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A Debilitating Adverse Reaction of Pityriasis Rubra Pilaris Due to Statin Therapy in A Low-Risk Patient: Case Report

Reich IJ[1]* | Keller KL[2]

***Correspondence:** Isaac Reich
Address: [1]Computational Biology, University of South Florida in Tampa, FL; [2]Peninsula Dermatology, Burlingame, CA
e-mail ✉: ijreich2022@gmail.com
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ABSTRACT

A 57-year-old male cardiologist with no previous cardiac history nor a positive family history of cardiovascular disease was started on atorvastatin to treat an LDL of 140 mg/dL. Within one month he developed a debilitating dermatologic reaction that initially was thought to be life-threatening Stevens-Johnson Syndrome. Biopsy demonstrated the reaction was Pityriasis Rubra Pilaris (PRP) an incurable dermatologic disease which on average lasts more than a year before resolution. As of the writing of this case report, 6 months after starting atorvastatin, the symptoms persist. This is only the second reported case of PRP resulting from statin therapy.
Keywords: *Statin, Pityriasis Rubra Pilaris, Lipid Therapy*

Introduction

Statins are among the most used medical therapies in the U.S. The frequency of their use is often not questioned. For example, 35 million Americans are taking statins and advocates contend twice that many should be taking them [1]. A quarter of American men over 45 years and half over 65 years of age are on a statin (Quick Stats, 2018). As a result, in 2013 the pharmaceutical industry generated profits of over 29 billion dollars on this class of medication [2].

While no one questions patients at high-risk should receive lipid lowering medication, there is significant controversy whether the use of this medication in low-risk patients is justified especially considering 20% of patients report an adverse event (Redberg and Katz, 2012) [3]. Research on the use of statins in low-risk patients has not demonstrated an improvement in serious cardiac events nor mortality [3] (Squizzato *et al*., 2011; Cholesterol Treatment Trialists, 2012). The reduction of risk is reported to be an absolute benefit equal to 0.46% (NNT=217) or one non-fatal heart attack avoided for every 217 low-risk patients who take statins [3].

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Physicians have alleged there is a financial conflict of interest which affects the research used to justify this therapy (Redberg and Katz, 2012). A Cochrane Database study reviewed 14 studies comprising over 33,000 patients and found a limited cost-benefit in low risk patients taking statins but concluded selective reporting of outcomes, questionable inclusion criteria, and failure to report adverse events made any conclusion of a benefit difficult (Taylor *et al*., 2011). The independent analysis performed by the Cochrane Database determined 10 of the 14 studies had been financed by the pharmaceutical industry (Redberg and Katz, 2012; Taylor *et al*., 2011). Further documenting the bias issues highlighted by Cochrane Database, these critics point out these studies excluded as many as 30% of patients from analysis because of a past medical history as benign as having muscle pain (Redberg and Katz, 2012). Cochrane Database also published a meta-analysis on the effect of statins in preventing stroke and found no benefit partly because 7 of the 8 included trials were considered by the authors to have a high risk of bias (Squizzato *et al*., 2011).

This case report involves the experience of a previously healthy 57-year-old male started atorvastatin based on the recommendation of his primary care provider and cardiology partner. He never smoked, ran 2 miles a day, and has no significant family history of cardiac disease. Within a month he suffered a debilitating adverse reaction which continued to restrict his activities 5 months after the event was first noted and the medication discontinued.

Case Report

A 57-year-old cardiologist with no risk factors for cardiovascular disease had a routine fasting lipid profile performed on August 2, 2021. His total cholesterol was 250 mg/dL, with an HDL of 42 mg/dL, and a calculated LDL of 140 mg/dL. Previous lipid profiles also demonstrated an elevated LDL but because of a consistently elevated HDL, therapy had previously not been recommended. This time statin therapy was recommended, and a prescription for atorvastatin was written. The medication was started on August 20, 2021.

On September 10, 2021, the patient broke out in a rash affecting his mucous membrane (Fig. 1). The atorvastatin was discontinued. Initial concern was for Stevens-Johnson Syndrome, a potentially lethal skin condition (Fig. 2). The rash spread to his entire body (Fig. 3).

A biopsy performed on September 28, 2021, diagnosed the condition as Pityriasis Rubra Pilaris (PRP), a rare and potentially debilitating condition with no known cure (see histology, Fig. 4) (Gajinov *et al*., 2013) [4]. The rash spread to the feet producing pain and inability to walk for two months. The hallmark of PRP is bright red hands that peel and are painful. The bright red painful hands, with ensuing

disabilities involving the ability of the patient to use his hands has continued for at least 5 months (Fig. 5).

