Is Etanercept Safe for Treating Plaque Psoriasis in a Patient With Chronic Hepatitis C Virus Infection?

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Clinical Question: Is the use of anti–tumor necrosis factor (TNF) therapy, specifically etanercept, effective and safe in the treatment of severe plaque psoriasis in a patient with chronic hepatitis C virus (HCV) infection?

Background

A 58-year-old man was evaluated for a 7-year history of severe plaque psoriasis with 20.0% body surface area. Previously, his psoriasis had showed marked improvement with methotrexate. He had discontinued use of methotrexate 1 month into therapy after serum alanine transaminase levels had increased to 9 times the normal value. He was found to have IgG hepatitis C viral antibody–positive status. Initial hepatitis C virus (HCV)–RNA was considered insignificant at 1350 IU/mL (normal levels generally defined as below 800 000 IU/mL). Liver biopsy demonstrated Metavir grade 2-3 (mild to moderate) inflammation with stage 3 bridging fibrosis. Other psoriasis systemic therapies such as acitretin and cyclosporine were not selected because of the concern that hepatotoxic and immunosuppressant activity from these agents could potentiate liver damage by chronic HCV infection. Our patient completed a 1-year course of combined therapy with narrowband UV-B and different trials of topical corticosteroids such as triamcinolone acetonide ointment, 0.1%, fluocinonide ointment, 0.05%, and betamethasone dipropionate ointment, 0.05%, without any improvement. Efalizumab treatment was initiated prior to the drug’s withdrawal from the market after considering our patient’s financial limitations, available prescription assistance, and literature describing minimal hepatotoxicity. The accumulated data concerning the successful use of efalizumab in patients with psoriasis and concomitant chronic HCV is limited to a case report and 1 case series. Data from these observational studies show reduction in plaque psoriasis body surface area involvement during treatment, without laboratory or clinical evidence of hepatic decompensation. Despite initial improvement with efalizumab, our patient’s psoriasis worsened with an acute generalized guttate-type flareup. This result was most likely associated with efalizumab use; there was no change in hepatic function and HCV-RNA levels during treatment. With continuing worsening, alternative therapy was sought.

Tumor necrosis factor is implicated in hepatocyte destruction during chronic HCV infection, although its exact pathogenic mechanism is still unclear. One study showed greater reduction in HCV-RNA levels after etanercept was used in combination with interferon alfa-2b and ribavirin for 24 weeks compared with placebo. Anti–TNF therapy may therefore provide benefit for chronic HCV infection and severe plaque psoriasis. The aim of this article is to determine from the available evidence whether etanercept would be an effective and safe treatment option for patients with severe plaque psoriasis in the setting of chronic HCV infection.

Literature Search

We searched PubMed and the Cochrane Controlled Trials Register for “psoriasis AND Chronic Hepatitis C AND etanercept” from inception until September 30, 2009.

Appraisal of the Evidence

We found 2 case series and 4 case reports that retrospectively reported clinical outcomes of etanercept therapy in patients with chronic HCV infection and psoriasis and/or psoriatic arthritis.

- The 2 case series highlight successful use of etanercept in patients with psoriatic arthritis and underlying chronic HCV infection. The first study illustrates 3 patients with moderate to severe psoriasis of long duration who developed HCV infection and started treatment with etanercept. As with our patient, 1 patient’s condition did not respond to phototherapy, topical agents, or efalizumab. All 3 patients had undergone prior treatment for their chronic HCV infection with pegylated interferon or interferon alfa/ribavirin that had eventually exacerbated their psoriasis. During treatment with etanercept, all 3 patients received consultation with a gastroenterologist, as well as serial evaluations of liver function tests and HCV-RNA levels using polymerase chain reaction. There was no worsening of liver function and no reported adverse events; a reduction in HCV-RNA levels was seen with etanercept therapy in all 3 patients. The second study described 2 similar patients who received 3-month interval screening of liver function and HCV-RNA levels during treatment with etanercept. These patients had stable serum liver function tests and decreased HCV-RNA levels for 12 months of therapy while also having regular evaluation by a gastroenterologist.

