However, both a coronary artery and a coronary A-V fistula must traverse the myocardium and the factor of myocardial relaxation, which plays an important role in augmenting coronary blood flow during diastole, is present. The myocardial relaxation factor, however, is not present in the ruptured aneurysm of the aortic sinus of Valsalva into the right heart. However, if the aneurysmal opening is within the right ventricle, a mechanism similar to the myocardial relaxation factor might be a result of the decrease in intraventricular pressure during diastole. In hemodynamics, the analogy to a coronary artery and a coronary A-V fistula is applied to a ruptured aneurysm of the aortic sinus of Valsalva into the right ventricle.[1,5]

Therefore, in the ruptured aneurysm of the aortic sinus of Valsalva into the right ventricle, the pressure gradient between the opening of the right ventricle and aortic sinuses is maximal during diastole and minimal during systole. Under these circumstances, maximal flow of left-to-right shunt through the opening would be during diastole and contributed to diastolic accentuation of continuous murmur. This accentuation correlated with the cineangiogram which demonstrated that most of the flow was in diastole.[9] This case showed only a diastolic murmur without aortic regurgitation. In this case, since the opening was small without a ventricular septal defect and was through the myocardium of the ventricular septum, during systole the opening might be constricted and presumably closed with myocardial contraction. The pressure gradient between the aortic sinuses and right ventricle might disappear in systole and the left-to-right shunt did not occur during systole through opening. Therefore, the blood flow through the opening was only during diastole and contributed only to a diastolic murmur. Furthermore, in this case, ventricular septal defect and aneurysmal obstruction of right ventricular outflow tract, which lead to systolic murmur, were not seen.[2,6,8] Thus, this patient demonstrated only a diastolic murmur without aortic regurgitation.

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Acute Respiratory Failure following Severe Arsenic Poisoning*

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A 47-year-old man had an episode of severe respiratory failure after acute intoxication with arsenic. Features of the initial clinical presentation included nausea, vomiting, and diarrhea, acute psychosis, diffuse skin rash, and marked pancytopenia. A peripheral neuropathy then developed which resulted in severe weakness of all muscles of the limbs, the shoulder and pelvic girdles, and the trunk. The neuropathy continued to progress despite treatment with dimercaprol (BAL in oil). Five weeks after the initial exposure, the patient was no longer able to maintain adequate ventilation and required mechanical ventilatory support. Improvement in the patient's neuromuscular status permitted successful weaning from the ventilator after one month of mechanical ventilation. Long-term follow-up revealed no further respiratory difficulty and slow improvement in the strength of the peripheral muscles.

The clinical features of arsenic poisoning have been well described and include a peripheral neuropathy which may be severe.[1] Although respiratory failure may complicate a wide range of neuropathic processes, including the Guillain-Barre syndrome, poliomyelitis, and acute intermittent porphyria, there are no detailed reports of respiratory failure as a sequel of acute arsenic intoxication.

We report a case of respiratory failure due to extreme weakness of the respiratory muscles in a patient who survived an acute intoxication with arsenic. The report details the time course of this complication of arsenic poisoning and documents the eventual reversibility of the respiratory failure.

Case Reports

A 47-year-old farmer was admitted to a local hospital with nausea, vomiting, and diarrhea. During the fourth hospital day, mental changes consisting of delusions and hallucinations developed, and the patient was referred to the Minneapolis Veterans Administration Medical Center.

The patient, at the time of transfer, was unable to give any coherent history. An interview with the patient's wife established that he was a farmer and had exposure to several kinds of insecticides. He used no drugs and was not a heavy drinker of alcohol.

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Physical examination revealed normal vital signs. The patient was alert but was agitated and uncooperative; he was oriented to person but not to place or time. He was paranoid and felt that the medical staff was attempting to harm him.

Examination of the skin revealed a morbilliform macular rash prominent on the trunk but sparing the face and extremities. No adenopathy was noted. Chest examination revealed decreased breath sounds at both lung bases. Cardiac and abdominal examination results were normal. Further neurologic examination revealed absent reflexes but no focal abnormalities. The patient moved all extremities but would not cooperate for testing of muscle strength or for the sensory examination.

Laboratory data on admission included a hemoglobin value of 11.3 gm/100 ml. The WBC count was 1500/cu mm, with 71 percent neutrophils. The platelet count was 40,000/cu mm. Serum electrolytes, glucose, calcium, and phosphorus values were all normal as were the prothrombin time, partial thromboplastin time, and thrombin time. Liver function tests revealed an increase in SGOT (177 IU) with a bilirubin value of 0.7 mg/100 ml and an alkaline phosphatase value of 70 IU. Renal function was normal, and the urinalysis was unremarkable. A toxicology screen for aspirin, alcohol, and sedative and antidepressant drugs was negative. Serum B_{12} and folate levels were normal.

