The involvement of ferroptosis on cisplatin-induced nephrotoxicity

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Background: Ferroptosis has been identified as iron-dependent regulated cell death, and it participates with a various disorder including kidney disease. Cisplatin, a classical anti-cancer drug, causes nephrotoxicity, which is inhibited by iron chelator. In the present study, we examined the involvement of ferroptosis on cisplatin-induced nephrotoxicity.
Methods: We used male mice with cisplatin-induced nephrotoxicity that were pretreated with vehicle or a ferroptosis inhibitor. Mice were sacrificed at 48 hours later.
Results: Cisplatin administration actually augmented ferrous iron and hydroxyl radical production in the kidney. Cisplatin-induced COX-2 expression, as well as lipid peroxide, was increased by cisplatin-treated kidney. An inhibitor of ferroptosis also suppressed cisplatin-induced increased of COX-2 expression and lipid peroxide. Mice with cisplatin administration developed kidney injury with renal dysfunction, and showed augmented oxidative stress, increased apoptosis, and elevated inflammatory cytokines. However, most of these symptoms were suppressed by a ferroptosis inhibitor.
Conclusion: Ferroptosis is suggested to involve cisplatin-induced nephrotoxicity.