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ABSTRACT

A rare clinical case of rhabdomyolysis occurred after habitual and non-intense physical exercise, in a male, 34 year-old patient, as well as the probable triggered factors involved and their clinical implications will be discussed. Moreover, the expressive increase, which is pioneering compared to other research such as on creatine kinase, hepatic enzymes, as well as clinical measures adopted for serum renal complications and with severe risk to the patient under study will be highlighted.

Keywords: rhabdomyolysis, physical exercises, statins, finasteride, ethnic group

INTRODUCTION

Rhabdomyolysis (RB) is characterized by compromising of the skeletal muscle tissue where its intracellular components, including electrolytes, myoglobins and other sarcoplasmic proteins are noticeably released from the creatine kinase (CK) as well as from the alanine aminotransferase (TGO) and aspartate aminotransferase (TGP) among others, releasing them from the circulation⁽¹⁾. It can present many causes, which will be discussed and connected to the present clinical case. This presentation was referred and shown to the patient in question and with his permission; its publishing was approached by its scientific interest. Firstly, the laboratory levels reached are highlighted, and subsequently, we call attention to the condition asymptomatic continuation during the clinical follow-up, during his hospital submission and his ambulatory evolution.

CLINICAL CASE REPORT

Male white patient, with third degree Asian heritage, current age of 34 years who looked for us firstly on 08/01/1997, at 21 years of age, for a routine cardiac evaluation since he regularly practiced running between 8 and 10km per session, 4 to 5x/week, and mean of 50 to 60 minutes per session. In his first visit, he reported occasional increase of blood pressure firstly noticed in a recent evaluation, with no relation to the sports practice. He was asymptomatic and with no use of specific medication or illicit drugs. He reported have been a premature and have presented an indefinite cardiac complication at 20 days of life and that he did not need subsequent follow-up. Amigdalectomy at eight years old, with no history of hepatic and/or blood diseases. Family history of maternal grandmother underwent nephrectomy for kidney stones, mother with blood hypertension and dyslipidemia, sister with dyslipidemia and father with sudden death by valvulopathy "sic" at 42 years of age. Normal physical exam, with height of 1.78m, weight of 79.400kg, BP 120mmHg x 80mmHg layed, no postural alteration on both upper limbs, normal peripheral pulses, HR = rhythmic 68bpm, normal heart sounds and absence of murmurs. Lungs and abdomen not worth of note. Eletrocardiogram (ECG) at rest, normal. Ergometric test (ET) with normal response to physical exertion, with no ischemia and/or arrhythmia, BP normal behavior and

reaching 13MET, normal echodoplercardiogram (ECO) and normal 24h BP ambulatory mapping (MAPA). Laboratory data found: fast glycemia (GL) 103mg/dl; triglycerides (TG) 100mg/dl; total cholesterol (TC) 247mg/dl; LDL-C 186mg/dl; HDL-C 41mg/dl; urea 34mg/dl; creatinine 0,9mg/dl; potassium (K) 4,0mg/dl; normal I urine; normal hemogram. A that time, patient and us chose to be treat him diet and specific nutritional guidance as well as maintenance of his habitual running physical activities and periodical follow-up was required. However, he was absent from his evolutionary clinical control for about four years, returning at the following dates.

23/07/2001 – asymptomatic, normal cardiac evaluation, normal ECG, keeping his mentioned physical activities. Laboratory data: TC 229mg/dl, LDL-C 165mg/dl, HDL-C 47mg/dl, VDL-C 17mg/dl, TG 87mg/dl, GL 93mg/dl, uric ac. 6.0mg/dl. Kept with diet and physical exercise. Weight 80.600kg. Control after four months required and again he did not have it, returning only on the following date.

23/01/2003 – asymptomatic, normal cardiac evaluation, normal ECG, keeping his habitual physical activities, laboratory data in mg/dl: TC 197, LDL-C 129, HDL-C 54, TG 72 and normal reactive C protein. Weight 80.500kg. Control TE required and not performed by patient.

