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RESEARCH ARTICLE

STATIN INDUCED MYOPHATY - CASE REPORT

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ABSTRACT

We present the case of a 28-year-old woman, who began suffering 6 months prior to admission with weight loss, malaise, dysphagia to solids and progressive dyspnea. Anterior mediastinoscopy and lymph node biopsy were performed. In recovery it presents respiratory difficulty, CO2 80mmHg; Suggamadex is administered. Enter intensive therapy for assessment and management, is found elevation of muscle enzymes. Muscle biopsy with necrotizing myopathy associated with statins. Management with prednisone and immunoglobulin; graduating for improvement. Statin-related myopathy usually manifests after 6 months of therapy. The risk factors include: characteristics of the patient, agents that cause an increase in the half-life of the drug or an increase in its concentration at the muscular level and factors that increase the susceptibility of the muscle. It is recommended to stop statins days before major elective surgery. The pharmacogenic myopathies are frequent. They appear after a time of exposure to the responsible drug. They may present with myalgia, proximal weakness and increased muscle enzymes. The withdrawal of the drug leads to the cure of the disease in most cases.

INTRODUCTION

The pharmacogenic myopathies are frequent. The incidence is unknown. Clinical manifestations vary from myalgias and weakness to rhabdomyolysis. To date, more than 150 causes of rhabdomyolysis are described (Olivé, 2010). The most frequent are shown in Table 1.The objective is to review the literature with definition of clinical variables and complications, specifically muscular by use of statins and impact of their identification and timely treatment.A bibliographic search was carried out in the PubMed, MD Consult and EBSCO databases, with the key words: «Statin Myopathy», «Statin rhabdomyolysis», «Statin side effects», «Pharmacogen myopathies». Different articles were selected for review, and by their content allows a correlation and analysis of the present case.The case of a 28-year-old woman is presented. Background of importance: Dyslipidemia in treatment with statins specifically simbastatin 20mgs every 24 hours 8 months ago. Starts 6 months ago with decreased stools of consistency without mucus or blood, partially cedes administration of antidiarrheal, since then weight loss of approximately 13 kg. Two months ago general malaise was added asthenia, adynamia, hyporexia, drowsiness, chills, fever with profuse diaphoresis, predominantly nocturnal, in addition to nonproductive cough, dyspneizing, not cyanozating, and a week ago with dysphagia to solids, with gradually progressive dyspnea , which is why it is carried out with an optional tomographic study in which ganglia with enlarged anterior and superior mediastinum, pulmonary aorto window, carina and subcarinal region of probable inflammatory etiology are appreciated. The admission was decided on a scheduled basis for anterior mediastinoscopy and lymph node biopsy.

Balanced general anesthesia is performed with propofol, fentanyl, rocuronium and maintenance with sevoflorane 2vol%. Non-invasive monitoring the operation with surgical time of 3 hours, minimal bleeding, with administration of 1200mL of crystalloid solutions, uresis 200ml, neutral balance. Non-pharmacological emersion and extubation with 95% TOF and adequate protective airway reflexes.Upon admission to the post-anesthesia care unit, there is muscle weakness and respiratory distress that requires assisted ventilation with a face mask. Venous gasometry is taken, which reports PCO2 of 80mmHg, a single dose of 200mg of sugammadex is administered to rule out residual relaxation, without changes. Ventilation is started with BiPaP and the admission of intensive therapy unit for assessment and management is decided. Because of weakness in the lower limbs, an approach is made as myopathy, finding elevation of muscle enzymes meaning CPK, aldolase. A vastus lateralis muscle biopsy was performed with evidence of myositis and myolysis, findings compatible with necrotizing myopathy associated with statins, which is why management with prednisone and immunoglobulin boluses was initiated in the intermediate care unit. Infusions were maintained with bicarbonate for 48 hours; intravenous and oral fluid support was maintained; Clinical and laboratory continued favorable evolution. After 72 hours of admission, a clear decrease in the biochemical markers and phosphorus phosphate was detected, and it was discharged after 5 days for improvement. Statins, inhibitors of 3-hydroxy-3methylglutrayl-coenzyme A (HMG-CoA) reductase, reduce the synthesis of mevalonate, an important precursor for the production of cholesterol, which causes the decrease of low density lipoproteins (low density lipoprotein (LDL for its acronym in English)) in 25 to 50% (Perler, 2007).

