpox bioterrorism.

Second, the long-term sequelae of myopericarditis due to smallpox vaccination remain unknown. Subclinical or overt abnormalities due to vaccinia viremia or its immunologic responses, such as direct viral toxicity or immune-mediated myocyte necrosis, persistent myocardial inflammatory infiltrates, or development of myocardial fibrosis, may manifest years later, with ventricular dysfunction, conduction system abnormalities, or sudden death. Although almost all recently vaccinated patients with myopericarditis recovered clinically, the possibility of residual low-grade myocardial inflammation and fibrosis cannot be excluded or prevented.

Third, endomyocardial biopsy probably is of greater than “limited utility” after smallpox vaccination. We advocate endomyocardial biopsy for all patients with suspected new-onset ventricular dysfunction (ejection fraction ≤45%) and symptoms of heart failure after smallpox vaccination. The rationale for this approach is the documentation of possible steroid responsive cosinophilic myocarditis, which occurred in one recent patient after smallpox vaccination, and the need to exclude uncontrolled vaccinia virus replication within the myocardial that may be responsive to immune globulin. Endomyocardial biopsy under echocardiographic guidance is a relatively safe procedure in experienced hands and may provide a definitive actionable diagnosis in high-risk patients (6).

It is a profound tragedy that vaccination against an eradicated disease whose elimination marked the single greatest human success against a communicable disease is now required for U.S. soldiers because of the threat of biowarfare. Current smallpox vaccine appears to carry significant risks of serious adverse events. The true incidence and long-term sequelae of current smallpox vaccine remain unknown.

Appor S. Gami
Joseph Murphy, MD
*Leslie T. Cooper, Jr., MD
*Mayo Clinic
Cardiovascular Division, Mayo East 16B
200 First Street SW
Rochester, MN 55905
E-mail: cooper.leslie@mayo.edu


REFERENCES


REPLY

We appreciate the comments on our review (1) of myopericarditis associated with smallpox vaccination. The recently published rates of myopericarditis may indeed be underestimates, for they are based on reporting of clinical encounters with symptomatic patients from an occupational cohort, as we noted previously (2). To better assess the true incidence rate, we will soon enroll volunteers in a prospective trial of smallpox vaccinees with baseline and follow-up electrocardiography, laboratory markers, and questionnaires.

We described the need to follow patients diagnosed with postvaccinal myopericarditis to establish whether long-term sequelae exist (1), and we recently have published the results of such follow-up (3). On the basis of these data, long-term sequelae are
not yet apparent, and recovery rates based on objective markers are high. We intend to continue follow-up for the next two to five years, while looking to evidence of any long-term sequelae.

The utility of endomyocardial biopsy after smallpox vaccination is uncertain. Given the inherent risks and low diagnostic yield of endomyocardial biopsy (1,4), as well as the high likelihood of full objective recovery after smallpox vaccine-associated myopericarditis (3), we would be remiss to recommend a potentially harmful procedure in all patients with depressed left ventricular function.

Although there has been one case of eosinophilic myocarditis that improved shortly after receiving corticosteroids (5), this one case is insufficient to conclude that corticosteroids will always be beneficial, even when eosinophils are seen on biopsy. However, the possibility that corticosteroids may uniquely benefit patients with eosinophilic myocarditis does warrant continued evaluation. Therefore, although we support endomyocardial biopsy in patients with symptomatic moderate or worse left-ventricular dysfunction, eosinophilic myocarditis does warrant continued evaluation.

ties not previously noted, demonstrating the need for continued caution when performing these exams.

A 48-year-old man with a left-sided, dual-chamber pacemaker placed on August 1, 1997, for neurogenic syncope (Thera DR 7960i, Medtronic Corp., Minneapolis, Minnesota) had metastatic multiple myeloma and significant pain. The MRI was performed to evaluate lower extremity neurologic deficits after attempted intrathecal catheter implantation.

The thoracic and lumbar spine regions were evaluated by sagittal fast spin echo (FSE) T2-weighted pulse sequences with fat saturation and pre/post contrast T1-weighted FSE pulse sequences in the sagittal and axial planes. Compared to previous computed tomography (CT) myelogram, MRI revealed more extensive cord compression at T9–10 from epidural tumor. The MRI demonstrated no epidural hematoma, possibly preventing an unnecessary laminectomy. A CT examination performed one month previously, because of pacemaker contraindication to MRI, demonstrated no epidural involvement.

Pacemaker evaluation immediately before MRI showed adequate battery voltage and impedance (Fig. 1) with DDDR pacing (lower rate 60, upper sensor and tracking rates 135 beats/min). M.A.R. (an anesthesiologist “facile in the ways of pacemaker programming”) disabled pacemaker rate responsiveness and monitored the patient with pulse oximetry plethysmography and electrocardiography (Millenia 3155 MVS monitor, In Vivo Research, Orlando, Florida). This monitor has no pacemaker artifact enhancement in the remote (MRI) mode.

Upon entering the MRI room, pacemaker magnet mode was activated (DOO pacing, 85 beats/min) until patient alignment with the MRI tunnel (heart rate returned to 74 beats/min). During MRI, pacing appeared to remain in DDD mode, with heart rates between 68 and 82 beats/min. Occasional pseudofusion beats were noted, but the ECG tracing was unreliable during MRI sequences. PVCs were noted during and between MRI scan cycles. No medication was given, and the patient did not complain of palpitations or chest pain (although he had back pain). He was quickly removed from the MRI upon completion of the 1.5-h exam.

Immediate pacemaker interrogation revealed onset of elective replacement (ERI) with a programming change to VVI pacing at 65 beats/min despite normal battery voltage and impedance (Fig. 2). This change eliminated all pacemaker diagnostic data storage. The “STATUS RESET” function in the programmer returned the pacemaker back to DOO pacing.