CASE REPORT

CE 1.0 Contact Hour

Psoriasis Management

Quality, Cost, and Coordination

Jennifer Nicpon

ABSTRACT: Psoriasis is a complex inflammatory disorder of the skin that affects up to 3.2% of the people in the United States. It is associated with psoriatic arthritis, a potentially debilitating inflammatory joint condition. Psoriatic patients also have an increased risk of lymphoma, heart disease, Type II diabetes, obesity, and metabolic syndrome. The degree to which each patient is affected with and by psoriasis can vary greatly. The treatment available for these patients includes topical products, phototherapy, traditional systemic medications, and biologics. With the high cost of healthcare in the United States, as healthcare providers, we must consider the direct and indirect costs of psoriasis. The annual cost of psoriasis in the United States for the year 2013 was approximately $112 billion. Current guidelines, which utilize evidence-based practice recommendations, help to provide patients with the most cost-effective treatment to yield the best results.

Key words: Biologics, Evidence-Based Practice, Healthcare Costs, Psoriasis, Traditional Systemic Therapy

Psoriasis is a chronic inflammatory skin condition that affects approximately 3.2% of people in the United States (Brezinski, Dhillon, & Armstrong, 2015). This is a disease that affects much more than only the skin. Increased risks of lymphoma, heart disease, metabolic syndrome, diabetes, and obesity are known comorbidities (American Academy of Dermatology Work Group et al., 2011). Smoking, alcohol consumption, depression, and suicide are also linked with psoriasis (American Academy of Dermatology Work Group et al., 2011). The life-span of those affected with severe psoriasis is approximately 5 years shorter than that of someone without psoriasis (American Academy of Dermatology Work Group et al., 2011). The direct costs for treating psoriasis in the United States were estimated in 2013 at $51.7–$63.2 billion (Brezinski et al., 2015). Indirect costs of this disease were $23.9–$36.4 billion in 2013. The cost of comorbidities was estimated at $36.4 million yearly (Brezinski et al., 2015). This disease contributes to physical and mental distress along with significant costs on our healthcare system. Providing evidence-based care of psoriasis to patients will help ensure quality treatments, help with cost containment, and help to provide our patients with coordination of care.

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CASE PRESENTATION

A 58-year-old female presented to the clinic for evaluation and treatment of psoriasis. She has plaque psoriasis affecting her scalp, back, gluteal cleft, elbows, forearms, and legs. Her palms and soles are clear. She has pitting on all 10 fingernails. High-dose topical steroids have been used in the past with good results; however, they are no longer working. She now has started experiencing joint pain in her knees, back, and hands with early morning stiffness. She has greater than 5% but less than 10% body surface area (BSA) involvement. Her body mass index is 53. She has a history of hypertension, degenerative joint disease, asthma, and allergies. Her surgical history was significant for a hysterectomy performed over 30 years ago. She is a widow and lives with her daughter and son-in-law.

INITIAL PRESENTATION AND TREATMENT

After listening to the patient and assessing her disease, her psoriasis was classified as moderate, being greater than 5% and less than 10% BSA. Current guidelines classify psoriasis as mild if less than 5% BSA is affected. Psoriasis is considered moderate if the BSA affected is greater than or equal to 5%, but less than 10%. It is considered severe if the BSA affected is 10% or greater (American Academy of Dermatology Work Group et al., 2011). It is estimated the 20% of patients with psoriasis have moderate-to-severe plaque psoriasis (Schaefer et al., 2015). The possibility of psoriatic arthritis (PsA) was suspected in this patient with her new complaint of joint pain. PsA is reported to occur in up to 42% of patients with psoriasis (American Academy of Dermatology Work Group et al., 2011). This patient

has never seen a rheumatologist and does not currently have a diagnosis of PsA. What should be the next step in treatment of this patient's psoriasis?

