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AN EXCEPTIONAL PRESENTATION OF ANTABUSE REACTION

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Abstract :

Disulfiram is a drug commonly used in India for alcohol deaddiction. Due to its aversive nature of the reaction with alcohol, Patients tend to discontinue alcohol use. Usual clinical manifestations of disulfiram-ethanol reaction (also known as antabuse reaction) are generalized body warmth, urticaria, pruritus, conjunctival ingestion, light headedness, vertigo, nausea, vomiting. However here, we report a case of antabuse reaction mimicking NON ST ELEVATION MYOCARDIAL INFARCTION to emphasize the variability in its presentation and potential hazards associated with its use.

Keyword :ANTABUSE REACTION, HYPOTENSION,NON ST ELEVATION MYOCARDIAL INFARCTION.

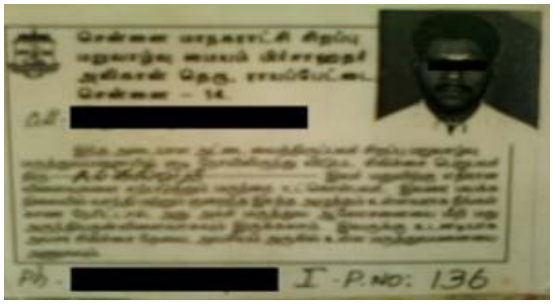
Disulfiram ethanol reaction (antabuse reaction) is potentially a toxic reaction seen in patients using disulfiram for alcohol deaddiction,who consume ethanol recreationally or accidental exposure to substances that contains alcohol (cough syrups, mouth wash,after shave lotions)4.It usually begins with in 15-30 minutes following exposure to alcohol and peaks between 30 minutes to 1 hr1. Peak can be delayed as late as 12 hrs. Even a minimum quantity of alcohol is suffice to induce this reaction1.This toxic reaction can happen during any time up to 2 weeks following the discontinuation of disulfiram.Cardiovascular manifestations like chest pain, dyspnea and palpitations are also observed in these cases.But ECG changes following antabuse reactions are extremely rare and if detailed patient history is not considered, it can lead to a possible misdiagnosis.

CASE REPORT

A 35 year old male presented to our hospital emergency department with complaints of central chest pain which was burning in nature and radiating to back. He complained that his chest pain was associated with profuse sweating and palpitations for about 30 minutes duration. Patient was dyspneic and there was no history of orthopnea or paroxysmal nocturnal dyspnea. Also, the Patient had 2 episodes of vomiting at the time of admission. He had no prior history of coronary artery disease, diabetes mellitus, or hypertension. Patient had consumed alcohol about half an hour prior to the onset of chest pain. At the time of admission he was dyspneic, tachypneic, febrile and hypotensive (80/50 mmHg) with breath smells of alcohol. His JVP was not elevated, auscultation of the heart and lungs were normal.

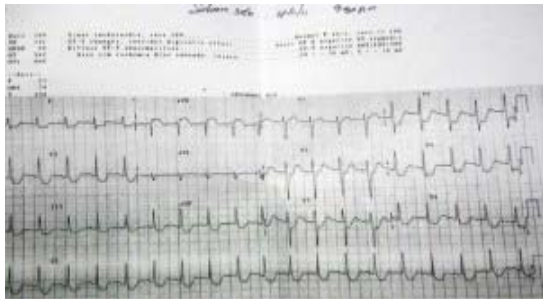
ECG showed ST depression of more than 2mm in lead II,III,aVF and V2 to V6 with ST elevation of 1mm in aVR (FIG 1). Detailed personal history revealed that patient was an alcoholic for the past 12 years and, at the time of admission was undergoing deaddiction programme for 3 months on disulfiram dosage 250 mg B.D.

Patients deaddiction registration card.



