cardial effusion. Cutaneous tests were negative for tuberculosis and trichinosis, and examinations of the stool showed no parasites. The antinuclear antibody test and lupus erythematosus cell test were negative. The electrocardiogram remained abnormal, with a Q-S complex in leads V1 through V6, and a vectorcardiogram was interpreted as consistent with a destructive myocardial process, rather than infarction. Therapy with steroids was tapered over six weeks, the murmur of mitral regurgitation disappeared, and four months after the acute event, therapy with both prednisone and digoxin was omitted.

Studies subsequently performed at the Peter Bent Brigham Hospital, Boston revealed both cellular and humoral hypersensitivity to cromolyn sodium. Lymphocytes from this patient produced migration-inhibiting factor and incorporated additional amounts of tritiated thymidine in response to administration of cromolyn sodium in vitro. Serum was shown by Farr's technique to bind tritiated cromolyn by a fraction of IgE. This binding approached normal control levels by 4 and 12 months after therapy with cromolyn sodium was terminated.

At 36 years since the initial episode, the patient has experienced no further cardiovascular symptoms. The total eosinophil count remains below 1,000/cu mm. The findings from cardiac examination are normal. The electrocardiogram is unchanged.

**Discussion**

A variety of adverse responses to therapy with cromolyn sodium have been reported. In addition to cases of cutaneous eruption and pulmonary infiltrates, the occurrence of urticaria, angioedema, anaphylaxis, and polymyositis has been noted. Regardless of the type of hypersensitivity, eosinophilia has been an almost invariable feature.

This patient represents the first reported example of primary cardiac involvement, with evidence of pericarditis with tamponade, left ventricular failure, transient mitral regurgitation, and persistent electrocardiographic abnormalities. Peripheral eosinophilia, with total counts ranging from 8,000/cu mm to 12,000/cu mm, accompanied the syndrome.

The association of marked eosinophilia and cardiac disease was first recognized by Löffler, and numerous subsequent reports have related peripheral eosinophilia to endocardial fibrosis, myocarditis, pericarditis with effusion, and abnormalities of the conduct system. Pathologic examination has revealed extensive fibrotic reaction of the endocardium and subendocardial regions, with superimposed fibrin-platelet thrombi, myocardial scarring, and occlusions of small vessels.

There was no initial or subsequent evidence for an alternate source of the profound eosinophilia in this patient. Furthermore, serologic hypersensitivity to cromolyn sodium could be demonstrated. In light of these observations and the prompt resolution of symptoms after withdrawal of therapy with cromolyn sodium, this agent is presumed responsible for initiation of the marked eosinophilia, which in turn resulted in severe cardiac compromise.

Patients receiving cromolyn sodium, especially those with a past history of eosinophilia, should be monitored carefully for evidence of increasing peripheral eosinophilia and signs of cardiac damage. If significant eosinophilia occurs, withdrawal of therapy with cromolyn sodium should be considered.

**Acknowledgments**

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**References**


Rhabdomyolysis and Renal Failure following Status Asthmaticus*

**Kirpal S. Chugh, M.D.; Pravin C. Singhal, M.D.; and Gajendra K. Khatri, M.D.**

Acute renal failure developed in a 25-year-old man following status asthmaticus. He was found to have myoglobinuria. Vigorous contraction of the respiratory muscles and hypoxia were considered to be responsible for the development of myoglobinuria. Associated dehydration, in the presence of myoglobinuria, also contributed to the development of acute renal failure.

Recently, there has been a trend identifying the occurrence of nontraumatic rhabdomyolysis in an increasing number of conditions. Nontraumatic rhabdomyolysis has also been found to be an important factor in the genesis of acute renal failure after severe exercise, heat stroke, seizures, prolonged coma, and viral myositis;*
however, the occurrence of this condition in status asthmaticus and its contribution to the development of acute renal failure have not been stressed so far. We now report such a case.

CASE REPORT

A 25-year-old man known to have bronchial asthma was admitted with complaints of wheezing and respiratory difficulty of three days' duration. Prior to admission, he received intravenous therapy with aminophylline (500 mg) and oral therapy with ephedrine (25 mg three times daily). Physical examination revealed an orthopneic, dehydrated, and cyanotic subject. His respiratory rate was 62/min. Blood pressure was 110/70 mm Hg. Rhonchi were audible all over the chest. Examination of the cardiovascular and nervous systems did not reveal any abnormality.