04/08/2004 – asymptomatic in mg/dl: TC 267, LDL-C 186, HDL-C 55, TG 128, uric acid 6.6, TGO 30 U/L, TGP 48 U/L, TSH 1.2uIU/ml, normal I urine), Normal TE for ischemia with 15.33 MET, normal BP behavior, weight 86.100kg (much above the previous one). Conduct kept and received orientation for nutritional follow-up and return also delayed.

10/07/2006 – two years after last control, asymptomatic and with normal routine cardiac evaluation, normal ECG, BP 120 x 80mmHg, normal ECO, TE with 18,46MET, normal and normal BP behavior and MAPA with threshold indices of systolic at vigil and normal at night. Weight 75.800kg.

27/09/2007 – asymptomatic, keeping usual running rhythm and habitual sports and with normal cardiac evaluation, normal ECG, and we obtained: TC 211mg/dl; LDL-C 132mg/dl; HDL-C 63mg/dl; fasting GL 111mg/dl and post-prandial 83mg/dl; glycated Hb 5.7%; TG 82mg/dl; TGO 21U/L, TGP 18U/L; uric acid 5.9mg/dl, TE reaching 15.38MET, normal and at SBP peak of 230mmHg X DBP of 110mmHg and returning to normal values after four minutes; normal ECO; weight 74.600kg; MAPA (required) with load

percentage at threshold values both for systolic and diastolic BP at vigil and normal at night. Kept his habitual physical exercises program and also at that occasion practice of recreative society soccer 1h, 1x/week.

25/06/2008 – asymptomatic at normal routine cardiac evaluation, normal ECG with fasting GL 102mg/dl, glycated Hb at 5.6%, HDL-C 58mg/dl, LDL-C 135mg/dl, TC 213mg/dl, TG 101mg/dl, weight 76kg, kept with his running training 40km/week and soccer 1x/week. Control required in six months.

23/04/2009 (Thursday) – routine periodical evaluation and slight fatigue after usual exercises: hemogram with discreet leukopenia (3.86), normal red series, normal glycemic curve, fasting GL 89mg/dl, glycated Hb 5.6%, TC 229mg/dl, LDL-C 152mg/dl, HDL-C 58mg/dl, TG 96mg/dl, total testosterone 582mg/dl and cortisol morning 16.3ug/dl (these two last ones due to overtraining suspicion), normal TE with 18.46MET and normal BP behavior, normal ECO. Since during these years his lipid levels at certain occasions were above normal values and at 34 years of age (13 years after his first evaluation) and with family history, we decided to begin with statin, linked to habitual physical exercises and diet guidance. We introduced rosuvastatin (RO) of 10mg at night for 30 days and control exams after this period.

25/04/2009 (Saturday) – two days after last control, played society soccer, at 20h during 1h30 minutes at a very warm night (sic) and referred slight muscle pain during practice which did not stop him from going on, having attributed it to the exercise and spontaneously stopped. At his home arrival at 23h, noticed urine with “darker color” (tea color) sic and attributed it to a self-prescribed vitamin in use, not referred in the visit and asymptomatic. He did not present important muscular trauma during this sports activity, his diet was routine-like and did not use alcohol or other substances, denied fever or other manifestations of infection suspicion. On the following morning the same urine ‘color’ was observed and he went to the hospital on 26/04/2009 (Sunday) at 9h00 with no symptoms. Feverish with normal physical exam except for his suspicion of discreet jaundice reported by the doctor on call, who asked for laboratory evaluation: leukocytosis hemogram 13.800, segmented 10.902 and discreet lymphocytopenia, TGO 1.303U/L, TGP 238U/L, gama GT 24U/L, alkaline phosphatase (ALP) 78U/L, amilase 51U/L, lipase 206U/L, lactic dehydrogenase (DHL) 6.304U/L, urea 31mg/dl, creatinine 1.03mg/dl, sodium (Na) 140mmol/l, K 4.2mmol/l, total bilirubin (BT) 2.2mg/dl, indirect bilirubin (BI) 2.0mg/dl, direct bilirubin (BD) 0.2mg/dl, creatin kinase (CK) 80.000U/L (normal 260U/L), urine I proteins +++, 20.000 red cells and 20.000 leukocytes, hemoglobin (Hb)+++; IgG 1.270mg/dl (normal 1.600mg/dl) IgM 144mg/dl (normal until 230mg/dl), sorology hepatitis A, B, C negative. Laboratory alterations caused him to be admitted with diagnosis of RB and for prevention of acute renal failure (ARF). Remained in hospital for seven days and with medication for hydration with important replacement volume, besides other therapeutic measures for renal protection, and for possible pertinent general hydroelectrolytic and metabolic corrections (standard hospital protocol). Remained asymptomatic and at good general status during his entire hospital admission period and with gradual regression of the sequence laboratory controls performed and hospital discharge on 01/05/09: TGO 118U/L, TGP 132U/L, DHL 208U/L, CK 4.859U/L, urea 20mg/dl, creatinin 0,87mg/dl, K 4,2mmol/l and normal urine I. Normal total specific abdomen