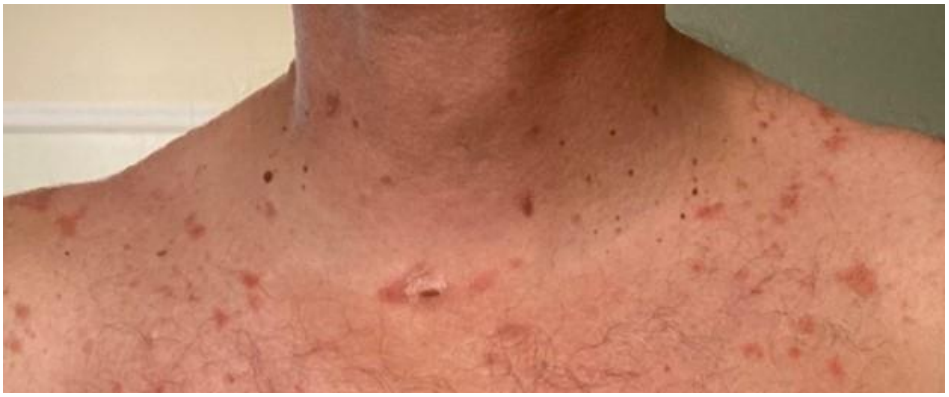

Figure 1: The initial presentation of PRP, September 11, 2021. The rash consisted of macules, papules, and blisters. The rash spread to the hands and feet where it persists and results in cracking and pain.

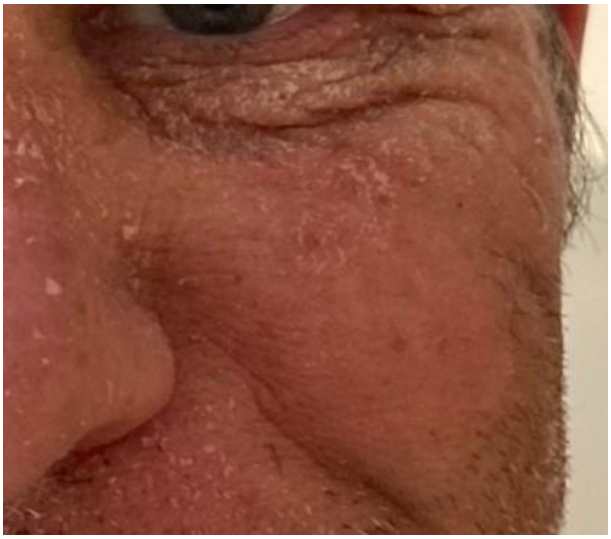

Figure 2: Left side of the patient's face, September 20, 2021. The blistering and the proximity of the lesions to the eye and the nose raised a concern for Stevens-Johnson Syndrome.

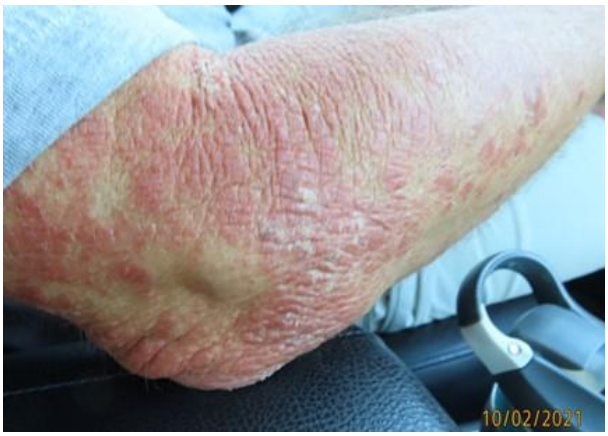

Figure 3: The rash affecting the patient's right elbow, October 2021.

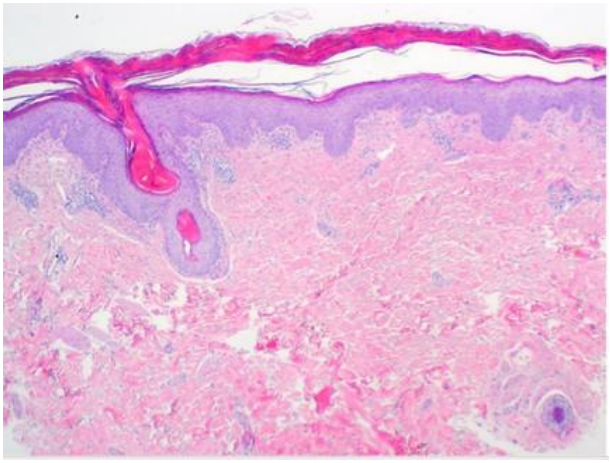

Figure 4: Skin biopsy read as consistent with Pityriasis Rubra Pilaris by the Johns Hopkins Dermatopathology Quality Assurance Conference: epidermal acanthosis, parakeratosis, and follicular plugging.

