CASE REPORT

ONLINE EXCLUSIVE

THE PATIENT

24-year-old woman

SIGNS & SYMPTOMS

– Large joint arthralgias
– History of type 1 diabetes, seizures, migraines

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THE CASE

A 24-year-old woman with a history of type 1 diabetes, seizure disorder, and migraines presented to a rural Federally Qualified Health Center (FQHC) with progressive and severe symmetric large joint arthralgias of several weeks' duration. The patient's existing medications included etonogestrel 68 mg subdermal implant, levetiracetam 1500 mg bid, insulin glargine 26 units subcutaneously nightly, and insulin lispro 20 units subcutaneously tid (before meals).

An examination revealed symmetrically edematous elbows, wrists, and fingers. Subsequent serologic analyses and a telemedicine consultation with a rheumatologist confirmed a diagnosis of rheumatoid arthritis (RA). The patient's lab work was positive for antinuclear antibody titers (1:40), rheumatoid factor (513 IU/mL), and anticyclic citrullinated peptide antibodies (248 units/mL). Treatment was started with prednisone 60 mg PO daily, methotrexate 20 mg PO weekly, and hydroxychloroquine 400 mg PO daily. (The benefits of prednisone in treating this patient's severe arthralgias outweighed concerns over its use in a patient with diabetes.)

After 2 months of receiving RA therapy, the patient underwent further work-up to assess its effectiveness. Liver function testing was performed, and she tested positive for hepatitis C virus (HCV) antibodies. Viral polymerase chain reaction confirmed active HCV infection. Lab work revealed a viral load of 15,000,000 IU/mL; transaminase, 173 U/L (normal range, 4-36 U/L); and aspartate aminotransferase, 246 U/L (normal range, 8-33 U/L). A liver sonogram demonstrated no findings of cirrhosis or fibrosis.

Upon receiving a diagnosis of active hepatitis C, the patient acknowledged that she'd had unprotected heterosexual intercourse and shared used insulin syringes with friends.

THE DIAGNOSIS

Consideration was given to a diagnosis of HCV arthropathy, which can present as an RA-like arthritis in HCV-infected individuals, in the differential diagnosis.[1] A cohort study found HCV-associated arthropathy occurred in 6.8% of those with chronic HCV infection.[2]

However, the symmetrical involvement of shoulders and knees as the patient's primary arthralgias, and a rheumatologic work-up showing the presence of anticyclic citrullinated peptide antibody levels, confirmed the diagnosis of RA with coexisting HCV.

DISCUSSION

Delivering interdisciplinary care in a rural area

Although evidence-based guidelines and online HCV Treatment Path programs guided the initial evaluation of potential treatments for this patient, her multiple comorbidities prompted us to seek out additional, interdisciplinary advice through a resource for underserved communities called Project Extension for Community Healthcare Outcomes (ECHO; see "What is Project ECHO?[3,4]"). The patient's case was presented virtually, without identi-

fying information, to a multidisciplinary HCV team. Two treatment options were suggested:

- sofosbuvir/velpatasvir (400 mg/100 mg) for 12 weeks or
- glecaprevir/pibrentasvir (100 mg/40 mg) for 8 weeks.

Both are evidence-based and recommended treatment options according to the HCV treatment guidelines issued jointly by the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.[5]

In most patients with HCV, treatment is guided by a number of factors, including pill burden, access to care, duration of therapy, drug interactions, and patient-specific needs. After analyzing all aspects of this patient's case, 2 major concerns guided our shared decision-making process on treatment.

The best treatment is what works for the patient

Owing to the patient's multiple comorbidities and prescribed medications for chronic diseases, concerns about possible medication interactions with the HCV treatment options were a factor in her HCV treatment plan. Additionally, the patient had significant social determinants of health barriers that made continued treatment and follow-up challenging.

The potential interaction of HCV infection treatment with the patient's current methotrexate therapy for her RA was a primary concern. To determine the risk for interactions, the team used the University of Liverpool HEP/HIV Drug Interactions Checker, which helps identify possible interactions with these disease-specific medication therapies.[6]

Both sofosbuvir/velpatasvir and glecaprevir/pibrentasvir have a potential interaction with methotrexate and are driven by a similar mechanism. Methotrexate is a substrate of the Breast Cancer Resistance Protein efflux transporter (BCRP), and the components of both sofosbuvir/velpatasvir and glecaprevir/pibrentasvir are inhibitors of BCRP.[7] The inhibition of this efflux transporter can lead to an increased concentration of methotrexate, increasing the risk for methotrexate toxicity.[7]

Since no quantitative data exist regarding the degree of inhibition that these HCV drugs exert on BCRP, the team considered sofosbuvir/velpatasvir and glecaprevir/pibrentasvir to have equal risk with regard to potential for drug interactions.

The patient's barriers to treatment were another area of concern that directed our therapy decision. The patient had multiple barriers, including poor access to health care because of transportation issues, multiple children requiring care, a variety of chronic diseases, and other life stressors. Shared decision-making ensured our patient's autonomy in choosing a specific treatment.

The patient's social situation and preference narrowed the team's basis for medication choice primarily down to the duration of therapy: 8 weeks of glecaprevir/pibrentasvir vs 12 weeks of sofosbuvir/velpatasvir. The patient mentioned multiple transportation challenges for follow-up visits to the clinic and therefore wanted to utilize the shorter treatment duration. Follow-up is needed every 4 weeks, so the patient was able to go from 3 to 2 visits.

For problems, there are solutions. Following careful consideration of these patient-specific factors and preferences, the team decided to begin therapy with glecaprevir/pibrentasvir. The patient worked with an outreach specialist at the FQHC to coordinate care and complete paperwork for the Project ECHO consultation. The outreach specialist also assisted the patient in completing paperwork for the Patient Assistance Program for HCV treatment. Because the patient is being cared for at an FQHC, the clinic's in-house pharmacy was able to utilize the 340B Federal Drug Pricing Program, which makes otherwise out-of-reach medicines affordable for patients such as ours.

Our patient has had no issues with treatment adherence, adverse effects, or follow-up appointments. The patient's RA symptoms have improved significantly without any discernable worsening of her HCV infection.

THE TAKEAWAY

This case shines a light on the multiple challenges (clinical, geographic, and financial)

This case shines a light on the multiple challenges that could have come between our patient and proper treatment—but ultimately, did not.

What is Project ECHO?

Project Extension for Community Healthcare Outcomes (ECHO) began as an avenue to connect hepatitis C virus (HCV) treatment experts to providers in underserved communities within New Mexico. Specialists can offer their clinical guidance to community clinicians without seeing the patient themselves.[3] Project ECHO now has expanded to connect community clinicians across the United States and globally to specialists who treat other chronic conditions.[4] More information about Project ECHO can be found at hsc.unm.edu/echo.

> that could have come between our patient and proper treatment—but ultimately, did not. The Project ECHO model of care remains a viable way to provide patients who live in rural and underserved communities and who have active HCV and other underlying chronic conditions with interdisciplinary care that can improve health outcomes. JFP

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