Table 1. Most frequent causes of rhabdomyolysis

Myopathies due to direct toxicity
Glucocorticoid
Antipalúdic
Colquicine
Statines
Cocaíne
Zidovudine
Ipecuaco
Etretinato
Isotetrinoine

Table 2. Adverse effects of statin therapy

Headache
Alteration of liver enzymes
Paresthesias
Gastrointestinal disorders
Myopathies / myalgias
Rhabdomyolysis
Rash
Hipersensibility

Table 3. Myopathic syndromes related to statins

Concept	Definition
Statin myopathy	Any muscular disorder associated with the use of statins
Myalgia	Muscle disorder without elevation of serum CK
Myositis	Muscle disorder with elevation of serum CK
Rhabdomyolysis	CK levels> 10 times above the upper limit associated with Renal Failure

Table 4. Risk factors associated with myopathies

Advanced age
Female sex
Low rate of muscle mass
Multisystemic disease
Diseases that affect kidney or liver function
Hypotirioidism without treatment
Drug interactions
Vigorous exercise
Excess alcohol
Concurrent infections
Surgery or major trauma
Diet
Genetic factors (Eg: Cytochrome P450 isoenzyme polymorphisms, inherited defects of muscle metabolism, characteristics that affect the oxidative metabolism of fatty acids.)

These effects together contribute to the reduction of cardiovascular risk, increase of long-term survival and, therefore, decrease in mortality in patients with or without risk of coronary disease, which makes these drugs the most effective option for the patient. Treatment of hyperlipidemia (Mihaylova *et al.,* 2006). The extensive use of these drugs, considered safe and well tolerated, has also allowed the possibility of reporting different adverse effects related to prolonged use. Current evidence shows a different range of adverse effects that, in certain cases, lead to the discontinuation of its use by patients (Table 2). Among these, myopathies stand out due to their potential severity (Patel *et al.,* 2011). There are certain drawbacks when describing the epidemiology of this condition. Myopathy, myalgia, myositis and rhabdomyolysis are terms that are used inconsistently in different studies. To solve this problem, the American Heart Association in conjunction with the American College of Cardiology and the National Heart, Lung and Blood Institute have defined 4 myopic syndromes related to statins (Table 3) (Quiceno *et al.,* 2007). The myopathy related to statins usually manifests from 6 months after the start of therapy, although there are reports of adverse effects presented at 3 and even at 1 month of treatment (Patel *et al.,* 2011; Sathasivam *et al.,* 2008). In a meta-analysis it was reported that the incidence of myopathies occurs in 5 patients per 100 000 people / year. According to the FDA Adverse Event Reporting System, the incidence of fatal rhabdomyolysis is estimated at 1.5 deaths per 10 million written medical prescriptions (Sathasivam, 2008). It has been described that the frequency of true myositis fluctuates between 1 to 5% and that of myopathy associated with monotherapy is observed in 0.2% to 7%. According to reports, the interaction with other medications increases this incidence by 1% .8 Finally, the presence of asymptomatic CPK elevation is widely reported in 11 to 63% of the cases.9 Currently, statins have a higher rate of effects. myotoxics are atorvastatin and simvastatin. Among the risk factors that increase the possibility of the development of myopathy, there are different variables that operate before or during the consumption of statins and that include: characteristics of the patient, agents that cause an increase in the half-life of the drug or a increase in muscle concentration, the use of concomitant medications, and factors that increase muscle susceptibility (Table 4) (Quiceno *et al.,* 2007).

Clinical presentation

Although the safety profile of statins is excellent, myalgias are the classic clinical data, without necessarily showing functional muscle deterioration. In general, clinical manifestations are not well established, but muscle pain and weakness can often be found. Observational studies have found a myalgia rate of 10-15% among patients who took. Statins, in a low percentage fulminant rhabdomyolysis was found that is potentially fatal (Gounden and Blockman, 2008). The best strategy to minimize myopathy due to statins is prevention. It is recommended to use the lowest dose to achieve the therapeutic objectives, avoid as much as possible the concomitant therapy with drugs that increase the risk of myopathy and careful prescription to susceptible patients. Likewise, it is recommended to suspend statins a few days before elective major surgery, to avoid postoperative effects mentioned in the clinical case (Catarralá, 2009).

Conclusion

The pharmacogenic myopathies are frequent. The pharmacological history is essential for its diagnosis. They usually appear for the first time after a period of exposure to the drug responsible. They may present with myalgia, proximal weakness and increased muscle enzymes. The withdrawal of the drug leads to the cure of the disease in most cases, however, it is important to make a detailed clinical history during the preoperative assessment emphasizing the use of drugs with which side effects can develop due to their chronic use, and in this way can be given a more appropriate management and even indicate the suspension of certain medications before a scheduled surgery.

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