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• One case report showed similar findings to the case series after following 1 patient with chronic HCV infection and psoriasis for 12 months.10
• Another case report revealed a patient being treated with methotrexate and biweekly 25-mg subcutaneous injections of etanercept for 12 months with marked improvement in psoriasis and no adverse reactions or elevations in HCV-RNA values with treatment.11
• Another case report discussed the successful result of etanercept therapy in a 49-year-old man with generalized psoriatic flareup after liver transplantation for his chronic HCV infection. The severe posttransplantation flareup occurred despite the patient’s having taken systemic immunosuppressive agents. Etanercept 25 mg subcutaneous biweekly was used for 3 months with complete clearance and no worsening of liver function.12
• Behnam et al13 reported a case of etanercept used as prophylaxis to prevent psoriatic flareups in a patient with chronic HCV and psoriasis. The patient initially presented with 15% body surface area psoriatic plaques, undetectable HCV viral load, and unremarkable laboratory evaluation. Despite relative contraindication, oral acitretin was used in combination with topical steroids. 15% body surface area psoriatic plaques, undetectable HCV viral load, and unremarkable laboratory evaluation. Despite relative contraindication, oral acitretin was used in combination with topical steroids. After 20 months, abnormal liver function test results developed and clinically significant increase in HCV RNA levels. Extensive liver fibrosis required interferon alfa therapy. There was a 7-month period between discontinuing acitretin and starting etanercept regimens. Etanercept therapy, 50 mg once weekly, was initiated 4 weeks prior to starting interferon alfa therapy. At the end of 24 weeks, there was reduction of liver enzyme and HCV-RNA levels and clearance of psoriasis.

Limitations of the Critically Appraised Topic
To our knowledge, the existing evidence concerning the use of etanercept in patients with chronic HCV infection and psoriasis is limited to retrospective studies. All the large randomized placebo-controlled phase 3 trials of the major biologic agents (including etanercept, adalimumab, and infliximab) have excluded patients with chronic active HCV infection. Therefore, these patients are not well studied. Selection and reporting bias associated with available retrospective reports make it difficult to interpret the safety and efficacy of etanercept in patients with chronic HCV infection and severe plaque psoriasis. It is unknown what effect longer duration of etanercept would have on this group of patients.

Clinical Bottom Line
Hepatitis C virus infection can coincide in patients with severe psoriasis and offers a therapeutic challenge. The association and prevalence of HCV infection in patients with psoriasis is unknown. The use of systemic agents in the treatment for this group of patients is limiting owing to hepatotoxic adverse effects that may worsen chronic HCV infection. Presently, there is no evidence from randomized, controlled trials to support the use of etanercept in patients with plaque psoriasis and chronic HCV infection. The available observational studies have demonstrated benefit, but longer-term observation and additional studies are still needed to determine the safety and efficacy of etanercept in multiple patients with psoriasis and chronic HCV infection. Our article amplifies recent consensus14 that anti-TNF therapy merits strong consideration if patients with psoriasis and chronic HCV infection develop an insufficient response to topical agents and phototherapy. Unfortunately, the high cost associated with etanercept prevents accessibility. Evidence-based studies involving lower-cost anti-TNF therapies are therefore also needed.

What Happened to Our Patient?
Our patient qualified to receive financial assistance and was started on etanercept therapy, 50 mg twice weekly. He refused interferon therapy despite recommendation from his gastroenterologist. Quantitative HCV-RNA levels were measured every 6 weeks by using hybridization following reverse transcriptase polymerase chain reaction (Roche Cobas AmpliCyclic HCV Monitor Test, V2.0; SeraCare Life Sciences, Millford, Massachusetts) throughout the course of his psoriasis treatment. Over the past year, HCV-RNA levels became undetectable, serum transaminase levels normalized, and his plaque psoriasis almost cleared. He has continued using etanercept without adverse reactions and maintains a normal review of systems.

REFERENCES