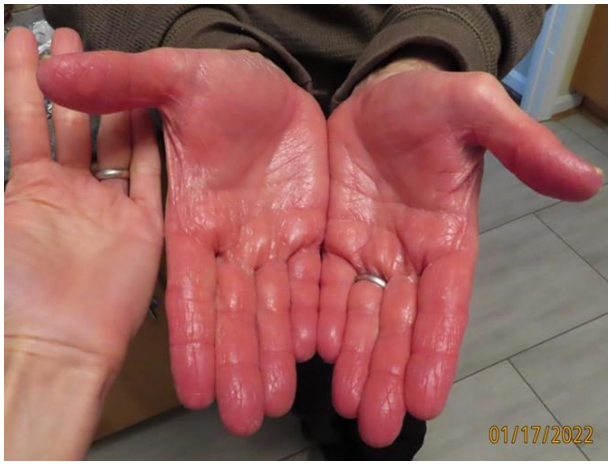

Figure 5: The patient's hands 5 months after diagnosis with his wife's hand for comparison. Notice the hallmark of PRP-the bright red inflammation of the hands and feet. It has not resolved and is associated with painful cracking.

The case was reported to the FDA Adverse Event Reporting System (FAERS). The patient was contacted by the manufacturer who performed an analysis of quality control at the factory the atorvastatin was produced. No aberrations in production were identified. A laboratory evaluation did not find alternative etiologies in this patient.

On October 22, 2021, after atorvastatin had been discontinued for a month and a half, the fasting lipid profile was repeated. The total cholesterol was now 223 mg/dL with an HDL of 43 mg/dL and a calculated LDL of 118 mg/dL. The determination was there was no longer an indication to initiate lipid therapy.

As of the writing of this report in January 2022, the PRP has not resolved. The patient is being managed with acitretin and secukinumab.

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Discussion

PRP as an adverse event caused by statin therapy has only been reported one time previously (Gajinov *et al*., 2013). According to the National Organization of Rare Disorders, PRP is associated with a number of long-term disabilities including: difficulty walking, hearing loss, and joint pain. Usually, patients experience a remission in 1-3 years but not always [4]. There are management strategies for symptoms but neither the U.S. Food and Drug Administration nor the European Medicines Association has approved a medication for the management of PRP [4]. In addition to the well-described phenomenon of PRP being caused by medication, other potential causes of PRP include infections, malignancy, and family history. A commonly tested cause is HIV infection [4].

The controversy regarding the use of statins in low-risk patients can't be resolved with a single patient. However, while this specific complication is rare (it is presumably underreported), the risk of severe, life-threatening, and debilitating adverse events after starting statin therapy is not. In addition to Stevens-Johnson Syndrome being reported as a fatal consequence of statin therapy, other serious long-term adverse events include diabetes, cognitive impairment, liver impairment, renal impairment, cataracts, and rhabdomyolysis (Noordally *et al*., 2012; Hippisley-Cox and Coupland, 2010). One study reported a low-risk patient on a statin is more likely to develop diabetes as a complication of statin therapy (1 in 204 patients) than avoid a non-fatal myocardial infarction as a benefit of statin therapy (1 in 217 patients) [3].

In the authors' opinion the medical literature contains an element of disbelief, discreditation, and condescension regarding adverse events caused by statins, referring to these adverse events as "perceived" or a "nocebo" (Adhyaru and Jacobson, 2018) [1]. In blog posts and readers' comment sections patients express frustration and outright anger about their experience with a medical community that refuses to acknowledge real persistent problems caused by this class of medication [5]. An example of disbelief, is the physician recommended strategy of re-introducing statins after a serious adverse event (Simons *et al*., 2015). Re-introduction is a logical strategy for drugs with an immediate life-saving benefit for which there is no other therapy (e.g. vancomycin), but statins have a small distant benefit and other therapeutic options for hyperlipidemia are well established (Redberg and Katz, 2012). Advocating a strategy of reintroducing statins after the patient has suffered a serious adverse event indicates these adverse events are not taken seriously (Adhyaru and Jacobson, 2018).

