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Case Report

Exercise-induced urticaria with muscle injury: a case report

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ABSTRACT

Exercise has become an integral part of life in this modern era due to sedentary lifestyle. Although, urticaria patients are being evaluated for all the common triggering factors like food, environmental allergens and infections, an entity called exercise induced urticaria often get missed. Exertional and asymptomatic rhabdomyolysis must be kept in mind during evaluation. A 27 year male patient was diagnosed with severe exercise induced urticaria with muscle injury. Patient developed urticaria within 30 minutes of strenuous exercise. Clinical history was insignificant for any allergen exposure except for clear history of urticaria once weekly after strenuous exercise. Patient also reported need for oral analgesics on the day of strenuous exercise indicating muscle injury. Asymptomatic phase correlated with abstinence of exercise. His lesions gradually got relieved with anti-histamines. Routine blood investigations were normal except elevation of aspartate aminotransferase (AST-354U/L), Lactate dehydrogenase (LDH-619U/L) and normal alanine aminotransferase (ALT-51U/L), altered AST/ALT ratio more than 6. Creatinine kinase (CK) can increase ten folds in healthy individuals following strenuous exercise. Hence, CK was not done for this patient. Aminotransferases may remain elevated even after normalisation of CK up to 2-3 weeks. LDH was done as an additional investigation. Simple routine investigation for altered AST and confirmation with LDH or CK for its source from muscle injury can be done. Severe exercise induced urticaria with muscle injury can be managed with moderation of exercise intensity along with short course of antihistamines owing to the benefit of exercise. This patient was followed up for 2 years and there was no episode of urticaria after stepping down the exercise intensity. Detailed history of exercise duration and intensity is required along with basic investigations for evaluating exercise induced urticaria. A sub-entity called severe exercise induced urticaria with muscle injury must be kept in mind due to the risk of asymptomatic or exertional rhabdomyolysis.

Keywords: Urticaria, Severe exercise-induced, Muscle injury urticaria, Exertional rhabdomyolysis

INTRODUCTION

Urticaria affects 15-25% of population at least once in their lifetime. Release of vasoactive substances like histamine, prostaglandins and kinins are involved in its pathogenesis.[1] Majority of urticaria cases are attributed to food, environmental allergens, infections, idiopathic and physical triggers.

Any kind of physical exertion like mechanical or thermal can trigger physical urticaria. Physical urticaria occurs on cholinergic background. Cholinergic urticaria comprise of 30% physical urticaria and 7% of chronic urticaria cause. It is believed to be due to non-specific stimulation of mast cells. [2]

A study done on aetiology of chronic spontaneous urticaria (CSU) found that average age group was 20-40 years in all types and male: female ratio was about 1:1. In patients less than 20 years, infective focus was the major cause. The 70% of cases were diagnosed to be idiopathic.[3]

The spectrum of exercise induced urticaria included cholinergic urticaria, exercise induced anaphylaxis and its

variants. Cholinergic urticaria occurs due to increase in body temperature without vascular collapse. Exercise induced anaphylaxis occurs due to exercise with vascular collapse. Variants include familial type with autosomal dominant inheritance and food-dependent.[4]Autologous serum skin test (ASST) is used to identify autoimmune aetiology in CSU.[2]

Studies from literature have cited that increased sweating during exercise induces cholinergic urticaria. Interestingly, studies have studies have stated that there was an aggravation of urticaria in both summer and winter due to different pathogenic mechanisms.[5]

AST (Aspartate transaminase) is a cytosolic and mitochondrial isoenzyme which is found in liver, cardiac and skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes and erythrocytes. AST is less sensitive and specific for liver. ALT (Alanine transaminase) is a cytosolic isoenzyme mainly in liver and it is more specific to the liver.[6]

LDH is a ubiquitous enzyme present in almost all body tissues making it not an ideal biomarker. Anaerobic metabolism during excessive physical exertion increases LDH. LDH can also show false high value due to haemolysis of blood sample.[7]

