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Rheumatology Second Opinion - Extended Written Report

Date: 2022-09-16

Patient: Jane Doe

Discussion:

The patient is well known to me as I was her rheumatologist until March 2016. She has giant cell arteritis which has been resistant to prednisone (requiring in the past persistent moderate to high doses for adequate control) and has developed multiple adverse effects from it, including steroid-induced diabetes mellitus. As a result, Actemra was initiated in February 2016 as a steroid sparing medication.

Actemra has been shown to an effective steroid sparing agent for patients with giant cell arteritis, as evidenced by several case series and case reports (1,2), as well as a recent randomized, double-blind, placebo-controlled trial (3). Actemra is known to induce elevation in liver transaminases (AST and ALT) as well as elevations in lipid parameters (total cholesterol, LDL, HDL, triglycerides) (4).

Laboratory tests from 4/28/16, 6/21/16, 7/19/16 and 7/22/16 are provided for review. Liver enzymes AST and ALT were noted to increase from April 2016 to July 2016. The ALT went from 1.5 times the upper limit of normal in April to 3.3 times the upper limit of normal in July. The cholesterol, triglycerides and lipoprotein panel showed marked elevation of the total cholesterol, elevation of the triglycerides, and marked elevation of the LDL. The blood test from 7/22/16 also showed insufficiency of vitamin D level.

Regarding the rate of monthly tapering of chronic prednisone dosage, there are no specific standards of care. The goal of tapering prednisone is to use a rate of change that will prevent both recurrent activity of the underlying disease and symptoms of cortisol deficiency due to persistent hypothalamic-pituitary-adrenal axis (HPA) suppression.

Recommendations:

I will start by saying that I do not have the baseline (prior to initiation of Actemra) liver enzymes and lipid tests available for comparison. In addition, no other diagnostic studies such as liver ultrasound are available for review. Therefore, the abnormalities in the presented blood tests are assumed to be the result of the current treatment with Actemra.

In case of liver enzymes elevation greater than 1 to 3 times the upper limit of normal, Genentech, Actemra's manufacturer, recommends reducing the dosage to 4 mg per kg or hold the intravenous Actemra until the ALT or AST have normalized (4). For liver enzymes elevation greater than 3 to 5 times the upper limit of normal, the manufacturer recommends holding Actemra until the levels are less than three times the upper limit of normal. For persistent increases greater than three times the upper limit of normal, it is recommended to discontinue the medication.

Based on above guidelines, the dose of Actemra should have been decreased to 4 mg per kg or held following

the blood test results from 4/28/16 which showed the ALT of 1.5 times the upper limit of normal. In addition, based on the latest test from 7/22/16 which showed a 3.3 times the upper limit of normal elevation of the ALT, Actemra should be held and the liver enzymes repeated every 2 weeks to monitor their decrease. When Actemra can be resumed (either when the liver enzymes levels are less than 3 times the upper limit of normal or when the liver enzymes have normalized), the dose should be resumed at half the original dosage (4 mg/kg). The liver enzymes should be monitored every 2 to 4 weeks.

The blood tests from July 2016 showed marked elevation of the lipids. Again, I don't have any pre-Actemra lipid panel for comparison but it is safe to assume that this medication contributed significantly to the elevation the lipid parameters. This lipid elevation usually responds to lipid-lowering agents, which should be initiated if not already done.

As stated above, there are no specific standards of care dictating the rate of decrease of chronic prednisone dosage but in general, the goal is to prevent both recurrent activity of the underlying disease and symptoms of cortisol deficiency due to persistent HPA axis depression. Symptoms of cortisol deficiency may include exhaustion, dizziness, low blood sugar, diffuse body aches. In general, prednisone is tapered by 10% every 2 to 4 weeks. That usually means 2.5 mg per day every 2 to 4 weeks at prednisone doses between 20 and 10 mg per day, 1 mg per day every 2 to 4 weeks at prednisone doses between 10 and 5 mg per day, and 0.5 mg per day every 2 to 4 weeks at prednisone doses from 5 mg per day down. Therefore, if the prednisone dosage was decreased by 2.5 mg every four weeks down to 2.5 mg per day currently, it is possible that the decrease in dosage could have been done a little slower once the dose of 10 mg per day was reached. However, many patients can tolerate this rate of tapering. If there is a concern for cortisol deficiency based on the presence of symptoms, this can be addressed by the endocrinologist with a low dose ACTH stimulation test. If there are no symptoms to suggest cortisol deficiency, I do not recommend any action.

Questions:

The patient wants an opinion concerning her blood test results (liver enzymes and cholesterol) during her treatment with Actemra (Which was started in February 2016). Also the prednisone was decreased each month after March by 2.5 mg and the patient's endocrinologist is concerned about the possibility of adrenal insufficiency.

References:

1. Loricera J, Blanco R, HernÃ¡ndez JL, et al. Tocilizumab in giant cell arteritis: Multicenter open-label study of 22 patients. Semin Arthritis Rheum 2015; 44:717.
2. Sciascia S, Rossi D, Roccatello D. Interleukin 6 blockade as steroid-sparing treatment for 2 patients with giant cell arteritis. J Rheumatol 2011; 38:2080.
3. Villiger PM, Adler S, Kuchen S, et al. Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet 2016; 387:1921.
4. Actemra (tocilizumab) [prescribing information]. San Francisco, CA: Genentech Inc; October 2013.

Electronically Signed by: , MD on 09/16/2022 03:25:59 AM

Board Certified: Rheumatology