Patient skipped the evening dose of tablet disulfiram on the day of consumption of alcohol. Patient had consumed approximately 90 ml of alcohol prior to the reaction. Patient denied any drug intake apart from tablet disulfiram in the morning of the presentation. Hence a diagnosis of possible disulfiram – ethanol reaction was made.

FIG.1 ECG at the time of admission



Considering the age of the patient and ECG changes, antiplatelet drugs were used at the time of admission in emergency room as it was our institutional protocol. Cardiac biomarkers was not done at the time of admission as the time window was only 30 minutes. Nitrates was not used as the patient was hypotensive.

In the cardiac care unit patient's hypotension was managed with crystalloids and dopamine (10 to 20 mic/kg/min.) and patient's hemodynamics did not improve with dopamine, subsequently Norepinephrine was used at the dose of 0.05 mic/kg/min. Later hemodynamic status improved with norepinephrine support, which is a classical feature of an antabuse reaction. Patient was treated with antiemetics, H1 & H2blockers along with dexamethasone. TROPONIN T was done 4 hrs and 8 hrs after admission and both were negative.

As per the institutional protocol, Cardiologist opinion was sought and was opined that considering the clinical background, which were more in favour of antabuse reaction and the global ST T changes seen in this patients ECG was possibly due to myocardial ischemia induced by hypotension, correcting hypotension there would be a high probability of reversion of ECG changes. More over the description of chest pain did not fit in to the characteristics of unstable angina and to heparinize if the patient's serial ECGs show any progressive or persistent ST-T changes irrespective of nature of chest pain and if cardiac biomarkers were to be positive. But the patient's subsequent ECG showed normalization of ST segment with negative cardiac biomarkers and also the symptoms reverted with supportive measures, heparin use was deferred, even though the initial differential diagnosis was unstable angina.

The NSTEMI (NON ST ELEVATION MI) was excluded based on negative cardiac biomarkers and reversal of ECG changes following administration of crystalloids, supportive measures and subsequently antiplatelets were withheld. Patient symptomatically and hemodynamically improved with supportive measures. The next ECG taken 4 hours after admission showed normalization of ST segment with sinus tachycardia (FIG 2). However, the normalization of ST segment ruled out tachycardia induced ST T changes as the tachycardia was present in the ECG which was taken at the time of admission and 4 hours later.

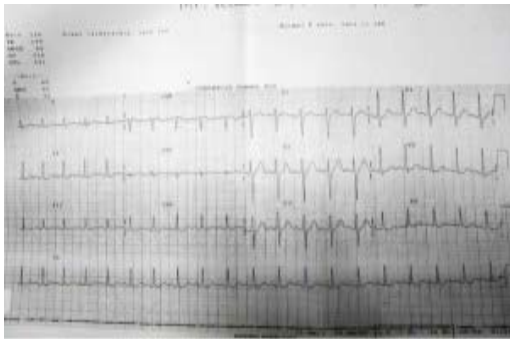


FIG 2. ECG Taken 4 hours after admission.

The complete blood count,serum electrolytes, liver function tests, blood sugar,urea,creatinine, lipid profile, serum amylase all were with in normal limits. An ultra sound scan of abdomen showed fatty liver and no other abnormalities detected, Chest X ray was normal. Screening ECHO done which showed Ejection fraction of 67%, No Regional Wall motion Abnormalities detected, normal chamber dimensions and all valves were normal.

Serial ECG taken at 8 hrs after admission was normal apart from sinus tachycardia.

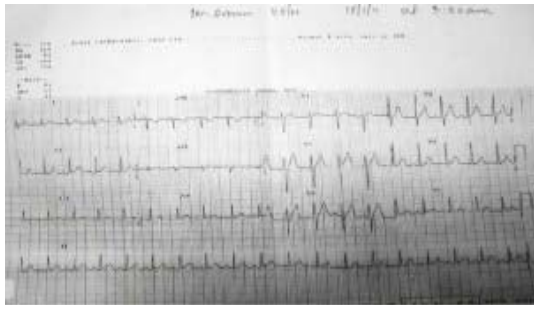


FIG .3. ECG taken after 8 hrs.