Rhabdomyolysis is due to disruption of skeletal muscle integrity leading to direct release of myoglobin, CK, aldolase, LDH and electrolytes. Rhabdomyolysis ranges from asymptomatic illness to acute kidney injury (AKI). Increased temperature and humidity during exercise/ exertion may also play a role in higher rates of rhabdomyolysis.[8]

CASE REPORT

A 27 year old male with history of erythematous itchy wheals suggestive of punctate, papular and few plaques type of urticaria lesions involving whole body at least once in a week after 30 minutes of severe exercise. No history suggestive of angioedema for the past four months and lesions resolved with anti-histamines (Figures 1-4). Asymptomatic phase of 2 months correlated with lack of exercise. No history suggestive of food, drug or environmental allergens exposure and systemic involvement. Family history was insignificant. Patient used to self-medicate oral analgesics on the day of severe exercise. All blood parameters were normal except elevated AST (354U/L), normal ALT (51U/L) and altered AST/ALT ratio>6. Isolated elevation of AST could be due to muscle injury. LDH was done as a supportive investigation to confirm muscle source and it was found to be elevated (619 U/L). Urticaria after exercise and before intake of oral analgesics along with evidence of muscle pain and injury ruled out analgesics induced urticaria. Severe exercise-induced urticaria with muscle injury was diagnosed. Consent for photograph and publication was obtained.

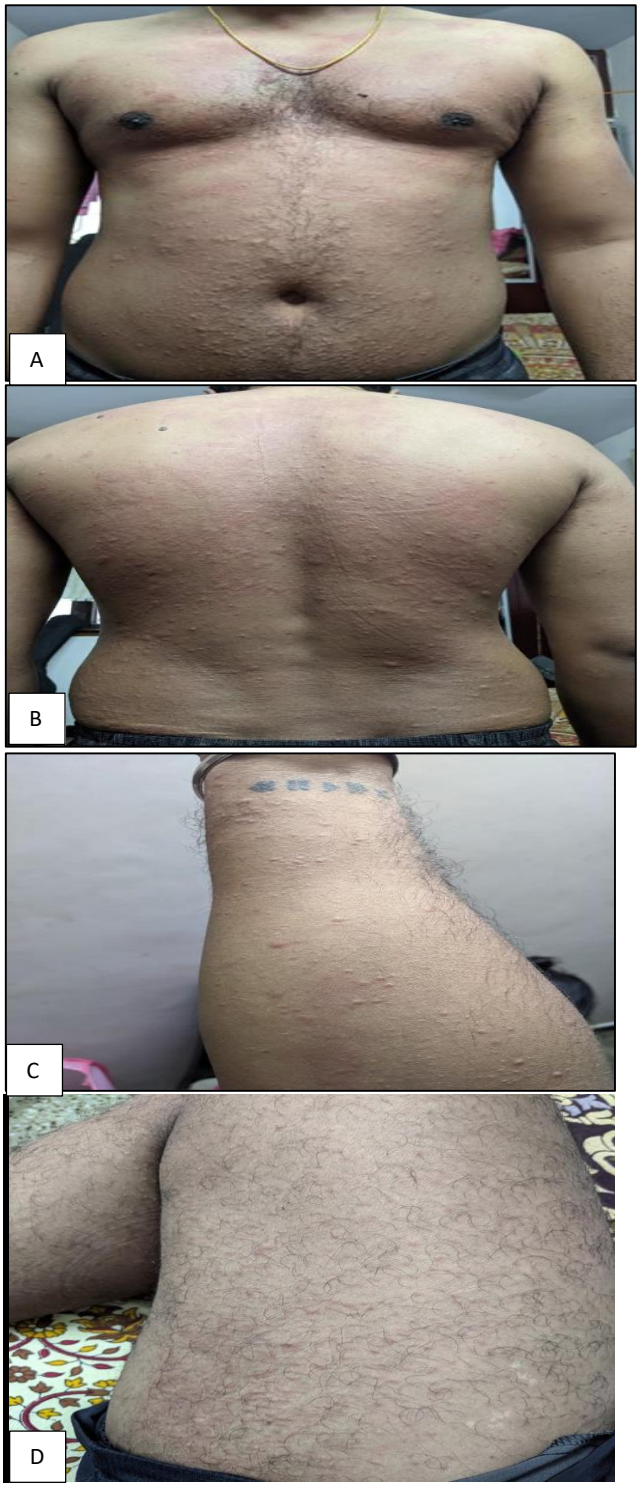

Figure 1 (A-D): multiple erythematous urticarial punctate papules and plaques involving front and back of the trunk, volar aspect of hands and thighs.