USING EVIDENCE-BASED PRACTICE

Evidence-based practice, as defined by Sigma Theta Tau International Research and Scholarship Committee (2008), is "the process of shared decision-making between practitioner, patient, and others significant to them based on research evidence, the patient's experiences and preferences, clinical expertise or know-how, and other available robust sources of information" (Cullen, Hanrahan, Tucker, Remple, & Jordan, 2012, p. 333). With the goal of providing care according to evidence-based practice, the National Guideline Clearinghouse was used to search for recent guidelines. The 2011 guidelines by the American Academy of Dermatology along with the National Institute for Health and Clinical Excellence (NICE, 2012) for the treatment of psoriasis and PsA provide similar recommendations. Using these guidelines, it is recommended that topical therapies be used for mild diseases. They may be used independently of or in conjunction with phototherapy (American Academy of Dermatology Work Group et al., 2011). Topical treatments include corticosteroids, Vitamin D analogs, topical tazarotene, and topical tacrolimus (American Academy of Dermatology Work Group et al., 2011). Emollients and ointments are also used. Cost can vary greatly depending on the topical product used and size dispensed. Costs can range from $8 (for a 15-g tube of triamcinolone 0.1% ointment) to $834 (for a 100-g tube of Vectical) per tube of topical medication (GoodRx, 2015b). However, this patient is classified as having a moderate disease; therefore, topical treatment alone is not recommended. Moderate and severe diseases should be treated with traditional (nonbiologic) systemic medications or biologics (American Academy of Dermatology Work Group et al., 2011; NICE, 2012). Methotrexate is the first-line systemic agent (NICE, 2012). It is the most cost-effective medication and has the most amount of safety follow-up (American Academy of Dermatology Work Group et al., 2011). The costs of this medication at 1 year were estimated and reported to be $4382.93–$5678.77 (D'Souza & Payette, 2015). Other options include cyclosporine, which is useful during flares, and acitretin (American Academy of Dermatology Work Group et al., 2011). Cyclosporine estimated yearly costs range from $11,710.51 to $15,710.87 depending on dose (D'Souza & Payette, 2015). The estimated yearly cost of acitretin ranges from $16,847.01 to $61,094.85 depending on dose (D'Souza & Payette, 2015). There is significant cost savings with methotrexate compared with other traditional systemic medications.

Using the current guidelines in providing evidence-based practice, this patient was started on methotrexate. Her starting dose was 15 mg weekly, and she was increased up to 20 mg weekly by her third month of treatment. complete blood count comprehensive metabolic panel were checked at the start of treatment, at 1 week, and then monthly for 3 months. The patient's laboratory results were normal, and she tolerated the medication well. Her psoriasis was responding well, and her joint pain improved.

METHOTREXATE

Methotrexate has been used to treat psoriasis for over 50 years as an anti-inflammatory medication (Yelamos & Puig, 2015). Methotrexate is U.S. Food and Drug Administration Category X. It is teratogenic and mutagenic (Yelamos & Puig, 2015). This medication should not be given to women who are pregnant or are breastfeeding. Pregnancy is not recommended until at least 3 months have elapsed since the last dose of methotrexate (Yelamos & Puig, 2015). The patient in this case study is 58 years old and has had a hysterectomy, eliminating this potential risk. Methotrexate is used when phototherapy and topicals are ineffective and in moderate-to-severe diseases. It is relatively inexpensive (Czarnecka-Operacz & Sadowska-Przytocka, 2014). Typically, it is dosed 7.5–25 mg weekly. These are much lower doses than hematology/oncology use and are considered to have a good safety profile (Yelamos & Puig, 2015). Liver fibrosis is a concern with long-term use; however, new studies are suggesting that fibrosis is not correlated to cumulative dose, but with concomitant factors (Yelamos & Puig, 2015). When used alone, results may take 1–8 weeks to occur, with some studies showing better results at 12 weeks (Yelamos & Puig, 2015). The patient's methotrexate should not be discontinued or the dose should not be changed for 4–8 weeks unless the patient is experiencing side effects or laboratory abnormalities (Czarnecka-Operacz & Sadowska-Przytocka, 2014). Regular blood tests are needed to monitor for bone marrow toxicity and hepatotoxicity. It is recommended to monitor renal function, liver enzymes, and complete blood count at baseline, at 2 weeks, and every 3 months (Yelamos & Puig, 2015). A liver biopsy should be performed when liver enzymes increase five- to nine-fold or when a cumulative total of 4 g is reached (American Academy of Dermatology Work Group et al., 2011; Yelamos & Puig, 2015). In a recent review, methotrexate was found to be the least costly systemic therapy, with average monthly costs being $794.05–$1502.51 (D'Souza & Payette, 2015). Since the patient is not of childbearing potential, methotrexate is a good choice for her psoriasis treatment.

Methotrexate not only can help to treat psoriasis but also may help cardiovascular comorbidities in patients with systemic inflammation like psoriasis. In a systematic review and meta-analysis by Micha et al. (2011), methotrexate was associated with a lower cardiovascular disease risk (21%). This finding was also seen in a study by Prodanovich et al. (2005). Methotrexate decreased the incidence of vascular disease in people with psoriasis or rheumatoid arthritis, possibly because of its anti-inflammatory properties (Prodanovich et al., 2005). The addition of folic acid

decreased the occurrence of vascular disease further. This does appear to be a good choice for our patient; however, other options need to be considered as we are coordinating her care with the primary care provider (PCP).