and renal ultrasound, sorology Epstein Barr Virus negative. He was told to avoid physical exertion until ambulatory control in seven days and return to his habitual laboratory activities.

10/05/2009 (event on 25/04/09) – already under ambulatory evaluation: TGO 18U/L, TGP 44U/L, gama GT 19U/L, BT 1.70mg/dl, BI 1.34mg/dl, BD 0.36mg/dl, CK 170U/L, DHL 165U/L, urea 32mg/dl, creatinine 0.93mg/dl, FA 64 U/L, VHS 1mm/h, normal urine I, LDL-C 177mg/dl, TC 249mg/dl, HDL-C 52mg/dl. At this first visit after discharge, revealed to have regularly used for two years (720 approximate days) finasteride 1mg daily prescribed by another doctor for hair loss and that he had forgotten to mention it for finding it not important, totaling hence approximately 720mg of finasteride in that period. Asymptomatic and at good general status, was released to return with gaits 1h, 3x per week, 18 to 20km week. Finasteride use was prohibited, which already occurred in the admission period and control in 30 days.

29/06/09 – routine control, asymptomatic and gait physical activity mentioned above results 2 days after last gait: TGO 18U/L, TGP 17U/L, DHL 150U/L, CK 174U/L, gama GT 14U/L, ALP 47U/L, BT 1.84mg/dl (normal 1.30mg/dl), BI 1.45mg/dl (normal up to 1.10mg/dl), BD 0.39mg/dl (normal up to 0.30mg/dl), normal urine I, TC 225mg/dl, LDL-C 150mg/dl, HDL-C 55mg/dl, TG 100mg/dl. Oriented to increase intensity of interval exercises (gaits – *jogging* – 5km total in each session) for 30 minutes, 3 to 4x/week.

04/07/09 – told to collect samples immediately after 7km jogging, results were: CK 260U/L (normal up to 174U/L), DHL 163U/L, TGO 19U/L, TGP-18U/L, gamaGT18U/L, ALP 58U/L; TC 238mg/dl, HDL-C 49mg/dl, LDL-C 172mg/dl, BT 2.2mg/dl, BD 0.5mg/dl, BI 1.7mg/dl. Due to bilirubin vales above evaluation with hematologist was recommended. Gilbert's Syndrome diagnosis (persistent increase of BI and BT and normal BD) and released by the professional in question to normal activities and also with no restriction to physical exercises due to the benignity of this pathology, in medical report sent to us.

25/08/09 – sample collected after 48h of 7km jogging – results – TGO-TGP-GGT-ALP-DHL- within normality, CK 189U/L (normal 174U/L), BT 1.9mg/dl (up to 1.2mg/dl), BD 0.3mg/dl, BI 1.6mg/dl (normal 1.0mg/dl), normal urine I, normal hemogram, glycemia 107mg/dl, TG 123mg/dl, TC 205mg/dl, LDL-C 136mg/dl, HDL-C 44mg/dl, K 4.5mmol. Released to his exercise routine, 50 minutes/session jogging, 4x/week, 30 to 40km /week and general sports practice.

