Anakinra/hydrocortisone/hydroxychloroquine

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Toxic myopathy following drug toxicity: case report

A woman in her 40s [*exact age at onset not stated*] developed toxic myopathy during treatment with unspecified steroids, hydrocortisone, anakinra and hydroxychloroquine for juvenile idiopathic arthritis (JIA). Additionally, hydroxychloroquine related drug toxicity was also noted [*not all routes stated; durations of treatment to reactions onset stated*].

The woman, who had a history of JIA along with various concurrent conditions, presented from a nursing home following a mechanical fall at the age of 42 years. She had been receiving SC anakinra 100mg daily, hydroxychloroquine 200mg twice daily and hydrocortisone 20mg every morning and 10mg in the afternoon for JIA. On arrival, imaging revealed indeterminate C7 vertebral fracture. She had also been of unspecified steroid therapy since the age 18 years.

The woman received a cervical collar and unspecified medications for pain control. Her hospital course was complicated by acute on chronic hypoxic and hypercapnic respiratory failure. She required rescue bilevel positive airway pressure (BiPAP) support and was admitted to the intensive care unit. She became encephalopathic. Her arterial blood gas showed respiratory acidosis with CO_2 retention of greater than 105mm Hg. She was intubated. CT thorax revealed a left-sided opacification initially suspected and treated as left sided pneumonia. However, her respiratory status failed to improve despite on unspecified antibacterial therapy. She also failed recurrent spontaneous breathing trials while sedation was weaned. The findings were suggestive of significant neuromuscular weakness and lung collapse secondary to diaphragmatic weakness. On day 13 of admission, she underwent percutaneous endoscopic gastrostomy and a tracheotomy for long-term ventilator support. Her anamnesis revealed that she had recurrent admissions including an admission due to fall from bed with subarachinoid haemorrhage and fall from stairs resulting in comminuted fracture of her distal left tibia. Given her prolonged hospital course, recurrent hospital admissions and diaphragmatic weakness, there was concern that she had been exhibiting progressive weakness prior to the admission. History taking was limited due to nonverbal status and mechanical ventilation. She had reported progressive muscular weakness over the past year which resulted in recurrent hospitalisations leading to deconditioning. She did not require supplemental oxygen previously. During admission, her serum aldolase was elevated initially, which normalised 4 days later. Thyroid-stimulating hormone, ALT and AST were also elevated. Rheumatology was consulted. She had been on various medications for JIA. She had been on hydroxychloroquine for about 10 years. Hydroxychloroquine was withheld in her mid 20s to 40 years. She was on stable dose of 200 mg twice daily from the age of 40 to 42 years. Hydroxychloroquine was discontinued and later re-initiated due to concurrent synovitis in both hands prior to admission. Anakinra was discontinued due to septic shock secondary to concurrent *Enterococcus faecalis* urinary tract infection [*aetiology unknown*]. Based on the clinical presentation and diagnostic testing, a primary muscle pathology was suspected and muscle biopsy light microscopy was performed. It revealed type II fiber atrophy with scattered inflammation and granular myopathy with rimmed vacuoles. A diagnosis of toxic myopathy attributed to chronic use of hydrocortisone and hydroxychloroquine was made. Laboratory investigations and physical examinations were consistent with synovitis in her bilateral hand joints, it was elected to continue hydroxychloroquine and hydrocortisone until electron microscopy result. Hydroxychloroquine levels were 763 ng/mL suggestive of drug toxicity. Electron microscopy revealed granular material identified by the eosin and haematoxylin stains including numerous abnormal autophagosomes and vacuoles with curvilinear bodies. Immunohistochemical staining for CD68, CD20 and CD3 showed histiocytes and T lymphocytes in the perimysium and endomysium with decreased B lymphocytes. The findings were suggestive of an inflammatory response to muscle injury. Gomori trichrome sections revealed scattered vacuoles and fiber size variation consistent with myopathy attributed to hydroxychloroquine. Also, the myopathy was secondary to steroids including hydrocortisone and anakinra. Hydroxychloroquine was discontinued. Her condition improved to her prehospitalisation baseline.

Pillittere J, et al. Hydroxychloroquine-Induced Toxic Myopathy Causing Diaphragmatic Weakness and Lung Collapse Requiring Prolonged Mechanical Ventilation. Journal of Investigative Medicine High Impact Case Reports 8: no pagination, 12 Aug 2020. Available from: URL: http://doi.org/10.1177/2324709620950113 803500918