Clinical Case Reports

WILEY

Clinical Case Reports Open Access

CASE REPORT OPEN ACCESS

A Rare Case of Blastomycosis in a Psoriasis Patient Treated With Ustekinumab (Stelara)

Fatima Ghaffar[1] | Ahmed Hassan[2] | Masab Ali[2] | Hafiz Noman Ijaz[3] | Sajjad Jameel[4] | Monika Kumari[5] | Muhammad Husnain Ahmad[6]

[1]Department of Internal Medicine, Southeast Georgia Health System, Brunswick, Georgia, USA | [2]Department of Internal Medicine, Punjab Medical College, Faisalabad, Pakistan | [3]Shaikh Khalifa Bin Zayed Al-Nahyan Medical and Dental College, Lahore, Pakistan | [4]UofL Health—Jewish Hospital, Louisville, Kentucky, USA | [5]Liaquat National Medical College, Karachi, Pakistan | [6]Department of Medicine, Tentishev Satkynbai Memorial Asian Medical Institute, Kant, Kyrgyzstan

Correspondence: Muhammad Husnain Ahmad (husnainahmad601@gmail.com)

Received: 11 April 2025 | **Revised:** 27 July 2025 | **Accepted:** 20 September 2025

Funding: The authors received no specific funding for this work.

Keywords: blastomycosis | bronchoalveolar lavage | endemic mycosis | immunosuppression | opportunistic infection | psoriasis | ustekinumab

ABSTRACT

Psoriasis is a chronic inflammatory skin condition mediated by T-helper 1 (Th1) and T-helper 17 (Th17) cytokines, including interleukin (IL)-12, IL-23, IL-17, and tumor necrosis factor alpha (TNF-α). Ustekinumab, a human monoclonal antibody against the p40 subunit of IL-12/23, has revolutionized treatment of moderate to severe psoriasis but carries a risk of opportunistic infections due to impaired cell-mediated immunity. We describe a 54-year-old man from Kentucky with type 2 diabetes and chronic sinusitis, receiving ustekinumab for 1 year for plaque psoriasis. He presented with recurrent pneumonia unresponsive to multiple courses of amoxicillin-clavulanate, azithromycin, and levofloxacin. Chest imaging consistently demonstrated left lower lobe airspace opacities, initially attributed to nonresolving bacterial pneumonia or possible malignancy. On bronchoscopy with bronchoalveolar lavage, scattered broad-based budding yeast were visualized, and culture confirmed *Blastomyces dermatitidis*. The patient was initiated on oral itraconazole, resulting in symptomatic relief and gradual radiographic resolution over 6 months of follow-up. Although pulmonary blastomycosis is rare (1–2 cases per 100,000 in endemic areas), clinicians should maintain a high index of suspicion for endemic mycoses in immunosuppressed patients on biologic therapies presenting with persistent pulmonary infiltrates. Early invasive diagnostics and targeted antifungal therapy are critical to prevent morbidity and improve outcomes.

1 | Introduction

Psoriasis is a chronic inflammatory skin disorder that affects approximately 3.2% of the U.S. population. Its pathogenesis involves dysregulated immune activation, with T cells and dendritic cells producing pro-inflammatory cytokines such as interleukin (IL)-17, IL-23, and tumor necrosis factor-alpha (TNF-α), which drive keratinocyte proliferation and inflammation, resulting in characteristic psoriatic plaques [1, 2]. While mild to moderate disease can often be controlled with topical corticosteroids, vitamin D analogs, and emollients, moderate-to-severe or refractory cases frequently require systemic biologic therapy [3]. Ustekinumab, a fully human monoclonal antibody targeting the p40 subunit shared by IL-12 and IL-23, has emerged as a cornerstone in biologic treatment, particularly after the PHOENIX trials demonstrated its efficacy and safety [4]. By inhibiting IL-12 and IL-23 signaling, ustekinumab downregulates the Th1 and Th17 pathways, reducing inflammation. However, this immunomodulatory mechanism may also impair host defenses, particularly cellular immunity, increasing susceptibility to opportunistic

Summary

- Blastomycosis should be considered in immunosuppressed patients with persistent pneumonia in endemic regions, even when treated with biologics like ustekinumab.
- Early diagnosis and antifungal therapy can prevent complications.

infections [5]. Most adverse effects reported with ustekinumab include nasopharyngitis, upper respiratory tract infections, and injection site reactions. Nevertheless, more serious infections, including tuberculosis (TB), viral reactivations, and fungal infections, have been documented. Among fungal infections, deep mycoses such as histoplasmosis and pneumocystis pneumonia (PCP) have been described. Blastomycosis, however, remains exceedingly rare in this setting.