13/02/2010 - control – asymptomatic and total running weekly rhythm 30 to 40/km, divided in sessions of 10km, 50 at 1h/session. Normal cardiac exam, BP 120mmHg x 85mmHg, weight 77.200kg and we highlight the results 48h after running: TC 190mg/dl, LDL-C 122mg/dl, HDL-C 52mg/dl, TG 80mg/dl, TGO 17U/L, TGP 15U/L, BT 2.72mg/dl, BD 0.45mg/dl, BI 2.27mg/dl, CK 157U/L. Last control concerning the case presented.

Among the main causes for RB, we highlight⁽²⁾:

- General as well as mechanical trauma by high voltage electrical current, extensive burns.
- Intense and prolonged physical exercises.
- Muscular hypoxia: compression on the lower limbs at prolonged immobilization situations and/or consciousness loss.
- Genetic defects: glicolisis alterations or glycogenolysis; in the lipid metabolism; in the mitochondria; in glucose-6-phosphate dehydro-

genase. Metabolic myopathies like McArdle disease and muscular atrophy.

- Inflammatory myopathies: Poliomyositis and Dermatomyositis.
- Infections: *influenza A* and *B* virus; *Coxsackie*; *Epstein-Barr*; immunodeficiency; *legionella*; *estafilococcias*; *estreptococcias*; *escherichia coli*; *rickettsia species*; *salmonella species* among others. Fungi (*Candidiasis* and *Aspergillosis*); parasites (*Plasmodium species*).
- Body temperature alterations: thermal shock; malignant hyperthermia; malignant neurological syndrome; hypothermia.
- Electrolytic and endocrine alterations: hyponatremia; hypernatremia; hypokalemia; hypophosphatemia; hypocalcemia; diabetic ketoacidosis; hypothyroidism and hyperthyroidism.
- Drugs or toxins: estatins; fibrates; salicylates; corticosteroids; tricyclic antidepressives; anesthetic agents (Malignant Hyperthermia); anti-histamines; alcohol; heroin; cocaine; spider bites; bees.
- Idiopathies

RB generally occurs in healthy individuals and is rarely mentioned as a cause of sudden death in competitive athletes⁽³⁾. In the United States, 26,000 cases a year are described in the general population and IRA occurs in about 30% of the cases⁽¹⁾. In a study conducted by Melli *et al.* IRA occurred in 46% in 475 hospitals seeing patients with RB diagnosis. In this same study, it occurred more frequently in illicit drugs users or alcohol abuse and among individuals post-trauma and coexistence of other known causal factors, with 3.4% of mortality⁽⁴⁾. It is estimated that seven to 10% of IRA in the United States are due to RB⁽⁵⁾, being it the reason for admission for its prevention.

Global mortality rate in the literature is described in up 5%, with greater prevalence among men^(1,2) and when mainly occurring after extensive muscular trauma, a fact referred and recorded during wars⁽⁶⁾. Its evolution is usually benign in those patients without IRA. Its mortality is linked according to the specific risk population studied, as well as the involvement of other organs and with presence of coexisting clinical causes, besides an important individualized response. Recovery of the renal function with occurred in about 80% of the cases, being its pathogenesis, only partly elucidated, suggested by the myoglobin participation (MIOG) with subsequent myoglobinuria, since MIOG is one heme protein of low molecular weight, without specific plasmatic ligation protein and freely filtered by the glomerule⁽⁷⁾. It is detectable in the urine in concentrations with glomerular renal levels above 0.5 to 1.5mg of MIOG/dL and produces alteration in urine color in concentrations above 100mg/dL⁽⁷⁾. MIOG has remarkable nephrotoxic action, especially at tubular level, as well as effects related to vasoconstriction and consequent renal ischemia, besides onset of tubular pigment obstruction. However, not all RB cases are associated with myoglobinuria⁽⁸⁾. The IRA risk, due to the CK plasma levels is not well-established, although it is more rare in serum doses lower than 15.000 to 20.000U/L, some investigations refer to levels lower than 5,000 U/L⁽⁹⁾. These data reinforce the individualized responses in the RB evolution, as recorded in the present case as well as mentioned and the early diagnostic and therapeutic attention in the IRA prevention⁽¹⁰⁾. Concerning the case exposed above, some predisposing hypotheses to the RB onset will be discussed.