Further course in the hospital was uneventful. Patient was discharged and referred for higher cenre for deaddiction.Coronary angiogram was done one month after the discharge showed a normal epicardial coronary arteries.Hence we conclude that this is a disulfiram- ethanol reaction.

The differential diagnosis in this case were: NSTEMI ,unstable angina, disulfiram like reaction – which is seen in patients on disulfiram but had not taken alcohol and seen with certain drugs(ex:Metronidazole). In the light of the typical history, negative serial troponin levels, normalization of ST segment with in few hours of supportive care,Hemodynamic respose to Norepinephrine and absence of other drug intake, the diagnosis of antabuse reaction was made even though the ECG was initially atypical. This case highlights the potential hazards associated with the use of disulfiram and also a rare case of atypical ECG with an antabuse reaction.

DISCUSSION:

Disulfiram use for alcohol deaddiction has been in practice for more than half a century. It's property of inducing adverse reactions was accidentaly discovered in rubber industry workers in early 1950s. Nowadays,it is commonly used as an adjuvant theraphy for alcohol addiction along with psychosocial therapies. Alcohol in liver metabolized by alcohol dehydrogenase in to acetaldehyde,which is further metabolized by aldehyde dehydrogenase in to acetate1.But disulfiram inhibits mitochondrial aldehyde dehydrogenase-2 irreversibly and causing acetaldehyde accumulation1.This accumulation of acetaldehyde leads to hypotension and cardiovascular collapse in antabuse reaction2.

Cardiovascular manifestations of disulfiram ethanol reaction are usualy hypotension, chest pain,dyspnea and palpitations, and in rare cases patient may have myocardial ischemia with ECG manifestations2,6.Also there are case reports of atrial fibrillation and sustained ventricular tachycardia following antabuse reactions6.

The commonest mode of presentation of these reactions are flushing, conjunctivalinjection, pruritus, urticaria, diaphoresis, lightheadedness, vertigo, headache, nausea, vomiting, and abdominal pain1,5. Mortality had been reported in these type of reactions, though rare1. There is a significant inter-individual and intra-individual variation in the intensity and duration of reaction noted

Diethyldithiocarbamate,the metabolite of disulfiram,inhibits dopamine hydroxylase from

which norepinephrine is produced5.The decreased levels of norepinephrine along with acetaldehyde(potential vasodilator),may be the reason for hypotension2.The hypotension that is refractory to crystalloids will respond to norepinephrine infusion1,5.Cutaneous manifestations are due to histamine release.The exact mechanism how the ischemic ECG changes occurs remains unclear,may be attributed to hypotension3.These patients are managed symptomatically with crystalloids,H1 blockers (Diphenhydramine),antiemetics and rarely with ionotropic support.

Fomepizole an alcohol dehydrogenase inhibitor, prevents the metabolisn of ethanol to aldehyde and could limit the effect of antabuse reaction7.

vitamin C can be used in antabuse reaction in large intravenous doses of 1 gram as flash oxidizer10.vitamin C is a co-factor for dopamine hydroxylase which is inhibited by diethyldithiocarbamate leading to depletion of norepinephrine stores8,9.In addition,the
*unstable acetaldehyde-protein adducts are stabilized by the use of large intravenous doses of vitamin C via its antioxidant action*11.*Antihistaminic action complements its use10. However,currently there no standard recommendation for its use in antab use reaction1.*

Our patient had not presented with typical manifestations of antabuse reaction like flushing,uriticaria,conjunctival injection or diaphoresis but with ischemic ECG changes. His hypotension was refractory to crystalloids and hemodynamic status was improved with norepinephrine infusion1.

This case report underscores the exceptional presentation of antabuse reaction and potential hazards associated with disulfiram use, though mortality is very rare. Therefore a clear knowledge about such rare presentations becomes necessary to manage these life threatening reactions.

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