Acute liver injury associated with glucosamine dietary supplement

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SUMMARY

A 55-year-old woman taking over-the-counter (OTC) glucosamine developed symptomatic hepatotoxicity. Several of her liver enzymes were elevated to 10 times the upper limit of normal. One week after discontinuing glucosamine, serum transaminases fell dramatically, with some returning to normal limits. Four weeks after glucosamine was discontinued, all her liver tests were normal. Rechallenge was not attempted. The potential causes of hepatocellular injury were evaluated. Glucosamine is a dietary supplement available in a wide variety of commercial preparations, primarily used for joint relief in osteoarthritis. Despite the extensive use of glucosamine supplements, significant elevations of transaminases are rare. The mechanism of hepatotoxicity in many OTC herbal preparations is unknown. It is vital for physicians to elicit a careful history of OTC medications and educate their patients on their potential adverse effects.

BACKGROUND

Glucosamine is a widely used over-the-counter medication purported to decrease the pain and cartilage loss of osteoarthritis. Glucosamine is an amino sugar and a prominent molecule in the biochemical pathways of synthesis of glycosylated proteins and lipids. It is also a major component of keratin sulphate and hyaluronic acid which are present in articular cartilage and synovial fluid, and are reduced in osteoarthritis. As such, glucosamine is not a herbal or botanical medication, but rather a dietary supplement. Glucosamine is commercially available and widely used for osteoarthritis and arthritic pain. Controlled trials of glucosamine have yielded conflicting results.¹⁻⁴ As use of over-the-counter medications and dietary supplements are becoming increasingly more popular in the US population, it is important for physicians to be aware of the indications, efficacy and adverse events related to these alternative remedies. Review of the current literature identified a single case series of three patients with glucosamine-induced liver injury, ranging from mild elevations of liver transaminases to fulminant liver failure.⁵

CASE PRESENTATION

A 55-year-old woman presented to the emergency department with complaints of generalised malaise and yellowing of the skin and eyes. Laboratory values revealed a mixed hepatocellular-cholestasis pattern, bilirubin 9.1, alkaline phosphatase 303 U/L, alanine transferase 1553 U/L, aspartate aminotransferase 897 U/L and γ -glutamyl-transpeptidase (GGT) 424 U/L. Medical history was significant for only

hypertension for which she has been taking Nebivolol, a β -blocker without incident. Further questioning of the patient revealed that she began using over-the-counter glucosamine supplements approximately 2 weeks prior to admission. The patient denied use of other over-the-counter drugs or alternative therapies. Her history was negative for alcohol excess or high-risk activities such as unsafe sexual contacts and intravenous drug use. Physical examination was remarkable for jaundiced with marked scleral icterus. The liver was non-tender without evidence of hepatomegaly or stigmata of chronic liver disease.

INVESTIGATIONS

Determination of hepatitis B surface antigen, hepatitis B e antigen, hepatitis B c antigen, cytomegalovirus and autoimmune screening tests (antinuclear antibodies, antimitochondrial antibodies, antiliver kidney microsomal antibodies, antismooth muscle antibodies) were negative. However, her work-up did reveal a positive Epstein-Barr virus (EBV) IgG and IgM, but had a normal peripheral smear, which strongly excludes EBV as a cause of her acute liver injury.

OUTCOME AND FOLLOW-UP

One week after discontinuing glucosamine, patient's liver function tests decreased dramatically. Over the next 4 weeks, all liver function tests were normal.

DISCUSSION

Glucosamine is a dietary supplement available in a wide variety of commercial preparations primarily used for joint relief in osteoarthritis. Known side effects include abdominal pain, drowsiness, headache and photosensitivity. There still remains little data on hepatotoxicity caused by over-the-counter herbal remedies, and the mechanisms are still poorly understood. The precise mechanism is unknown but may be secondary to the production of toxic metabolites when the herbal preparation is metabolised by the liver. Drug-induced liver injury may follow an acute course, mimicking acute hepatitis or may advance to chronic liver disease and cirrhosis, despite cessation of the inciting agent.⁵ Further investigation is needed to determine the exact mechanism of glucosamine-induced liver injury. It is vital for physicians to be cognizant of the potential adverse effects of seemingly harmless herbal preparations, and to account for any herbal exposure a patient may have had, as timely cessation of these products may prevent a potentially serious adverse reaction.

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Learning points

- ▶ Patients should be asked about the use of herbal and over-the-counter treatments as part of the medication history.
- ▶ Glucosamine-containing products may cause drug-induced liver injury, which may resolve upon discontinuation of the herbal product.
- ▶ Further investigation is needed to determine the exact mechanism of glucosamine-induced liver injury.

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