To justify this small but medically significant risk, there must be either a mortality benefit or a significant morbidity reduction demonstrated in low-risk patients treated with statins. The authors

respectfully acknowledge many cardiologists contend there is a morbidity benefit and different research could be presented to support their contention. However, a benefit-risk assessment requires the assessment of both benefit and risk to be free of bias. The supporting evidence for benefit is contaminated by research supported by or performed by the pharmaceutical industry and the risks are inappropriately diminished by a skepticism regarding prevalence and severity inconsistent with patient experience and much of the literature. Clinicians will not appropriately consider an alternative therapy if they consider the adverse effects of statins to be "perceived" (Adhyaru and Jacobson, 2018).

This case demonstrates it is reasonable statin therapy be excluded in low-risk patients until there is a consensus there is a mortality benefit or a morbidity benefit exceeding risk. The contention of benefit must be supported solely by studies done independently of the pharmaceutical industry and performed by and advocated by cardiologists who can demonstrate financial independence from the pharmaceutical industry. Alternative therapies should be the first line recommendation.

Nearly half of American men above 60 years of age are on a statin (Quick Stats, 2018). Because hyperlipidemia has many potential therapies, statin use must be carefully considered and the potential for rare but serious side effects should be acknowledged. Afflicted patients must be treated with respect.

In this case, an otherwise healthy patient with a risk of having a cardiac event much less than 1% developed a series of long-term debilitating adverse events due to a therapy which was no longer indicated a few weeks later.

Consent: Written informed consent was obtained from the patient.

References

Adhyaru BB, Jacobson TA. Safety and efficacy of statin therapy. *Nat Rev Cardiol* 2018; 15: 757-769.

Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, Voysey M, Gray A, Collins R, Baigent C. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet* 2012; 380: 581-590.

Gajinov ZT, Matić MB, Duran VD, Vucković N, Prcić ST, Vujanović LM. Drug-related pityriasis rubra pilaris with acantholysis. *Vojnosanit Pregl* 2013; 70: 871-873.

Hippisley-Cox J and Coupland C. Individualising the risks of statins in men and women in England and Wales: population-based cohort study. *Heart* 2010; 96: 939-947.

Noordally SO, Sohawon S, Vanderhulst J, Duttmann R, Corazza F, Devriendt J. A fatal case of cutaneous adverse drug-

induced toxic epidermal necrolysis associated with severe rhabdomyolysis. *Ann Saudi Med* 2012; 32: 309-311.

Quick Stats. Percentage of adults > 20 years of age told their cholesterol was high taking lipid lowering medication, by sex and age group. *Morb Mort Weekly Report* 2018; 67,771.

Redberg R and Katz M. Healthy Men Should Not Use Statins. *JAMA* 2012; 307: 1491-1492.

Simons JE, Holbrook AM, Don-Wauchope AC. Successful reintroduction of statin therapy after statin-associated rhabdomyolysis. *J Clin Lipidol* 2015; 9: 594-596.

Squizzato A, Romualdi E, Dentali F, Ageno W. Statins for acute ischemic stroke. *Cochrane Database Syst Rev* 2011; 8: CD007551

Taylor F, Ward K, Moore TH, Burke M, Davey Smith G, Casas JP, Ebrahim S. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2011; 1: CD004816.

Web-links:

1. Hurst TR. Considering statins? What a Cardiologist wants you to know. WebMD. Available at: https://blogs.webmd.com/heart-health/20210121/considering-statins-what-a-cardiologist-wants-you-to-know#

2. Batts V. Statins: A billion-dollar industry costing millions of lives. Statins.com. Available at: https://www.statins.news/2019-04-08-statins-a-billion-dollar-industry-costing-millions-of-lives.html

3. Abramason J. Statins in patients at low risk of cardiac disease. Am Fam Physician 2017; 96: Available at: https://www.aafp.org/afp/2017/1101/od1.html.

4. National Organization for Rare Disorders, Rare Disease Database, Pityriasis Rubra Pilaris, Pityriasis Rubra Pilaris - NORD (National Organization for Rare Disorders) Available at: https://rarediseases.org/rare-diseases/pityriasis-rubra-pilaris/

5. NY Times. October 18, 2018.
Available at: https://www.nytimes.com/2021/10/18/well/live/ldl-cholesterol-heart-attack.html#commentsContainer