Blastomycosis is a systemic fungal infection caused by *Blastomyces dermatitidis* and *Blastomyces gilchristii*, dimorphic fungi endemic to North America, particularly in areas surrounding the Great Lakes and the Mississippi and Ohio River basins [6]. Infection typically results from inhalation of fungal conidia, which convert into yeast forms in the lungs. Pulmonary involvement is the most common presentation and may resemble bacterial pneumonia or malignancy, often leading to diagnostic delays, especially in immunocompromised hosts. The reported annual incidence in the United States is ≤ 2 cases per 100,000 population, with hospitalizations averaging about 0.3 per 100,000 [7]. Among hospitalized patients, the case-fatality rate is typically 8%–10%, although CDC data reported a spike to 17% in 2021 despite stable hospitalization rates [7]. Mortality in published series ranges widely from 4% to 78%, with a pooled estimate of 6.6% based on a systematic review of 2820 cases [8]. Outcomes are significantly worse in immunocompromised patients and those with acute respiratory distress syndrome (ARDS), with ARDS being the most important risk factor for death [8].

In this report, we present a rare case of pulmonary blastomycosis in a patient receiving ustekinumab for psoriasis. This case underscores the diagnostic challenges posed by atypical infections in immunosuppressed patients and highlights the importance of considering endemic fungal infections in the differential diagnosis of non-resolving pneumonia.

2 | Case History

We present the case of a 54-year-old male from Kentucky presented with the chief complaint of worsening shortness of breath for 2–3 months, associated with cough and hemoptysis. He reported symptoms of fever, night sweats, chest and abdominal pain, nausea, vomiting, and a 20–30 lb unintentional weight loss over 6 months. His past medical history included psoriasis, type 2 diabetes, chronic sinusitis, back pain, and seasonal allergies. He denied smoking but reported recent travel to the Ohio River basin and contact with soil while gardening but no known animal exposure or recent international travel. His medications included ustekinumab for 1 year (90 mg subcutaneously every 12 weeks), metformin 1000 mg twice daily, and antihistamines as needed.

Six months prior to this admission, he had been treated for presumed pneumonia with amoxicillin-clavulanate. Two months later, he experienced similar symptoms and was prescribed amoxicillin-clavulanate and azithromycin (500 mg on day one, then 250 mg daily for 4 days). A chest x-ray at that time revealed left lower lobe airspace opacity with air bronchograms, suggestive of community-acquired pneumonia as shown in Figure 1.

Despite adherence to the prescribed medications, his symptoms persisted, and he returned to the emergency department on August 10, 2024. He was discharged with levofloxacin 750 mg daily for 7 days. Due to the lack of clinical improvement, a chest CT was performed, showing unresolved airspace opacity. While this was initially attributed to non-resolving pneumonia, the possibility of neoplasia could not be ruled out based on imaging, as shown in Figure 2.

3 | Differential Diagnosis, Investigation, and Treatment

On presentation to our facility, vital signs revealed a temperature of 98.8°F, pulse of 104 beats per minute, respiratory rate of 18, oxygen saturation of 100% on room air, and blood pressure of 143/77 mmHg. Physical examination revealed wheezes and rhonchi in the left lower lung field, but air entry was equal bilaterally, and the remainder of the exam was unremarkable. Laboratory results were notable for leukocytosis (WBC $16.1 \times 10^3/\mu L$), anemia (hemoglobin 9.4 g/dL), thrombocytosis (platelets $720 \times 10^3/\mu L$), hyponatremia (sodium 132 mmol/L), and hypoalbuminemia (albumin 3.0 g/dL). Procalcitonin was 0.27 ng/mL. Given his immunosuppressed state from ustekinumab therapy, persistent pulmonary opacity, and constitutional symptoms, the differential diagnosis included non-resolving bacterial pneumonia, endemic fungal infection (such as blastomycosis or histoplasmosis), TB, and pulmonary malignancy.

