EDITORIAL

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Myopathy, Drugs, and Mitochondria

Exposures to some drugs have been reported to bring about myopathy (1). When diagnosing a patient with myopathy, it is necessary to consider myopathy secondary to drugs. In the most of such cases, with discontinuation of the offending drug, myopathy subsides and muscle power recovers within couple of days or several weeks. An important exception to this condition is statin-induced immune-mediated necrotizing myopathy (2,3). But, in another form of statin-induced myopathy, self-limited and more benign one resolves several weeks after discontinuation of the drug.

The pathomechanisms underlying drug-induced myopathy can be categorized as 1) impairment of energy and protein metabolism, 2) autoimmune-mediated necrosis, 3) impairment of autophagy, and 4) mitochondrial dysfunction (1). First, impaired cellular energy and protein metabolism is the most common mechanism of drug-induced myopathy. Drugs that interfere with adenosine triphosphate (ATP) consumption, anaerobic glycolysis, and hepatic gluconeogenesis from amino acids can lead to myopathy. Three representative examples of this mechanism are glucocorticoids, statins, and alcohol. Second, in case of autoimmune-mediated necrosis, the patients suffer from severe weakness and pain of sudden onset, and fever may develop. Antipychotic drugs, such as haloperidol, risperidone, olanzapine, and clozapine, and selective serotonin reuptake inhibitors can lead to immune-mediated necrotizing myopathy. Labetalol, an antihypertensive drug, and propofol, an anesthetic agent, have also been reported to be rarely associated with necrotizing myopathy. Statins and alcohol can also induce this type of myopathy. Third, for examples of autophagy impairment, chloroquine, colchicine, vincristine, and amiodarone have been reported to induce myopathy which is associated with this mechanism. Lastly, as for mitochondrial dysfunction, there is a long list of offending drugs: statins, bupivacaine, antiepileptic drugs, such as phenytoin, valproic acid, and lamotrigine, and nucleoside reverse transcriptase inhibitors, such as zidovudine and clevudine. Bupivacaine inhibits mitochondrial complex I of the electron transport chain and cytochrome C oxidase. Valproic acid can inhibit oxidative phosphorylation, which may be associated with ragged red muscle fibers and cytochrome C oxidase-negative muscle fibers. Zidovudine, which is used against human immunodeficiency virus (HIV) infection, can decrease mitochondrial DNA expression, leading to the impairment of oxidative phosphorylation and the increased production of free radicals. Clevudine, an agent with activity against hepatitis B infection, may have similar mechanisms for mitochondrial toxicity to zidovudine. In this issue, Park et al. (4) elegantly report patients with clevudine-induced myopathy, and comprehensibly review previously reported cases of clevudine-induced myopathy, and finally discuss about clevudine's pathologic roles.

Collecting 95 cases of clevudine-induced myopathy by searching electronic databases and including their own seven cases, they analyzed the demographic data, clinical features, and pathologic findings. The mean duration of clevudine therapy before the development of myopathy was 14.2 months with a range of 5 to 24 months. Weakness mainly involved thigh muscles, and in around 13% of cases, bulbar or neck weakness was present. In majority of patients, creatine kinase was elevated to a median value of 887.7 IU/L with a range of 117.0 to 8,082.0, and myopathic abnormalities on electromyography were observed. Interestingly, muscle biopsy revealed features of mitochondrial myopathy in 90% of cases. After the discontinuation of clevudine, weakness improved within around three months. The authors proposed that careful attention for myopathy should be given to patients with long-term clevudine therapy, especially for longer than 14 months.

Thanks to this study, we learn the clinical features and pathologic findings of clevudine-induced myopathy. Furthermore, we gain more evidence that the link between muscle, mitochondria, and drugs can act in various clinical settings. In this report of clevudine-induced myopathy, not only neurologists but also hepatologists can get meaningful insights for patient care.

DISCLOSURE

The author has no potential conflicts of interest to disclose.

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REFERENCES

1. Jones JD, Kirsch HL, Wortmann RL, Pillinger MH. The causes of drug-induced muscle toxicity. *Curr Opin Rheumatol* 2014; 26: 697-703.
2. Mammen AL. Toxic myopathies. *Continuum (Minneap Minn)* 2013; 19: 1634-49.

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3. Apostolopoulou M, Corsini A, Roden M. The role of mitochondria in statin-induced myopathy. *Eur J Clin Invest* 2015; 45: 745-54.
4. Park SH, Park KS, Kim NH, Cho JY, Koh MS, Lee JH. Clevudine induced mitochondrial myopathy. *J Korean Med Sci* 2017; 32: 1857-60.

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