Statins

It is clinical domain that, despite rarely occurring, RB is suspected as consequence of routine use of statins in dyslipidemic patients, being usually preceded by myalgia, clinically manifested and or CK with increase of more than ten times the normal threshold⁽¹¹⁾. In clinical practice we also notice myalgia without enzymatic increase, as well as the reverse, that is to say, its increase with no myalgia, highlighting once again an individualized response in its onset. In the case under analysis, the rosuvastatine (RO) was prescribed in the dose of 10mg/day, and complications occurred with the second taking (second day of use), totalizing 20mg in 48h. Such fact was surprising to us and was a motivation to research on the published articles in RB cases associated with its use, specifically in Asian and their descendents, since the commonest is its onset related to increase of its habitual dose and time of use. Therefore, would that be the cause? Some investigations, as by Lee E *et al.*, demonstrated more systemic exposure of RO in Asians (Chinese, Malaysian, Indian) compared to the white population resident in Singapore and exposed to the same environmental factors, in the single dose of 40mg/day⁽¹²⁾. Our interest in these investigations is more specifically restricted to the daily doses used, dose total prescribed in the study, time of use, its tolerability noticeably aiming myotoxicity effects, involving possible descriptions of RB cases, the main case of this communication. Miyauchi K *et al.* CHALLENGER STUDY, assessed 50 Japanese patients aiming the RO action at LDL-C > or = 120mg/dl levels and the favorable consequences of its control, in atherosclerotic plaques and in carotid intima, assessed by resonance magnetic. The dose was 5mg/day, total of 96 weeks or approximate 602 days and therefore a total of 3010mg of RO and no record of severe myopathies complications was observed⁽¹³⁾. Kurabayashi M *et al.*, SUBARU STUDY, compared the effects in Japanese with hypercholesterolemia of RO 5mg/day with atorvastatin 10mg/day during eight weeks, approximate 56 days, total dose of RO 280mg. The effects were favorable in both with higher prevalence for RO, with no record of muscular complications⁽¹⁴⁾. Hua CX, in 30 male Chinese volunteers with single dose administration of 20mg of RO and evaluations of inflammatory markers before and after 72h of its administration also of its possible pleiotropic effects in with no record of muscular alterations⁽¹⁵⁾. Park SY *et al.*⁽¹⁶⁾ in a total of 392 Korean dyslipidemic patients, complied from the beginning of 06/2004 until the end of 08/ 2006, in the *Chungbuk National University Medical Center* in the doses: 5mg (n = 34); 10mg (n = 148) of atorvastatin and of 5mg (n = 94); 10mg (n = 82) of RO. The time of use oscillated in each clinical case and never lower than 30 days and no myopathies were recorded⁽¹⁶⁾. Chiang CE *et al.*, also tested the tolerability of RO in study comparing it with atorvastatin in Korean patients with dyslipidemia during 12 weeks (84 days), in the dose of 10mg day (total dose 840mg) and did not record important musculoskeletal effects⁽¹⁷⁾. In the DISCOVERY - Asia Study, the authors used during 12 weeks (84 days), in 1,482 patients from China, Hong Kong, Malaysia, Taiwan, and Thailand in the daily dose of 10mg of RO and it remained safe during its time of use⁽¹⁸⁾. A study with 12 Chinese volunteers (six men) who used in single doses 5, 10, 20mg of RO being its tolerability tested from zero hour and after that every hour until 72h. Two cases in the dose of 10mg presented bilirubin increase from 16.1 to 31.4mmol/L and another of CK from 141U/L to 307U/L, with return to normal values after Five days and asymptomatic, with-