The chest x-ray film showed bilateral pleural effusions, mild cardiomegaly, and normal pulmonary vasculature. Spirometry on the ward revealed an FEV_1 of 2.1 L with a FVC of 3.8 L. Arterial blood gas levels on room air revealed Po_2 of 68, Pco_2 of 29, and pH of 7.47. An ECG taken at the outside hospital was reviewed and showed prolonged QT interval of 0.50 m/sec, with a heart rate of 100 but was otherwise normal.

The pleural fluid was a transudate with 80 WBC and a protein of 1.8 gm/100 ml. The CSF was entirely normal with no cells, a glucose of 62 mg/100 ml, and a protein of 40 mg/-100 ml.

The patient's hemoglobin level dropped to 8.2 gm/100 ml; and the WBC on the third hospital day was 700/cu mm. A bone marrow examination revealed a hypercellular marrow with erythroblastic and megakaryocytic hyperplasia and neutrophilic hypoplasia. Megaloblastic changes were prominent, and there was also an increase in sideroblasts and siderocytes with an occasional ringed sideroblast.

The arsenic level on a urine sample obtained at the time of admission to the Minneapolis Veterans Administration Medical Center was 8.1 mg/L (normal < 0.05 mg/L). This result was available eight days after admission and therapy with dimercaprol (BAL in oil) was instituted.

The hospital course of this patient is summarized graphically in Figure 1. His mental status improved during the first hospital week, and the hematologic abnormality resolved within two weeks.

However, he developed progressive muscle weakness of such severity that he had essentially a flaccid quadraplegia within three weeks of the onset of his acute gastrointestinal symptoms. There was also a marked decrease in sensation over the entire body.

During the first two weeks of paralysis, the patient had no subjective awareness of dyspnea. On the 30th hospital day, he complained of an inability to cough effectively, and on the next day, he suddenly became extremely dyspneic. His pulse was 130 beats per minute and respirations, 32. Spirometry revealed an FEV_1 of 300 ml with an FVC of 500 ml. The maximum negative inspiratory force the patient could generate was —5 cm H_2O. Arterial blood gas levels showed a Po_2 of 48, with a Pco_2 of 45 and a pH of 7.39. Chest x-ray film revealed total collapse of the left lower lobe. A lung scan was normal except for slight decrease in perfusion of the left lower lobe.

The patient was intubated and mechanical ventilation was begun. After one month of mechanical ventilation improvement in the patient's neuromuscular status permitted successful weaning from the ventilator. The vital capacity was 1,400 ml at the time of weaning and improved over the next five weeks to 4,000 ml.

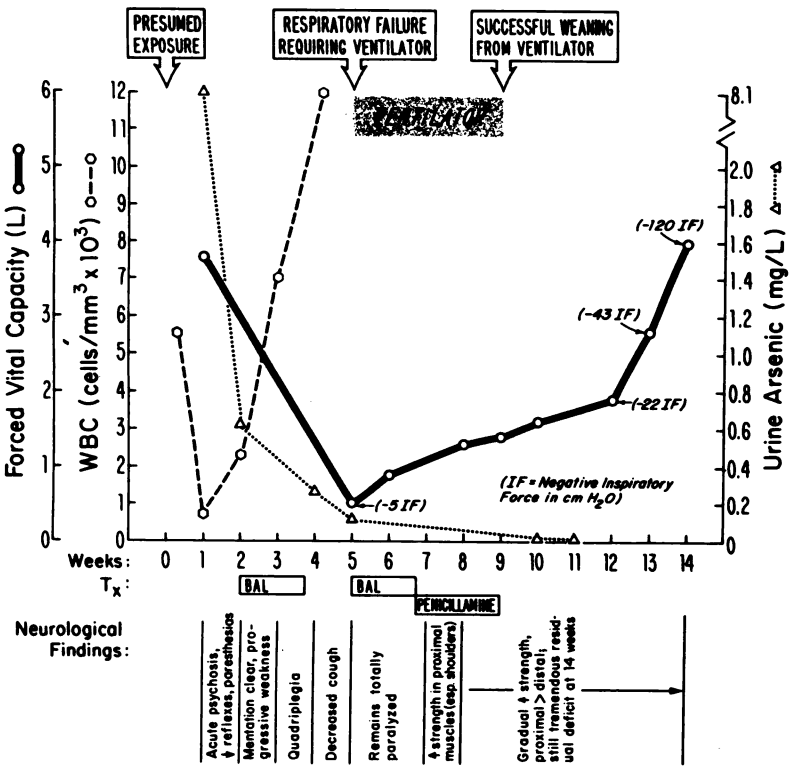

FIGURE 1. Hospital course of patient with respiratory failure following severe arsenic intoxication.