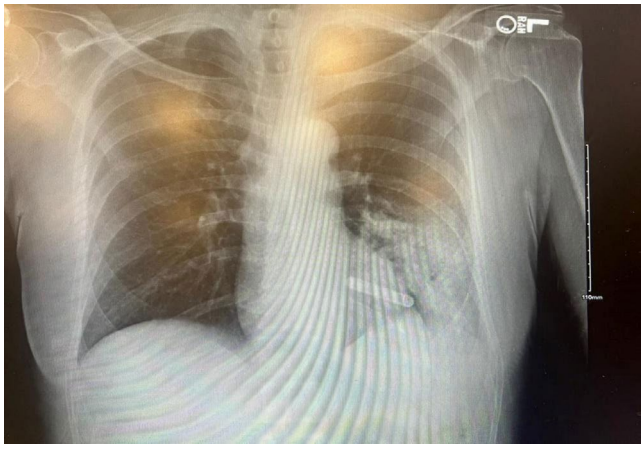

FIGURE 1 | Chest radiograph demonstrating left lower lobe airspace opacity. Frontal chest x-ray obtained on July 30, 2024, reveals a dense opacity in the left lower lung field with visible air bronchograms, suggestive of community-acquired pneumonia.

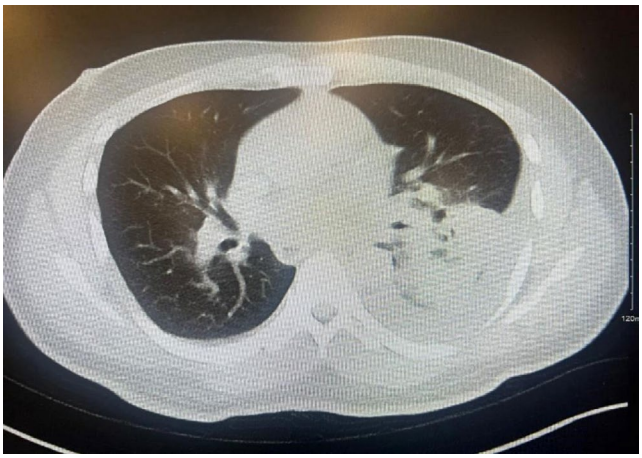

FIGURE 2 | Chest CT showing unresolved left lower lobe opacity. Axial chest CT performed in August 2024 demonstrates persistent consolidation in the left lower lobe despite appropriate antibiotic therapy, raising concern for non-resolving pneumonia and prompting further investigation.

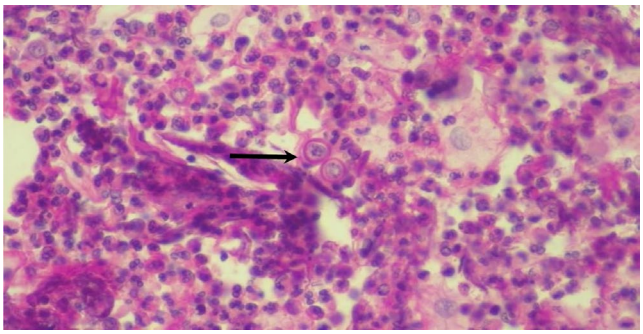

FIGURE 3 | High-power H&E stain highlighting fungal morphology. High-power view of the same H&E-stained lung tissue reveals well-defined broad-based budding yeast (arrow) within an inflammatory background, supporting a diagnosis of pulmonary blastomycosis. No malignant cells were identified.

4 | Outcome and Follow-Up

The patient was initially started on piperacillin-tazobactam 4.5 g intravenously every 8 h. A repeat chest x-ray demonstrated persistent left lower lobe opacification, and a CT scan of the chest revealed patchy opacification in the middle and lower lobes of the left lung with a small left pleural effusion. Given the lack of improvement, a bronchoscopy with bronchoalveolar lavage (BAL) was performed, which revealed broad-based budding yeast consistent with *Blastomyces* species; no malignant cells were identified (as shown in Figures 3–5).

The patient was treated with liposomal amphotericin B at a dose of 3 mg/kg intravenously daily for 14 days, followed by itraconazole 200 mg orally three times daily for 3 days and then 200 mg twice daily for a planned duration of at least 12 months. Ustekinumab was discontinued. The patient demonstrated significant clinical improvement initiation of antifungal therapy. Follow-up chest imaging is planned at 3 and 6 months to monitor radiographic resolution, and continued clinical monitoring is scheduled to assess for relapse or complications.

