

## Acute Myopathy Following Short-term Low-dose Oral Steroid Therapy

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### Abstract

*The chronic and acute forms of steroid myopathy are well described in literature. However, myopathy following short-term low-dose oral steroid therapy is uncommon. We report a 52-year-old man who developed acute onset myopathy within 10 days of initiating oral dexamethasone in a dose of 8 mg per day (prednisolone equivalent of 40 mg/day). Discontinuation of steroid therapy led to complete recovery over a 3-month period. Mechanisms of steroid-induced myopathy and relevant literature have been reviewed.*

### Introduction

Cushing first described steroid-induced myopathy in 1932<sup>1</sup>. The chronic form is more common and occurs after prolonged usage of oral corticosteroids<sup>2</sup>. The acute form, also known as critical illness myopathy, presents as acute quadriplegia, and usually occurs in ICU patients who receive high-dose IV corticosteroids and/or non-depolarising neuromuscular blocking agents to facilitate mechanical ventilation<sup>3-7</sup>. This report describes a patient who developed acute onset steroid myopathy following short-term low-dose oral steroid therapy but presented clinically as a limb girdle syndrome rather than acute quadriplegic myopathy.

### Case report

A 52-year-old male presented to us with a 2½ months history of two episodes of right focal motor seizures, accompanied by proximal weakness of both the lower limbs of 2 months duration. A CT scan of the head following the seizure revealed a left parietal granuloma. A presumptive diagnosis of neurocysticercosis was entertained by the treating physician. The patient received a one week course of albendazole therapy in a dose of 400 mg/day. He also received dexamethasone, 4 mg twice a day for 6 weeks, followed by 4 mg once a day for 3 weeks, and was subsequently shifted to prednisolone 40 mg per day, which he received for the next one week. Around 10 days after starting steroid therapy, the patient noticed a mild proximal weakness

in both the lower limbs, in the form of difficulty in climbing stairs and standing up from the squatting position. The weakness evolved over a period of 2 weeks and subsequently became static. The patient remained ambulatory but could not run or walk fast and also experienced difficulty in sitting up in bed from the supine position. A thinning of both the thighs was also noticed around one month after the onset of the weakness. There was no history of muscle twitching, pain, cramps or any accompanying weakness of the upper limbs, neck, cranial, and bulbar musculature. There was no history of loss of sensation, paraesthesias or any bowel-bladder disturbance. There was no past history of diabetes, hypertension, or any other systemic illness.

On evaluation at the time of presentation, general physical and systemic examination was normal. Higher mental functions and cranial nerves were intact. On motor examination, the upper limbs were normal. In the lower limbs, there was bilateral symmetric wasting of the thigh muscles with decreased tone and grade 4/5 power in all the muscle groups at the hip and knee. The legs and feet were spared with grade 5/5 power in the plantar and dorsiflexors of the feet. Weakness of neck flexors and trunk muscles was also present. All the deep tendon reflexes were elicitable and plantars were flexor in nature. Sensations were intact and there was no spinal tenderness or deformity.

On investigation, haemogram, blood sugar, KFT, LFT, serum CPK, calcium, phosphorus, alkaline phosphatase

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and electrolytes were in the normal range. TFT was normal and the patient was HIV negative. X-ray chest, EEG and nerve conduction studies were normal. On EMG, done from the quadriceps, insertional activity was normal and there was no spontaneous activity. A recording of short duration, low amplitude motor unit action potentials with a complete interference pattern however, confirmed the diagnosis of myopathy in our case. A follow-up CT scan head done at this stage, revealed a complete resolution of the granuloma that had been detected 2½ months back at the onset of the illness.

A diagnosis of a resolved left parietal granuloma (neurocysticercosis) and seizures with a steroid-induced myopathy was made. The steroids were tapered-off over the next two weeks. At a one-month follow-up, there was an improvement in the motor weakness by almost 50%. At a subsequent 3-months follow-up, the recovery was complete.

## Discussion

Myopathy has been recognised as a side-effect of glucocorticoid administration since its introduction as a therapeutic agent in the 1950s<sup>8</sup>. Cushing originally described it in 1932<sup>1</sup>. Muller and Kugelberg first studied it systemically in 1959<sup>1</sup>. An excess of either endogenous or exogenous corticosteroids is believed to cause the condition. It occurs more commonly with chronic usage of fluorinated steroids (such as dexamethasone, betamethasone, and triamcinolone) as compared to non-fluorinated ones (such as prednisolone or hydrocortisone)<sup>9</sup>.

The exact incidence of steroid myopathy is unknown but two distinct clinical patterns have been described in literature – chronic and acute<sup>2</sup>. The chronic or classic form of steroid myopathy is more common. It has an insidious onset and usually occurs after prolonged usage of oral corticosteroids in a daily dose of  $\geq 30$  mg/day<sup>2</sup>. Chronic administration of doses  $> 10$  mg prednisolone (or its equivalent) per day has also been reported to predispose patients to muscle injury<sup>10-12</sup>. Clinical presentation is that of a limb girdle syndrome. Neck flexor and proximal muscle weakness is more pronounced than distal muscle weakness. Pelvic girdle muscles usually are affected more

severely and earlier than pectoral girdle muscles; however, severe relative weakness of the anterior tibialis muscle can be found. Proximal muscle weakness of the lower and upper extremities is significantly related to the cumulative dose of steroid. Muscle bulk typically is normal, but muscle atrophy can occur. Muscle stretch reflexes are typically normal. Sensations are preserved. Patients with steroid-induced myopathy may also experience a significant decline in respiratory function, leading to symptomatic dyspnoea. The clinical course is usually reversible, with either improvement or resolution of weakness and respiratory impairment after drug withdrawal.