COMORBIDITIES STRIKE

Our patient returned to the dermatology clinic with worsening of her psoriasis shortly after her 3-month check. She had recently been hospitalized for a mild myocardial infarction and was diagnosed with two pulmonary emboli. During her hospitalization, her psoriasis medication had been stopped. She was started on warfarin, and this is being managed by her PCP. She had been out of the hospital for 2 weeks. Her psoriasis and joint pain had significantly worsened. On physical examination, the patient appeared frustrated with her disease. She was tearful during the examination and explained that she has started to have sleeping problems because of pain. Her psoriasis was now affecting 10% BSA, changing her classification to severe. This patient was in need of reinitiation of psoriasis treatment.

In our goal to provide evidence-based care, systemic (nonbiologic) treatment is still the treatment of choice (American Academy of Dermatology Work Group et al., 2011; NICE, 2012). Because the patient responded well initially to methotrexate, the plan was to restart her at the 20-mg weekly dose. Because of a possible interaction between methotrexate and warfarin, the patient's PCP was contacted (Facts & Comparisons, 2015). Recommendations are to monitor the International Normalized Ratio more frequently if a patient is on methotrexate and warfarin together. The PCP was opposed to restarting methotrexate. With methotrexate not being an option because of possible interactions with the patient's other medications, a different treatment was necessary to help this patient.

WHAT IS THE NEXT STEP?

Biologics can offer benefit to patients with psoriasis who have failed systemic therapies and have complex histories. Elevation of tumor necrosis factor (TNF) and other proinflammatory cytokines has been discovered in both the synovial fluid and psoriatic skin plaques of people with PsA (Brezinski & Armstrong, 2015). One class of biologics targets the TNF pathway and the TNF inhibitors. Another class targets a pair of cytokines: interleukin (IL)-12 and IL-23 (Brezinski & Armstrong, 2015). There are no relevant drug interactions with biologics, and they have less safety issues than traditional systemic therapies (American Academy of Dermatology Work Group et al., 2011). The TNF-alpha antagonists have no known drug interactions (American Academy of Dermatology Work Group et al., 2011). The TNF-alpha antagonists include the following:

- Etanercept (50-mg subcutaneous injection twice weekly for 3 months and then once weekly)
- Adalimumab (80-mg subcutaneous injection on the first week, 40 mg on the next week, and then 40 mg every other week)
- Infliximab (intravenous administration of 5 mg/kg every 8 weeks after loading doses at Weeks 0, 2, and 6)
- Golimumab (50-mg subcutaneous injection once per month)
- Certolizumab (400-mg subcutaneous injections at Weeks 0, 2, and 4 and then maintenance of 200-mg injections every other week; Brezinski & Armstrong, 2015)
- Golimumab and certolizumab are Food and Drug Administration approved for the treatment of PsA but not psoriasis alone (Brezinski & Armstrong, 2015).

Other biologic medications include the following:

- IL-12/23 inhibitor ustekinumab is another option (Brezinski & Armstrong, 2015). This medication is based on weight, at either a 45- or 90-mg subcutaneous injection at Weeks 0 and 4 and then every 3 months (Brezinski & Armstrong, 2015).
- A newly approved biologic, secukinumab, is a first of its kind of IL-17A antagonist (Garnock-Jones, 2015). This medication is also a subcutaneous injection of 150 or 300 mg at Weeks 0–4 and then once every 4 weeks (Garnock-Jones, 2015). Typical dosing is 300 mg per dose (Novartis, 2015). The approximate cost for two 150-mg syringes is $3,660 (GoodRx, 2015a).

There is an oral option that has been approved for moderate-to-severe plaque psoriasis, which is in a new class of drugs called phosphodiesterase 4 inhibitor:

> Apremilast is an oral medication that was approved for psoriasis in March 2014 but is not mentioned in the current guidelines. It inhibits an enzyme, phosphodiesterase, which is involved in inflammation within the cells (Celgene Corporation, 2014). This is an oral medication and is not a biologic. The dosing is 30 mg orally twice daily after initial titration (Wheeler, 2015). The approximate cost is $2,234 per month (MPR, 2015).