out important myalgias clinical consequences referred⁽¹⁹⁾. Saito Y *et al.*, tested 154 Japanese patients in the doses of 5, 10, 20mg of RO during eight weeks (56 days) and without pointed muscular collateral effects⁽²⁰⁾. From the IRIS trial, involving 740 South Asian patients residents in the United States and Canada, with 10 and 20mg of RO during six weeks (42 days), the same was well-tolerated⁽²¹⁾. In the COSMOS Study, in 200 Japanese patients for evaluation of the reduction of coronary plaque through intravascular ultrasound, after use of RO during 76 weeks, no cases of severe myalgia were reported including RB⁽²²⁾. Mabuchi H *et al.* in 37 Japanese with family heterozygote hypercholesterolemia in increasing doses of RO 10-20 until 40mg, reaching to 12-18 weeks (84 to 126 days) of use, two cases with CK increase, but without muscular symptoms⁽²³⁾. In a meta analysis, Strutt K *et al.*, involving six trials, with about 1,172 patients from Japan, in mean doses of 10mg Day of RO for mean period of 12 weeks (64 days) and total 640mg of RO, the drug was well-tolerated and without important collateral record⁽²⁴⁾. In a recent and interesting investigation, Kanazawa *et al.*, studied the effect with 2.5mg day of RO for a period of three months (approximately total 225mg) in 36 Japanese patients with type 2 diabetes and hypercholesterolemia, in the osteoblastic function, with its improvement, regardless of the decrease of the LDL-C levels and with no record of muscular complications⁽²⁵⁾. Tomilnson *et al.*, used RO in 305 Chinese with hypercholesterolemia, in daily dose of 10mg, under study to observe whether genetic variants interfere in the therapeutic results and did not record myopathy collateral effects either⁽²⁶⁾.

Therefore, despite some questioning, we cannot state with safety and evidence that the use of RO had been the probable isolate cause for this clinical complication in the present case, even due to the total dose used (20mg) and time of use (two days).

It is important to remember that some medication associated with statins boost the RB onset: mibefradil, fibrates, cyclosporine, warfarin, antibiotics, macrolides, digoxin, antifungicides, niacin, cyclosporine, nefazodone, clorzoaxone, all absent in the present clinical case.

PHYSICAL EXERCISE

It is described as a triggering factor, despite rare, of RB. Its onset is particularly and more frequently related to high intensities of physical exercises and in more competitive practitioners and therefore in extenuating physical activities. Practice in adverse weather conditions, such as high or low temperatures, favor this situation, besides inadequate previous hydration (heat) and during longer events, above 1h, without correct and suitable hydric and electrolytes replacement, especially K and Na. As illustration, we can mention a case report by Parolin BM *et al.*⁽²⁷⁾ describing a 36-year old runner who after 8km of rustic run developed fulminant hepatic insufficiency RB (CK 582UL) which developed to IRA and extreme increase of central body temperature (Exercise Induced Heat Stroke), being its clinical evolution favorable⁽²⁷⁾. In the present case he was practicing society soccer during 1h30 minutes, which was a usual activity and he did not perform any other previous physical exercise and had no important muscular trauma. He referred light muscular pain during the soccer practice on that day, without need to stop the activity and has attributed it to the exercise and no symptoms were reported.

We cannot affirm that the cause had been this physical activity performed and in the existing environmental conditions.

GILBERT'S SYNDROME

Its diagnosis was added to the present case and it was diagnosed by a routine hematologist after our demand. The Gilbert's Syndrome is a chronic and benign condition where indirect bilirubin increase is observed and CNA clinically manifest as jaundice. It can appear after stress or physical exercises, occurring more commonly among men and with prevalence estimated in 6% in the general population⁽²⁸⁾. Anesthetic acts under this clinical condition should be reevaluated. It is caused by a mutation in the gene GT1A1, aiding in the genetic laboratory diagnosis of this syndrome⁽²⁹⁾. After this evaluation and for its benignity, he was released to a normal life with no restrictions to physical exercises, with some guidance concerning use of anesthetics and certain medication, in report sent by the hematologist. It would not be the RB triggering in this case.