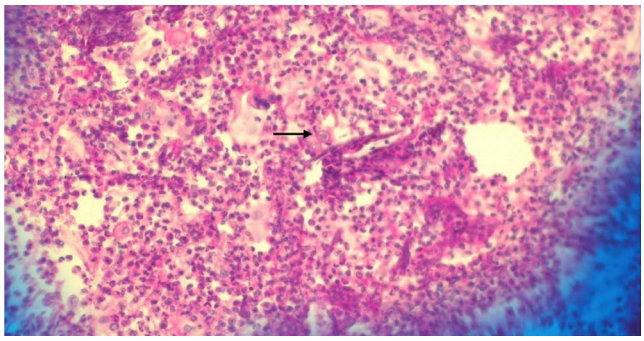

FIGURE 4 | Low-power H&E stain of lung tissue showing inflammation and yeast forms. Low-power hematoxylin and eosin (H&E) stained section of lung tissue obtained via bronchoalveolar lavage (BAL) shows scattered inflammatory infiltrates and early evidence of broad-based budding yeast (arrow), consistent with Blastomyces dermatitidis.

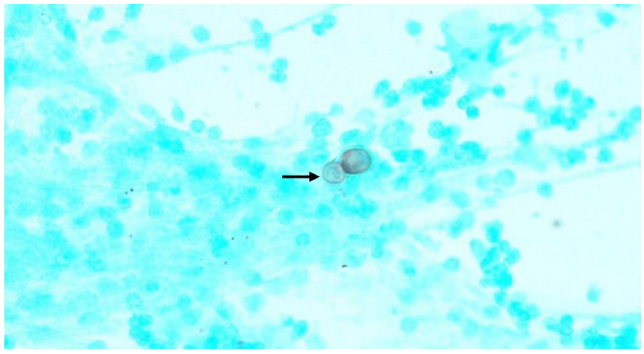

FIGURE 5 | GMS stain highlighting fungal organisms consistent with Blastomyces dermatitidis. Grocott-Gomori's methenamine silver (GMS) stain of bronchoalveolar lavage specimen showing dark-staining, broad-based budding yeast (arrow) against a pale background. These findings are diagnostic of Blastomyces dermatitidis infection.

5 | Discussion

Blastomycosis can present with a wide range of symptoms, from asymptomatic cases to dissemination to skin, bones and Central Nervous System (CNS). Pulmonary blastomycosis is the most common presentation and can range from mild symptoms to severe pneumonia and ARDS. Immunosuppressed patients are at higher risk for acute pulmonary disease, respiratory failure, and increased mortality [9, 10]. The most common symptoms involve respiratory complaints, such as cough, fever, and chills, which make it challenging to distinguish from bacterial or viral pneumonia. This often delays diagnosis, as treatment for bacterial pneumonia is frequently initiated first, as occurred with our patient. The American Thoracic Society recommends using multiple diagnostic tests, including direct visualization and culture of sputum, BAL fluid, or other biopsy material, as well as urine antigen testing and serum antibody testing [11] invasive tests like BAL are typically ordered only after a failure to respond to these treatments. Fungal culture remains the gold standard for diagnosing blastomycosis, with a diagnostic yield from BAL of approximately 94% in pulmonary cases, making it an essential tool in endemic regions [12]. Another significant challenge arises from the difficulty of distinguishing lesions caused by blastomycosis from other diseases based on imaging

studies alone. Mass lesions are frequently observed in blastomycosis and can often be mistaken for malignancy. Intermediate-sized nodules, often with satellite lesions, are another hallmark of blastomycosis. Cavitation, although less common, can also be seen in blastomycosis [13].

Ustekinumab is a monoclonal antibody targeting IL-12 and IL-23, cytokines that plays a key role in inflammatory diseases such as psoriasis and Crohn's disease. By inhibiting IL-12/23 signaling, ustekinumab suppresses Th1 and Th17 pathways, leading to reduced inflammation. However, this also suppresses immune defenses, increasing susceptibility to opportunistic infections. Notable opportunistic infections associated with ustekinumab include hepatitis B virus reactivation (HBVr), TB, and atypical mycobacterial infections (AMI) [14]. Documented risks include fungal infections such as histoplasmosis, candidiasis, and PCP has been reported with use of biologics but the risk of deep fungal infections like blastomycosis with use of ustekinumab are extremely rare [15].