The acute form of steroid myopathy is uncommon. It usually occurs in ICU patients who receive high dose IV corticosteroids and/or nondepolarising neuromuscular blocking agents to facilitate mechanical ventilation, but can occur with high-dose glucocorticoid use alone<sup>3-7</sup>. Though uncommon, myopathy following a single oral dose of prednisolone (40 mg) and acute myopathy following administration of a single low-dose of parenteral triamcinolone has also been reported<sup>1,13</sup>. However, the combined use of these drugs carries a greater risk for myopathy than does each drug separately. Acute steroid myopathy has also been referred to as acute quadriplegic myopathy, acute illness myopathy, critical illness myopathy, and myopathy associated with thick filaments. It may also develop in critically ill patients with sepsis, multi-organ failure, or transplant recipients receiving high-doses of IV corticosteroids during the perioperative phase<sup>14-16</sup>. The usual clinical presentation is with acute onset generalised muscle weakness, not limited to a mere proximal distribution. Muscle stretch reflexes are typically normal.

Our patient falls somewhere in the middle of the spectrum of chronic versus acute steroid myopathy. He developed acute onset myopathy (i.e., within 10 days of initiating steroid therapy) on relatively lower, oral steroid doses of 8 mg of dexamethasone/day (prednisolone equivalent of 40 mg/day). Moreover, the patient was not critically ill, malnourished, or suffering from any systemic or debilitating illness as is the usual case in patients who develop acute steroid myopathy. The clinical profile of the myopathy also resembled that of chronic steroid myopathy rather than that of the typical acute

quadriplegic steroid myopathy. Age and a sedentary lifestyle were possible contributory factors for the development of myopathy. Another unusual feature was the stabilisation of the weakness after a 2-weeks evolution despite the continuation of the initial steroid dosage of 8 mg of dexamethasone/day for another 2 weeks. The subsequent dose reduction of dexamethasone to 4 mg/day followed by a shift to prednisolone (40 mg/day) – a non-fluorinated steroid – probably prevented a further downhill course. Although wasting of the thigh muscles was noticed one month after the onset of weakness, there was no further worsening of muscle power. Also, unlike acute steroid myopathy in which muscle strength recovers slowly over several months in patients who survive, our patient made a significant recovery within one month of withdrawing steroids, and a complete recovery by 3-months time.

There are no specific laboratory findings in steroid-myopathy<sup>17,18</sup>. Unlike other drug-induced myopathies, serum CK and LDH concentrations are usually in the normal range or only moderately elevated<sup>19</sup>. An elevated urinary creatine excretion, if found, is more specific for this condition<sup>18,19</sup>. EMG is usually normal in the early phase, but may show low amplitude myopathic motor unit potentials later in the course<sup>f</sup>. In our case, the serum CK was not elevated but the EMG revealed myopathic potentials. Muscle biopsy usually reveals an increased variation in the diameter of fibres without muscle fibre inflammation or necrosis<sup>4</sup>. There is a preferential type II fibre atrophy in chronic steroid myopathy. Both types of fibres (type I and II) are affected in acute myopathy. A few necrotic fibres may present<sup>9,18</sup>. However, a diagnosis is often made on the basis of the clinical picture alone, without resorting to muscle biopsy<sup>9</sup>. In our case also, muscle biopsy was not performed since the patient stabilised and showed a significant improvement within a month of the steroid withdrawal.

The exact mechanism of the muscle weakness is unclear but may be related to decreased protein synthesis, increased protein degradation, hypokalaemia, and/or decreased sarcolemmal excitability<sup>20</sup>. The risk may be increased in elderly patients and those with cancer or negative nitrogen balance prior to onset of therapy<sup>21</sup>. Other contributory factors are a sedentary lifestyle, less

active muscles being preferentially affected; female sex, women being affected twice as commonly as men. Growth hormone and insulin-like growth factor-I (by decreasing the steroid-induced glutamine synthetase activity) have however been found to have a preventive effect on myopathy due to steroids<sup>17,18</sup>.

The weakness seen with steroid myopathy typically resolves after the corticosteroid dose is reduced or discontinued, although it can take weeks-to-months for recovery. An increase in muscle strength occurring within 3 – 4 weeks following dose reduction usually confirms the diagnosis of steroid-induced myopathy. This cause-effect relationship was very well established in our case. A reduction in the dosage prevented further worsening, while complete withdrawal of steroid therapy led to a remission and complete recovery. Chronic myopathy following prolonged treatment with high-doses of corticosteroids may however, at times, persist indefinitely.

## Conclusion

Our case highlights that acute myopathy may follow not only high-dose IV steroid therapy but may also develop with short-term, relatively low-dose oral steroid therapy and present clinically as a limb-girdle syndrome rather than acute quadriplegic myopathy. A possibility of steroid myopathy should be entertained in all patients who develop acute muscle weakness after starting oral or parenteral steroids. Early recognition of the problem and timely drug withdrawal carries a good prognosis for recovery. Our case once again highlights that steroids have side-effects and should be judiciously prescribed only after weighing the risk-benefit ratio in a given case. Non-fluorinated steroids should be preferred, and alternate day dosing considered when long-term steroid therapy is indicated.

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