Skeletal Muscle and Myocardial Injury Associated with Metal Fume Fever

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Metal fume fever, a syndrome affecting welders and foundry workers exposed to nascent oxides of various metals (especially zinc), is a well-described clinical entity.[1-5] Most often the symptoms, including upper respiratory tract irritation, dry cough, metallic taste, and delayed chills, fever, myalgias, nausea, and pleuritic chest pains (which typically appear in the evening after work), are self-limited. Symptoms may recur with daily exposure, but they usually have the tendency to diminish in severity during the workweek, giving rise to the popular designation "Monday fever." Occasionally rales may be found on physical examination, and if the more toxic cadmium oxide fume is inhaled, noncardiogenic pulmonary edema may develop.[6,7] A case of skeletal muscle and myocardial injury is reported in association with typical episodes of metal fume fever, an association heretofore unreported in the literature.

REPORT OF A CASE

A 29-year-old welder was admitted through the emergency room of a community hospital with complaints of left-sided pleuritic chest pain, nausea, and diarrhea of several hours' duration. He also gave the history of a steady bitemporal headache, lightheadedness, weakness, myalgias, and nightly shaking chills with a nonproductive cough over the previous four workdays. An athletic nonhypertensive nonsmoker with no family history of cardiovascular disease, the patient reported a work history of having welded on galvanized angle iron, beginning four days before admission, with no respiratory protective equipment, although the welding occurred outdoors. No co-workers were similarly affected, and the patient denied having welded on any parts wet with degreasers or coated with cadmium or other materials other than the galvanizing (zinc). The patient further related having run two to three miles on each of two evenings prior to admission as well as having suffered a mild upper respiratory tract infection three weeks earlier.

On admission the patient was alert with warm, dry skin; the oral temperature was 36 °C (96 °F), pulse rate 56/min, respirations 20/min, and blood pressure 120/66 mmHg. Meperidine and promethazine given intramuscularly produced significant relief of chest pain. A sinus bradycardia was noted on monitoring, and oxygen was administered by nasal cannula. The chest was clear to auscultation and percussion, and the cardiac examination revealed a regular rhythm without murmurs, gallops, or rubs. The admission electrocardiogram showed a sinus bradycardia with normal PR and QT intervals and QRS duration, an axis of +60°, 1- to 2-mm ST elevations in leads I, III, and aV_F, 0.5-mm ST elevations in leads I, V_5 and V_6, and 35- to 37-mm R waves in leads V_4 and V_5. The admission hematocrit was 37.4 percent and leukocyte count 9.2 × $10^3/\mu L$, with a normal differential count. The erythrocyte sedimentation rate was 3 mm/h (normal male 0 to 10 mm/h); creatine kinase (CK) 301 IU/L (normal 15 to 110 IU/L) with 12.4 percent CK-MB fraction. The chest roentgenogram showed a cardiothoracic ratio of 14.5:28.3, with no other cardiopulmonary abnormalities.

The patient was placed in a monitored unit, where he continued to experience intermittent chest pain; response was obtained to sublingual nitroglycerin and nitroglycerin ointment. The brief episode of junctional tachycardia that was observed terminated spontaneously. On the day following admission, the creatine kinase was further elevated at 2,507 IU/L, with 1 percent CK-MB fraction. Repeat electrocardiograms showed decreasing R waves in leads I, II, and V_4 through V_6 over the first six days of admission, with normalization of the ST segments. On the fourth hospital day the creatine kinase peaked at 3,146 IU/L, with 2 percent CK-MB fraction, and the erythrocyte sedimentation rate was noted to be 28 mm/h, with a

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leukocyte count of 5.6 × $10^3/\mu L$. Urine obtained on the sixth day was negative for myoglobin, while the total creatine kinase was down to 456 IU/L (100 percent CK-MM fraction). Other laboratory studies included a normal urinalysis on admission, normal electrolytes and arterial blood gases on room air (day 2), and elevations of aspartate amino transferase (454 IU/L, normal 9 to 50 IU/L) and serum lactic dehydrogenase (LDH) (735 IU/L, normal 75 to 196 IU/L) peaking on day 4, with particular elevation of the LDH-1 fraction. The serum cholesterol was remarkably low at 112 mg/dL.

The patient was discharged home ten days after admission, having been pain-free for nearly seven days. The following day he underwent cardiac catheterization, which showed only slight dilatation of the left ventricle and mild hypokinesis of the anterolateral wall. Ventricular end-diastolic pressure was normal. Coronary anatomy was normal, with no fixed obstruction, although catheter-induced spasm was observed in the proximal right coronary artery. Verapamil, 80 mg orally twice daily, was prescribed but was discontinued after two months. He has subsequently been symptom-free on no medications, with normal exercise tolerance, although he reports that his previous employers "are afraid to hire [him]."

DISCUSSION

By clinical history repeated episodes of metal fume fever clearly preceded the patient's hospitalization. Laboratory confirmation through the determination of urinary zinc[8] was not attempted because of lack of standardization.[5] The history of exercise and severity of rigors seems inadequate to explain the massive elevation of CK-MM, and rhabdomyolysis was not confirmed by urinalysis or specific assay for myoglobinuria. The electrocardiographic abnormalities, along with elevations of CK-MB and LDH-1, suggest that myocardial injury occurred, although the case is atypical for either myocarditis, pericarditis, or myocardial infarction. Isolated elevation of serum lactic dehydrogenase has been reported with metal fume fever.[2] CK-MB can be elevated with vigorous exercise without apparent myocardial injury,[9] although the reversible electrocardiographic changes here argue against this explanation. There appears to have occurred a diffuse insult to striated muscle, both skeletal and cardiac.

Besides zinc oxide fumes, no other complicating toxic exposures are postulated (eg, cadmium oxide fumes or phosgene gas from the pyrolysis of chlorinated solvents). Although an association between metal fume fever and either skeletal muscle or myocardial damage has heretofore been unreported in the literature, the possibility of a causal relationship should be entertained in this case.

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