Treatment of blastomycosis depends on disease severity and immune status. Immunosuppressed patients and those with moderately severe to severe pulmonary disease should receive initial therapy with amphotericin B (AmB), preferably a lipid formulation at 3–5 mg/kg/day or AmB deoxycholate at 0.7–1 mg/kg/day for 1–2 weeks or until clinical improvement, followed by oral itraconazole as step-down therapy [3, 16]. Itraconazole is initiated at 200 mg three times daily for 3 days, then 200 mg twice daily, and continued to complete at least 12 months of therapy in immunocompromised hosts (6–12 months for severe pulmonary disease) [3, 17]. For mild to moderate pulmonary blastomycosis, itraconazole alone (200 mg three times daily for 3 days, then once or twice daily) for 6–12 months is recommended. Serum itraconazole levels should be checked after 2 weeks to ensure adequate exposure [17]. Gastric acidity is essential for absorption, and therapeutic drug monitoring after 2 weeks is advised to ensure adequate exposure. Other azoles such as ketoconazole and fluconazole are less effective and generally not preferred; ketoconazole also carries a higher risk of adverse effects. Voriconazole may be considered for CNS involvement due to better cerebrospinal fluid penetration. All azoles are contraindicated in pregnancy [18]. Lifelong suppressive itraconazole (200 mg daily) may be required for patients with irreversible immunosuppression or relapse despite appropriate treatment. Adverse effects of AmB include nephrotoxicity, hypokalemia, anemia, fever, and infusion-related reactions, with the lipid formulation offering a more favorable safety profile.

Although our case is from an endemic region, the incidence rates of blastomycosis are approximately 1–2 per 100,000 people in endemic regions [19]. This makes immunosuppression by ustekinumab a significant factor in developing the infection in our patient. Regular monitoring is crucial for psoriasis patients on biologics like ustekinumab, as it enables the early detection and management of opportunistic infections [20].

6 | Conclusion

Our case report highlights the risk of blastomycosis in patients treated with ustekinumab, particularly in endemic regions. Although the infection is rare, it is important to keep it in differential diagnosis in patients taking immunosuppressants as early diagnosis can prevent complications.

Author Contributions

Fatima Ghaffar: conceptualization, data curation, formal analysis, validation, writing – original draft, writing – review and editing. **Ahmed Hassan:** project administration, validation, visualization, writing – original draft, writing – review and editing. **Masab Ali:** formal analysis, supervision, validation, visualization, writing – original draft, writing – review and editing. **Hafiz Noman Ijaz:** supervision, visualization, writing – original draft. **Sajjad Jameel:** investigation, methodology, resources, supervision, writing – original draft. **Muhammad Husnain Ahmad:** visualization, writing – review and editing. **Monika Kumari:** resources, visualization, writing – original draft.

Acknowledgments

We thank the patient for consenting to the publication of this case report and acknowledge the healthcare team involved in the patient's care.

Consent

Written informed consent was obtained from the patient to publish this report per the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data and materials are available upon request from the corresponding author.

References

1. C. L. Leonardi, A. B. Kimball, K. A. Papp, et al., "Efficacy and Safety of Ustekinumab, a Human Interleukin-12/23 Monoclonal Antibody, in Patients With Psoriasis: 76-Week Results From a Randomised, Double-Blind, Placebo-Controlled Trial (PHOENIX 1)," *Lancet* 371, no. 9625 (2008): 1665–1674, https://doi.org/10.1016/S0140-6736(08)60725-4.

2. K. L. Winthrop, S. A. Novosad, J. W. Baddley, et al., "Opportunistic Infections and Biologic Therapies in Immune-Mediated Inflammatory Diseases: Consensus Recommendations for Infection Reporting During Clinical Trials and Postmarketing Surveillance," *Annals of the Rheumatic Diseases* 74, no. 12 (2015): 2107–2116, https://doi.org/10.1136/annrheumdis-2015-207841.

3. S. W. Chapman, W. E. Dismukes, L. A. Proia, et al., "Clinical Practice Guidelines for the Management of Blastomycosis: 2008 Update by the Infectious Diseases Society of America," *Clinical Infectious Diseases* 46, no. 12 (2008): 1801–1812, https://doi.org/10.1086/588300.