Finasteride

Finasteride inhibits testosterone conversion in dihydrotestosterone (DHT) by inhibition of the intracellular enzyme 5- α -reductase. It is known that the DHT is a powerful masculinizing hormone and its action produces increase of the prostatic gland, increase in fat secretion by the sebaceous glands and hair growth. It is usually used in the dose of 5mg/Day for benign prostate increase control. During its use hair growth was observed, and it started to be administered 1mg/day with the aim to combat baldness (alopecia) and commonly used with no mandatory medical prescription for this purpose. According to lay publishing in our field, in 2008 1.7 million boxes were sold in Brazil (Veja Magazine-29/07/2009). This was the motivation for use by the patient in the present case, despite having been prescribed by another professional. We stress that in two years 720mg total were ingested and as mentioned, omitted by the patient until the onset of the complication. Had that actually played a role in the development of RB in this case? We did not find research in this dose of 1mg and in the habitual 5mg/day, specifically related to the RB onset, although additional care should be observed in patients with hepatic or renal failure, which is not the case of our patient. His previous laboratory exams show normality and slight unspecific increase in one of the TGP doses (24/08/2008), as described above. On that date he was already under use of finasteride 1mg/day, a fact he had omitted, as already mentioned. In studies of finasteride tolerability in 3,200 men light to moderate collateral effects were recorded, such as: libido alteration, ejaculation and erectile dysfunction in non-significant percentage in comparison to placebo and without report of muscular alterations⁽³⁰⁾. The question on if would be independently related as the cause for RB still remains.

This complication in the reported case would be linked to a combination of factors: use of finasteride (760mg in two years) + RO (total of 20mg, in two days) + usual and non intense physical exercise (society soccer 1h30 min.) + hotter temperature (very warm night-sic) + race (Asian - third generation) + individual and genetic predisposition + Gilbert's Syndrome accidentally diagnosed, would all factors add up to the etiological background or one factor would surpass the other? Important questioning

is relevant such as: 1) could we prescribe other statins to combat his dyslipidemia and in the specific case, rosuvastatine or not, as precaution? 2) Would he be restricted to more intense sports practice? 3) how can we identify a cause with genetic background ?

The clinical action taken with the purpose to answer those questions was:

To no initially prescribe statins and control his dyslipidemia with diet and habitual exercises, although mother and sister with dyslipidemia make use of simvastatin in usual doses and good tolerance without adverse effects.

Release to usually physically exercise as already reported in his clinical evolution and reguidance to practice of more intense exercises, especially at extreme temperatures, besides care with hydration and food ingestion.

Immediate suppression of finasteride and careful orientation in the use of medication, especially not prescribed by his follow-up doctor.

We lack a genetic evaluation due to its difficult performance in the clinical practice in the real world, for a possible neuromuscular substrate of neuromuscular disease and it related, and there is not a defined clinical guideline⁽³¹⁾. In recent publishing, remaining of myotoxicity symptomology, ranging from myalgias to more intense muscular weakening have been described after suppression of statin in 52 patients with CK remaining with mean

of 1.000U/L for over three months (up to six months) after suppression of statine and electromyography and muscular biopsy having been performed. In 47 patients with mean age of 22-86 years, muscular biopsy was normal (72% men) and in five patients (100% men), all older than 60 years (60-82 years), there was neuromuscular disease to biopsy: paraneoplastic polymyositis, amyotrophic lateral sclerosis, Kennedy's disease, muscular deficiency of phosphorylase b kinase, necrotic myopathy of indefinite cause⁽³²⁾. Thus, due to these results, the clinical and laboratory profile of the presented case does not fit into the mandatory performance of a muscular biopsy, facing it only as a complementary didactical aspect and obviously with discomfort from the patient.

To respect its individuality and send an alert message to athletes regarding the use of finasteride as a prohibited drug in competitive sports.

We understand it is important to communicate about this case so that opinions and suggestions for a complementary clinical approach are necessary, due to the remaining questions concerning the cause(s) of this complication reported here, since, according to the author: "doubts are more proper to the wise, while the absolute certainty is proper to the ignorant".

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