Scorpion Envenomation and Myocardial Damage

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Scorpion envenomation is quite common in India, Southern Asia, the southwest of the United States, and in the north (Golan Heights) and south of Israel. Although the yellow scorpion is considered the most dangerous of the species since it causes cardiac toxicity, several case reports have described temporary electrocardiographic changes following envenomation by the black scorpion. We present a patient who was stung by a black scorpion and sustained myocardial damage accompanied by reversible ECG changes.

Case Description
A healthy 50-year-old farmer from the Golan Heights was admitted to our hospital after having been stung by a black scorpion on the large toe of his right leg. He felt severe pain radiating to the right groin, and an hour later began to feel numbness in his hands and lips, as well as general fatigue and malaise.

The physical examination was normal except for the single sting wound in the large toe of his right leg; heart examination was normal, without a third or fourth heart sound, heart murmur, or any other abnormalities; and a neurological examination did not demonstrate any damage or deficits. Prothrombin time, partial thromboplastin time, hemoglobin and hematocrit were within normal limits. The sedimentation rate was high (36 mm in the first hour), without leukocytosis or thrombocytosis. The biochemical results were within normal limits except for high creatinine phosphokinase levels — 1,076 units/L on admission with 60 units/L CPK-MB that decreased gradually in the next few days to normal (478 units/L on the second day with 24 units/L of CPK-MB, 261 units/L on the third day, and 185 units/L on the fourth day). The electrocardiogram demonstrated a normal sinus rhythm, 65 beats/minute, with enlarged (high and wide) P waves (0.12 mm length and 0.08 mm high with a dicrotic notch), without a prolonged PR interval. The P waves returned to normal width and length after 2 days of hospitalization. The QRS axis was normal (60 degrees) and remained so throughout the follow-up period. QRS length was within normal limits. There were deep large inverted T waves in leads II, III, and AVF, with huge U waves in precordial leads V1-V4. On the third day the inverted T waves became smaller but still remained inverted (almost isodiphasic) and the U waves disappeared. Chest X-ray was normal. Echocardiography did not demonstrate regional wall motion abnormalities.

Comment
The Golan Heights is an endemic area for yellow and black scorpions. To the best of our knowledge, the patient described here is the first to exhibit ischemic ECG changes (partly reversible) with myocardial damage but without pulmonary congestion, edema or other adrenergic stimuli. He remained calm during the hospitalization and showed no signs of hyperadrenalinism; however, he did manifest signs and symptoms compatible with the diagnosis of acute myocardial infarction.

Envenomation by a yellow scorpion causes adrenergic systemic signs that include sweating, tachycardia, psychomotor disturbances, and elevation of blood pressure. Black scorpion envenomation also causes temporary ECG changes, and poison from the black scorpion has been shown to be cardiotoxic as well, but less so than the yellow scorpion toxin.

Of the 650 varieties of scorpions, very few are dangerous to humans. The dangerous species are indigenous to the southwest of the United States, India, and the Far East. In Israel they are found in the south of Israel, in Jerusalem, in the Judean desert, in the Lower Galilee region and the Golan Heights. Scorpion poison is stable in high temperatures and is composed of low molecular weight proteins. It has 65 amino acids that are connected by disulfide bridges. In vivo studies have shown that the poison concentrates in the presynaptic area (in the neuromuscular junction) and causes depolarization that leads to a rapid flow of calcium ions and a release of acetylcholine, which causes convulsions and tremor [1]. It was demonstrated that this poison is also cardiotoxic and increases the rate of contraction of myocardial fibers. In low concentrations it shortens the amplitude of the contraction, but in high concentrations it causes fibrillation of the heart muscle [1].

Gueron et al. [2] described five patients who were stung by yellow scorpions (Buthus quinquestriatus) and developed acute congestive heart failure with pulmonary edema and ECG signs of acute myocardial infarction. These changes reversed to normal within 48 hours. Another patient who was envenomated by a yellow scorpion developed hypertension, sweating, priapism, and ST-T
electrocardiographic changes. These changes returned to normal following treatment with alpha and beta blockers [3]. An additional two patients envenomated by black scorpions lived in a non-endemic area in Israel, and both suffered temporary cardiac involvement manifested by ECG changes that reverted to normal within 24 hours with myocardial damage [4]. In our patient, the ECG and the enzymatic picture were compatible with acute myocardial infarction.

References

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GAD, a Single Autoantigen for Diabetes

Type I diabetes is an autoimmune disease that affects 0.3% of the world’s population. It is caused by autogressive T cells that infiltrate the pancreas and eventually destroy the insulin-producing beta-islet cells. This results in higher glucose levels, which are normally kept in check by insulin. Autoimmune diabetes usually affects young people, who are then dependent on an artificial source of insulin for life. The identity of the self proteins in the pancreatic islets that target the cells for autoimmune destruction has long been debated. Yoon et al. have reported a real breakthrough in understanding the etiology of type I diabetes. They showed that a single self protein expressed by beta-islet cells — glutamic acid decarboxylase (GAD) — controls the development of diabetes in the non-obese diabetic (NOD) mouse.

There are two forms of GAD, GAD65 and GAD67, both of which are expressed in brain cells and in beta-islet cells, where their function is not clear. GAD65 has come under the scrutiny of diabetes researchers because some of the earliest autoantibodies found in prediabetic patients are GAD-specific, although other autoantibodies, such as those directed against insulin, are also present. Furthermore, intrathymic, intravenous, or oral administration of GAD65 has, in some instances, significantly delayed the onset of disease in NOD mice. Although intriguing, these observations still do not implicate GAD in the initiation of the disease process.

The simple and bold strategy adopted by Yoon et al. was to determine whether the development of diabetes in NOD mice required the expression of GAD. They accomplished this by generating transgenic NOD mice that expressed a GAD anti-sense gene exclusively in beta-islet cells, such that expression of both GAD isoforms was prevented in these cells (but not in brain cells).

This strategy would have failed had GAD an essential function to perform in β-islet cells, which apparently it does not. Yoon and his team were thus able to observe a strict correlation between the presence of GAD protein in beta-islet cells and the development of diabetes. In those animals that efficiently expressed the antigens, there was no beta-islet GAD expression and the mice remained free of diabetes.

Finally, there were fewer T cells reactive to other beta-islet-specific autoantigens such as insulin in GAD-less NOD mice but not in nontransgenic control animals. These results show that GAD is the essential autoantigen that initiates the disease by activating GAD-specific T cells. As the disease progresses, T cells reactive against additional beta-islet-specific antigens become activated.

The demonstration that a single self protein initiates autoimmune diabetes could have important consequences for therapeutic strategies, provided, of course, that these findings can be extended to the human disease. It is likely that GAD is also the initiating autoantigen in human type I diabetes because GAD-specific autoantibodies are among the first to appear in the prediabetic phase in human patients. Transplantation of human islets that are rendered GAD-less by introduction of an anti-sense transgene in vitro might benefit diabetic patients. Alternatively, if the relevant GAD autoantigenic peptides were expressed in all tissues of the body, including the thymus, it may be possible to induce GAD-specific tolerance. It is conceivable that such an approach might eliminate type I diabetes from the human population.

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