4. J. A. McBride, G. M. Gauthier, and B. S. Klein, "Clinical Manifestations and Treatment of Blastomycosis," *Clinics in Chest Medicine* 38, no. 3 (2017): 435–449, https://doi.org/10.1016/j.ccm.2017.04.006.

5. S. R. Mays, L. Bercovitch, and I. R. White, "Cutaneous Fungal Infections in Patients Receiving Tumor Necrosis Factor-Alpha Inhibitors," *Dermatologic Clinics* 30, no. 1 (2012): 113–121, https://doi.org/10.1016/j.det.2011.08.010.

6. American Thoracic Society, *Diagnosis and Treatment of Fungal Infections in Immunocompromised Patients* (ATS Clinical Guidelines, 2025), https://www.thoracic.org/.

7. CDC, "Data and Statistics on Blastomycosis," (2024), Blastomycosis, https://www.cdc.gov/blastomycosis/data-research/statistics/index.html.

8. A. Carignan, M. Denis, and C. N. A. Chakra, "Mortality Associated With Blastomyces Dermatitidis Infection: A Systematic Review of the Literature and Meta-Analysis," *Medical Mycology* 58, no. 1 (2020): 1–10, https://doi.org/10.1093/mmy/myz048.

9. J. A. Smith and C. A. Kauffman, "Blastomycosis," *Proceedings of the American Thoracic Society* 7, no. 3 (2010): 173–180, https://doi.org/10.1513/pats.200906-040AL.

10. E. Villacorta Cari, N. Leedy, J. A. Ribes, J. Soria, and T. Myint, "Risk Factors of Severe Blastomycosis and Comparison of Diagnosis and Outcomes Between Immunocompetent and Immunocompromised Patients," *Mycoses* 65 (2022): 239–246.

11. C. A. Hage, E. M. Carmona, O. Epelbaum, et al., "Microbiological Laboratory Testing in the Diagnosis of Fungal Infections in Pulmonary and Critical Care Practice: An Official American Thoracic Society Clinical Practice Guideline," *American Journal of Respiratory and Critical Care Medicine* 200 (2019): 535–550.

12. A. J. Furlan, F. F. Costa Filho, D. W. Gusfa, H. M. Tang, and B. S. Avner, "Blastomycosis Complicated by Adult Respiratory Distress Syndrome in an Immunocompetent Adult," *Cureus* 16 (2024): e52319.

13. W. Fang, L. Washington, and N. Kumar, "Imaging Manifestations of Blastomycosis: A Pulmonary Infection With Potential Dissemination," *Radiographics* 27, no. 3 (2007): 641–655, https://doi.org/10.1148/rg.273065122.

14. Y. Wang, X. Geng, X. Zhang, Y. Xiao, and W. Wang, "Hepatitis B Virus Reactivation and Mycobacterial Infections Associated With Ustekinumab," *Frontiers in Pharmacology* 13 (2022): 921084.

15. R. Romiti, A. L. D. S. Hirayama, A. M. Porro, et al., "Infections in the Era of Immunobiologicals," *Anais Brasileiros de Dermatologia* 99, no. 2 (2024): 167–180, https://doi.org/10.1016/j.abd.2023.08.004.

16. J. Lestner and W. W. Hope, "Itraconazole: An Update on Pharmacology and Clinical Use for Treatment of Invasive and Allergic Fungal Infections," *Expert Opinion on Drug Metabolism & Toxicology* 9, no. 7 (2013): 911–926.

17. K. D. Goughenour and C. A. Rappleye, "Antifungal Therapeutics for Dimorphic Fungal Pathogens," *Virulence* 8, no. 2 (2017): 211–221.

18. T. Baker, A. Patel, P. Halteh, et al., "Blastomycosis During Pregnancy: A Case Report and Review of the Literature," *Diagnostic Microbiology and Infectious Disease* 88, no. 2 (2017): 145–151.

19. T. M. Zhao, J. Gao, D. Y. She, and L. A. Chen, "Blastomycosis in China: A Case Report and Literature Review," *Chinese Medical Journal* 124, no. 24 (2011): 4368–4371.

20. A. Menter, B. E. Strober, D. H. Kaplan, et al., "Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics," *Journal of the American Academy of Dermatology* 80, no. 4 (2019): 1029–1072.