Emetine Toxicity with Electrocardiographic Abnormalities

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Seven case histories are presented illustrating various aspects of the noxious effects of emetine on the heart. T-wave changes, S-T segment deviations, and partial heart block are demonstrated. A case of frank myocardial infarction in a young man occurring during the administration of emetine is described. Finally, both persistence and lability of emetine-induced changes are illustrated.

Toxic effects of emetine on the heart have long been recognized and some deaths have been attributed to the use of this drug. Objective evidence of its untoward action on the myocardium has generally been presented in the form of electrocardiographic changes, but there have also been some confirmatory necropsy reports. In spite of the undoubted ill effects of this drug in some cases, the opinion is held that indications for its use still exist and that its toxic actions have been overemphasized. Although excellent cases have been documented, many have suffered from incomplete electrocardiographic investigation and inadequate control observations.

Approximately 50 per cent of patients receiving the usual course of emetine hydrochloride intramuscularly manifest some electrocardiographic abnormality. Most of the changes were transient, but some persisted many months. Klatskin and Friedman found electrocardiographic abnormalities in 49 of 93 patients who received emetine. The changes consisted of prolongation of the P-R interval, decreased amplitude or inversion of T waves, slurring and notching of the QRS, extrasystolic beats, a shifting pacemaker, and nodal rhythm. They also stated that the chest pain associated with emetine toxicity has none of the usual characteristics of coronary pain. Hardgrove and Smith reported a case that they initially considered as myocardial infarction on the basis of precordial pain that was not severe but lasted one hour during rest in bed. They dismissed the possibility of myocardial infarction, however, because changes in the S-T segments, Q waves, leukocytosis, increased sedimentation rate, friction rub, and fever were absent.

Change in S-T segments following emetine therapy have been quite rare; when present, they were usually depressions. In approximately 50 per cent of cases, abnormalities have persisted for two to four months. In other cases changes have not been seen for one to two weeks after cessation of treatment.

Seven cases are reported herewith in which electrocardiographic changes were associated with the administration of emetine hydrochloride. These cases were treated at Deer Lodge Veterans' Hospital from 1946 to 1955. Control and follow-up electrocardiograms were generally available.

Report of Cases

Case 1. A. H. M., a 21 year old man, suffered an attack of dysentery in October 1944 while in Italy. In February 1946 cysts of Entamoeba histolytica were found in the stool. An electrocardiogram on February 28, 1946, was normal (fig. 1). Emetine hydrochloride, grain I intramuscularly, was given daily from March 2 to March 10, 1946, for a total of 9 grains. On March 4, 1946, abnormal flat T waves were seen in leads I, II, and CF4. On March 21, 1946, the T waves were flat in lead I, inverted in lead II, and biphasic in CF4, CF3, and CF2. The P-R interval was 0.18 second, QRS 0.07, and the rate was 71/min. On May 7, 1946, and again on November 25, 1949, electrocardiograms were normal.

Case 2. C. D., a 22 year old man, had a normal electrocardiogram on October 17, 1946 (fig. 2). From November 27 to December 4, 1946, emetine, grain I, was given daily for the treatment of amebiasis. On December 6, 1946, the T was inverted in CF4, and...
ST was elevated with straightening of the ascending limb of the T wave in CF$_2$. The P-R interval was 0.15 second, QRS 0.07, Q-T interval 0.40, and the rate was 76/min. On December 20, 1946, T waves were flat in lead I and inverted in CF$_4$ and CF$_5$, but the ascending limb of T in CF$_2$ had regained its initial upward concavity.

**Case 3.** J. O. B., a 22 year old man, suffered with chronic abdominal pain, loose stools, anorexia, and mild nausea during service in Italy from 1943 to 1945. In June 1952, motile amebae and small cysts were found in the stool. On June 20, 1952, an electrocardiogram was normal (fig. 3) and emetine, grain 1 daily, was begun. On June 25, 1952, the T waves were inverted in V$_2$ and V$_4$, and flat in V$_5$ and V$_6$. The P-R interval was 0.15 second, QRS 0.10, Q-T interval 0.40, and the rate was 73/min. On June 26 emetine was discontinued. On June 27, 1952, T was upright in V$_2$. On June 30 T was inverted in V$_2$, V$_4$, and V$_5$. The P-R interval was 0.16 second, QRS 0.10, Q-T
0.40, and the rate was 75/min. An electrocardiogram on July 18, 1952, was unchanged, and on August 5, 1952, it was normal.

Case 4. D. L. M., a 28 year old man, was admitted on August 8, 1952, with chills and fever spiking up to 104 F. Malaria due to Plasmodium vivax was demonstrated, and motile and cystic forms of E. histolytica were found in the stool. On August 14, 1952, an electrocardiogram was normal (fig. 4); emetine hydrochloride, grain 1 intramuscularly, was given daily from August 14 to 21. On August 18 the electrocardiogram was unchanged. On August 22 the T wave was inverted in V4; the P-R interval was 0.16 second, QRS 0.09, Q-T 0.40, and the rate was 79/min. No follow-up study was obtained.