There is no specific order for the TNF-alpha antagonists to be used, according to the guidelines (American Academy of Dermatology Work Group et al., 2011). This is likely not true for the individual patient's insurance company. As with methotrexate, there is some research showing that biologics, as well as traditional systemic therapies, could decrease the risk of cardiovascular events (Roubille et al., 2015). Interestingly, patient satisfaction is also shown to be higher with biologics than traditional systemic treatments such as methotrexate (Schaarschmidt et al., 2015). The choice of when and what biologic medication to be used is a decision made by the provider with use of evidence-based practice, the patient, and insurance coverage.

Biologics are a much more expensive treatment option than traditional nonbiologic systemic treatments. In one study, it was estimated that there is greater than 10-fold difference in cost between biologics and traditional

systemic therapy (which did include phototherapy; Richard & Hönigsmann, 2014). Another study showed that the average cost per year for someone with moderate-to-severe plaque psoriasis for traditional systemic medications was $11,029 versus $26,708 for someone being treated with biologics (Brezinski et al., 2015; Schaefer et al., 2015). In yet another review, the costs of the biologics etanercept, adalimumab, infliximab, and ustekinumab were examined (D'Souza & Payette, 2015). Etanercept ranged from $34,431.77 to $63,036.77 yearly. Adalimumab ranged from $32,021.37 to $64,796.49 per year. Infliximab ranged from $44,821.74 to $73,644.68 yearly. Finally, ustekinumab ranged from $44,697.64 to $87,807.77 per year (D'Souza & Payette, 2015). However, direct costs are not the only consideration. Of those affected by moderate-to-severe psoriasis, 40% of patients stated that psoriasis was a problem or a very large problem daily in their lives (Brezinski et al., 2015). People who had severe psoriasis were less likely to work full time compared with those with mild disease (Schaefer et al., 2015). Psoriasis was the most common reason stated for not working within this group. Another consideration is of those who are working but the work needs to be modified (presenteeism). The loss of productivity because of psoriasis was estimated to equal $121 million every year, with $57 million being lost work days and $30 million in restricted days (Brezinski et al., 2015). Another staggering number was that $9.5 million is estimated to be lost in future earnings because of premature death related to this disease (Brezinski et al., 2015). There is much to consider when examining the cost of psoriasis for the treatment and quality of everyday life (Table 1).

UPDATED TREATMENT PLAN

After discussion with the PCP, a prior authorization was submitted for adalimumab; this was denied with the reason that phototherapy was never tried. This was interesting, as it was not following the recommended progression in the evidence-based guidelines. This treatment can add up cost quickly. The average cost for narrowband ultraviolet B light phototherapy is approximately $140/treatment (D'Souza & Payette, 2015). Narrowband ultraviolet B light phototherapy was arranged for this patient, and she completed three treatments weekly for 6 weeks. During this time, her psoriasis and joint pain worsened further. The patient became increasingly frustrated. At her follow-up appointment, another prior authorization was done for adalimumab. This was approved, and the patient tolerated this medication well with significant improvement of her psoriasis and joint pain.

TABLE 1. Approximate Yearly Costs for Psoriasis Treatment

Medication	Cost
Methotrexate	$4,382.93–$5,678.77[a]
Cyclosporine	$11,710.51–$15,710.87[a]
Acitretin	$16,847.01–$61,094.85[a]
Etanercept	$34,431.72–$63,036.77[a]
Adalimumab	$32,021.73–$64,706.49[a]
Infliximab	$44,821.74–$73,644.68[a]
Ustekinumab	$44,697.66–$87,807.77[a]
Secukinumab	$21,960–$58,560[b]
Apremilast	$26,808–$28,932[c]

[a]Adapted with permission from D'Souza and Payette (2015). [b]Approximate cost dependent on dosing of 150 or 300 mg (GoodRx, 2015a). [c]Approximate cost based on 30-mg oral dosing twice daily (MPR, 2015).

CONCLUSION

This patient's most beneficial treatment was delayed because of a variety of reasons. The preference of her PCP to not restart methotrexate was one reason. Methotrexate may have helped this patient's psoriasis if restarted after her hospitalization. The stepwise approach for psoriasis treatment required by the patient's insurance company resulted in further delay of the start of effective treatment for this patient. After a 6-week trial and documented failure of phototherapy, a biologic (adalimumab) was approved and worked well for the patient. The patient was and continues to be very satisfied with her treatment. Patient satisfaction impacts adherence to the treatment plan, thereby making both extremely important for successful treatment. In 2013, the annual estimated burden in the United States because of psoriasis ranged from $112 to $135 billion (Brezinski et al., 2015). We all need to be cost-conscious providers and balance the expense of treatments for psoriasis with the cost of not treating this disease. Evidence-based practice provides a great framework for navigating this complex problem. ■

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