Initially, the patient was given therapy with an infusion of aminophylline, parenteral administration of fluid (3.5 L), and supplemental oxygen. Subsequently, he was maintained on oral therapy with aminophylline (400 mg), ampicillin (500 mg), and prednisolone (20 mg three times daily). On the next day, the patient's respiratory rate decreased to 30/min, and he felt symptomatically better; however, he passed only 50 ml of dark brown urine despite correction of dehydration and subsequent massive therapy with a diuretic drug (furosemide; 200 mg). This young man had not passed dark brown urine (myoglobinuria) during the previous episodes of bronchospasms; however, none of the previous episodes was so severe or lasted for more than 24 hours, and his urine had never before been tested for the presence of myoglobin.

The following laboratory data were normal: hemoglobin level; hematocrit reading; leukocyte count; platelet count; prothrombin index; thrombin time; egulon lysis time; fibrinogen level; and serum level of electrolytes. The following levels were determined: blood urea nitrogen (BUN), 75 mg/100 ml; creatinine, 8.5 mg/100 ml; creatine phosphokinase, 90 Sigma units/ml (normal, 0 to 12 Sigma units/ml); uric acid, 13 mg/100 ml; aldolase, 75 units/ml (Sibley-Lehninger method; normal, 2 to 8 units/ml); calcium, 7.5 mg/100 ml; phosphorus, 7.2 mg/100 ml; and glucose (fasting), 110 mg/100 ml. Urinalysis showed a pH of 6.8, osmolality of 296 mOsm/kg, a sodium level of 76 mEq/L, and the presence of myoglobin by the technique described by Glaser et al.5 The urine yielded a negative reaction for fibrin degradation products. Microscopic examination revealed two to four white blood cells, occasional red blood cells, and two to three pigmented granular casts per high-power field. A chest x-ray film revealed a hyperinflated chest. An electrocardiogram showed no abnormality.

The patient remained oliguric (50 to 100 ml) for three days. On the fourth day of hospitalization, he went into a diuretic phase and thereafter showed steady improvement in renal function (Table 1).

DISCUSSION

Rhabdomyolysis is characterized by the triad of an elevated serum concentration of creatine phosphokinase, myoglobinuria, and the presence of pigmented granular casts in the urine.6 In the present case, too, markedly raised levels of creatine phosphokinase and aldolase and the presence of myoglobin and pigmented granular casts in the urine confirmed the diagnosis of rhabdomyolysis.

Myoglobinemia following severe exercise has been frequently reported.4 Vigorous and repeated contractions of intercostal, diaphragmatic, and accessory respiratory muscles during an asthmatic attack are equivalent to severe exercise. If the duration of the spasm is prolonged, as occurred in the present case, the degree of muscular injury is going to be greatly increased. Repeated coughing during the attack also involves vigorous contraction of skeletal muscles and adds to the severity of the myoglobinuria. In addition, hypoxia due to respiratory insufficiency leads to muscular ischemia and contributes to the muscular injury. In the present case, there was no suggestion of other reported causes of rhabdomyolysis, including hypokalemia, vascular occlusion, hyperpyrexia, heat stroke, convulsion, prolonged coma, and diabetic ketoacidosis.

The association between myoglobinuria and acute renal failure is well known. In the present case, deterioration of renal function and the pattern of urinary osmolality and excretion of sodium suggested the development of acute renal failure. Dehydration facilitates the induction of acute renal failure with myoglobinuria in experimental animals.6 Severe muscular exertion and poor intake of fluid because of physical exhaustion makes these asthmatic patients prone to develop dehydration. In the present case, too, dehydration facilitated the development of acute renal failure in the presence of myoglobinuria. We suggest that besides identifying myoglobinuria in such cases, prevention of acute renal failure can be accomplished by maintaining proper hydration during the period of the attack.

REFERENCES


Table 1—Laboratory Data

<table>
<thead>
<tr>
<th>Data</th>
<th>Day of Hospitalization</th>
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<tr>
<td>Urinary output, ml/24 hr</td>
<td>50  75  1,000  3,500</td>
</tr>
<tr>
<td>Urinary osmolality, mOsm/kg</td>
<td>286 290 300 380</td>
</tr>
<tr>
<td>Urinary sodium level, mEq/L</td>
<td>76  80  90  110</td>
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<tr>
<td>Serum aldolase level, units/ml</td>
<td>75  70  30  8</td>
</tr>
<tr>
<td>Serum creatine phosphokinase, Sigma units/ml</td>
<td>90  80  40  6</td>
</tr>
<tr>
<td>Urinary myoglobin</td>
<td>+  +  +  -</td>
</tr>
<tr>
<td>BUN level, mg/100 ml</td>
<td>75  100 110 20</td>
</tr>
<tr>
<td>Serum creatine level, mg/100 ml</td>
<td>9  11  10  2</td>
</tr>
</tbody>
</table>

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