Long-term follow-up revealed no further respiratory difficulty and slow improvement in the strength of the peripheral muscles. One year after admission, the patient was able to walk with leg braces. He had good strength in the shoulders and upper arms but marked weakness of his hands.

Discussion

This patient had many of the classic clinical findings of severe acute arsenic poisoning. As described by Jenkins,[1] the sublethal form has initial features of an acute gastrointestinal disorder with abdominal pain, vomiting, and diarrhea. During the next several days, diffuse organ involvement may manifest itself as jaundice, skin rash, cardiomyopathy, and evidence of renal, pancreatic, or hematologic dysfunction. The first manifestations of neuropathy usually appear in one to two weeks.

Our patient had an initial acute gastrointestinal illness. The next phase of the illness, that of diffuse organ involvement, was manifested by acute toxic psychosis, skin rash, and cardiac and hematologic dysfunction. Cardiac toxicity of arsenic is well described, and a massive dose of arsenic may produce death due to myocardial failure early in the course of the illness. Cardiomegaly and a transudative pleural effusion suggested a milder degree of heart failure in our patient. A prolonged QT interval was noted on ECG; this is the most common ECG abnormality associated with arsenic poisoning.[2] The profound hematologic abnormalities noted in our patient were similar to the abnormalities seen in six patients reported by Kyle and Pease.[3] Each of their patients also had a WBC of less than 1,000/cm mm and the bone marrow recovered in each two to three weeks after cessation of exposure. Megaloblastic changes have also been previously reported.[3,4]

The neuropathy that occurs in arsenic poisoning generally occurs later than the acute toxic effects on other organs; it is a symmetrical polyneuropathy with involvement of both sensory and motor function. Chhuttani et al[5] have described nine patients in whom a rapid spread of the neuropathy within two to ten days after onset of gastrointestinal symptoms resembled the Guillain-Barre syndrome. However, as emphasized by Heyman et al,[6] arsenical neuropathy is associated with more prominent sensory manifestations than is the neuropathy of the Guillain-Barre syndrome. In addition, high spinal fluid protein levels (found in Guillain-Barre syndrome) has usually not been encountered with arsenic poisoning.

Although the neuropathy associated with arsenic poisoning may be severe, the literature does not include a well-described account of respiratory failure as a sequel of arsenic intoxication. Heyman et al[6] do refer briefly to one patient with Aldrich-Mees lines, high spinal fluid protein level, and respiratory paralysis. However, there is no prior information documenting the duration of respiratory support which might be necessary. There is also no documentation of reversibility following such support of respiratory failure. Our patient required mechanical ventilation for five weeks and slowly regained normal respiratory function over an additional six-week period.

This case also emphasizes again the difficulty of recognizing respiratory muscle weakness in profoundly weak and immobilized patients. The decrease in ventilatory function occurred insidiously and the patient, despite a markedly reduced vital capacity, had no sensation of dyspnea until further compromised by collapse of the left lower lobe. Patients with the Guillain-Barre syndrome are observed closely for respiratory muscle weakness because of the frequency of respiratory failure in that setting; our experience suggests that similar vigilance is necessary when the polyneuropathy associated with arsenic poisoning is severe.

The source of arsenic in this case was not located despite a thorough investigation of this patient's farm by the Minnesota State Board of Agriculture. Specifically, none of the insecticides he had been using contained arsenic. Somewhat surprisingly, such a negative investigation is not at all unusual. In 24 of 41 patients reported by Heyman et al,[6] the source could not be documented. In only one of the six patients with severe poisoning reported by Kyle and Pease[3] was the source of the arsenic identified, despite thorough investigation.

The use of dimercaprol to treat acute arsenic poisoning has been shown to be effective in preventing the occurrence of peripheral neuropathy if given within 18 hours of ingestion. The results of dimercaprol treatment in patients treated later are generally poor because arsenic, once bound to the tissues, is very tightly held and cannot be displaced by chelators. Our patient was treated approximately 14 days after exposure and already had evidence of peripheral neuropathy. Despite receiving this treatment, his peripheral neuropathy progressed. Once respiratory failure developed, another course of dimercaprol was given, followed by penicillamine, in an attempt to increase the excretion of the arsenic. However, we failed to show any increase in the concentration of arsenic in the urine during chelation treatment.

Long-term follow-up indicates that the patient is making slow progress and has been able to walk with assistance 12 months following ingestion. Continued slow improvement for as long as three years has previously been reported in other patients with initial profound neurologic deficits. Cautious optimism is warranted in cases of severe arsenic poisoning and vigorous support of ventilatory function is mandatory since the respiratory failure may be quickly reversible and the eventual outcome may be favorable.

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