Patient reported urticaria only on the days of strenuous exercise (weekly once). Hence patient patient was instructed to avoid strenuous exercise and mild/moderate exercise was advised along with a short course of second generation of anti-histamines. Patient had not reported any episodes of urticaria for 2 years with mild/moderate exercise. Follow-up investigations for normalisation of

AST or LDH were not done because patient was not willing for any investigations when normal.

DISCUSSION

A simple history of urticaria following exercise and its association with severity of exercise with relevant investigations to confirm muscle injury will serve as a guiding tool to rule out severe exercise induced urticaria. Exercise challenge test can be done in a clinical set-up to confirm the diagnosis.[9] This test was not performed in our patient because his initial blood investigations threw light on suspicion of muscle source altered AST in the form of isolated AST elevation. LDH was done to confirm the diagnosis. In our case, there was evidence of severe muscle injury in blood investigations. Exercise challenge test can be done to confirm exercise induced urticaria without any symptom or investigations suggestive of muscle injury.

In acute rhabdomyolysis, there is initial elevation of AST followed by ALT and their ratio being greater than 3 and eventually ratio reaches 1 due to the decline in AST because of it's shorter half-life.[10]

Elevated AST levels in the absence of liver disease could be due to muscle injury and it is confirmed by elevated CK and LDH.

In exertional rhabdomyolysis, CK levels will naturally increase up to 10 times the higher limit of normal after strenuous exercise in almost all normal individuals.[11]

A study of healthy young men (18-45 years) demonstrated significant increase in AST, ALT, CK, LDH and myoglobin after 1 hour session of weight lifting and it normalised after 7 days whereas bilirubin, ALP and Gamma glutamyl transferase remained normal.[12]

A case report of exertional rhabdomyolysis found significant elevation of AST and CK in 24 hours and ALT may be normal even up to 48 hours. Peak AST and AST/ALT ratio increase occurs on day 3 of injury. Aminotransferases may remain elevated even after normalisation of CK upto 2-3 weeks.[11] Aminotransferases and CK normalised concurrently in 85% of patients. Treatment with intravenous fluid in rhabdomyolysis normalised CK rapidly compared to aminotransferases due to renal clearance of CK.[11]

CK level was not checked in our patient because there was an isolated elevation of AST and LDH along with symptoms of urticaria and muscle pain requiring analgesics on the days of severe exercise only; indicating a background of muscle injury triggering urticaria.

Our patient developed acute urticaria following severe exercise causing acute muscle injury. Substantial evidence of acute muscle injury was found in this patient with elevation of both AST and LDH along with AST/ALT ratio >6. This patient is a clear cut case of severe exercise-induced urticaria with muscle injury, may be a variant of cholinergic urticaria with muscle injury.

Exercise-induced urticaria is managed by avoiding food before and after exercise, use of mast cells stabilisers and antihistamines before exercise.[9] This is a case of severe exercise- induced urticaria with muscle injury with a risk of exertional rhabdomyolysis managed with moderation of exercise intensity and short course of anti-histamines.

CONCLUSION

Exercise-induced urticaria is generally managed by avoidance of exercise. Owing to the benefits of exercise, exercise induced urticaria must be categorised into with or without muscle injury. Exercise-induced urticaria with muscle injury can be managed by switching over to mild exercise instead of oral anti-histamines or avoiding exercise completely. This also highlights the need for detailed history like exercise duration and intensity in cases of acute urticaria and to do relevant investigations if necessary to rule out its association with muscle injury. A sub-entity called severe exercise-induced urticaria with muscle injury must be considered due to the risk of asymptomatic or exertional rhabdomyolysis.

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