Case 5. A. K., a 28 year old man, was found to have motile E. histolytica in the stool on July 30, 1952. On July 31 an electrocardiogram was normal, with a P-R interval of 0.17 second (fig. 5). Emetine, grain 1 intramuscularly, was given daily from August 1 to 9. On August 9 an electrocardiogram revealed a P-R interval of 0.21 second and a flat T wave in lead I. On November 26, 1952, an electrocardiogram was normal, with a P-R interval of 0.17 second.

Case 6. D. M. S., a 39 year old man, was found to have cysts of E. histolytica in the stools on July 15, 1948. On July 16 an electrocardiogram showed a flat T wave in lead I, P-R interval of 0.12 second, QRS 0.07, Q-T interval 0.36, and a rate of 60/min. (fig. 6). Emetine was given in a dose of 1 grain daily from July 19 to 26. On August 14, 1948, the T waves were flat in lead I and inverted in CF4 and CF6, the P-R interval was 0.17 second, QRS 0.07, Q-T interval 0.42, and the rate was 67/min. On August 26 the electrocardiogram was back to the pretreatment state and was unchanged in March 1949 and February 1950.

Case 7. H. M. W., a 35 year old man, showed E. histolytica in the stool on January 7, 1955. At that time the sedimentation rate was 3 mm. in 1 hour. An electrocardiogram on January 8 was normal (fig. 7). Emetine, grain 1 daily, was given from January 8 to 14. On January 15 T waves were flat in leads I, II, aV5, aVF, V4, and V6. P-R interval was 0.16 second, QRS 0.08, Q-T 0.38, and the rate was 65 per minute.

On January 17 the patient complained of squeezing retrosternal pain that lasted some hours and was worse on breathing. There were a large Q3 and S-T elevations in leads II, III, aVF, and V4-6. The sedimentation rate remained at 3 mm. in 1 hour. On February 8 the abnormalities had increased and were consistent with posterolateral infarction. There was no marked change on March 9. On April 4 the abnormalities were receding, but were still present on April 19. On October 25 the patient had severe stabbing pain deep in the midchest, radiating to the left shoulder, that was provoked by strenuous activity and was relieved after rest for 20 minutes. The sedimentation rate remained at 4 mm. After a period of observation in hospital, a Master step test was
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FIG. 6. Case 6, D. M. S. Electrocardiographic complexes.

FIG. 7. Case 7, H. M. W. Electrocardiographic complexes

done (fig. 8), which produced a paradoxical elevation of T in lead II and aVF, and to a lesser extent in V6. On completion of the exercise, mild retrosternal discomfort was present, which subsided quickly on resting. On November 28 2 bouts of retrosternal pain were provoked by short brisk walks; on both occasions nitroglycerin afforded quick relief.

DISCUSSION

In each of the 7 cases electrocardiographic changes were consequent upon emetine therapy. They included flattening and inversion of T waves, elevation and change in contour of S-T segments, prolongation of atrioventricular conduction time, and frank myocardial infarction. In addition, these changes showed both persistence and lability.

None of the patients had fulminating or severe dysentery, but amebae were discovered in routine investigation of the stools in patients either with mild bowel disturbances or who were known to have been in an endemic area. The possibility that the electrocardiographic changes were secondary to electrolyte disturbances consequent upon marked dysentery may therefore be dismissed. The changes may not be reasonably attributed to amebiasis itself; in 5 of the 7 cases the electrocardiogram was normal before treatment,
It is only possible to speculate about the role of emetine in the production of myocardial infarction. Although it is tempting to attribute this to an esoteric lesion such as coronary arteritis, it is perhaps necessary to accept the explanation that therapy and infarct were spuriously allied in time. The pain and the electrocardiographic changes possibly reflected a large area of myocarditis due to emetine, but in view of the subsequent history of angina pectoris, the diagnosis of coronary artery disease seems more reasonable.

Finally, from the very limited postmortem material in the literature, the underlying lesion in the majority of cases would appear to be an interstitial myocarditis of toxic rather than inflammatory origin.\(^4\)

**SUMMARY**

Data from 7 cases demonstrate electrocardiographic changes following the administration of emetine hydrochloride.

The history of a young patient who sustained myocardial infarction while receiving emetine has been presented.

**SUMMARIO IN INTERLINGUA**

Datos ab 7 casos demonstra alterationes electrocardiographic post le administration de hydrochlorido de emetina.

Es presentate le historia clinic de un juvene patiente qui suffreve infarcimento myocardial durante un curso de emetina.

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