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Commentary: great imitators in dermatology: II

Some diseases, whether in diagnosing them or for their response or lack of response to treatment, continue to be astonishing. This remains so, despite the fact that technology has greatly improved, that we can reach information more quickly, and that we have many more resources now than we had even a decade ago. Even with all of these changes and advances, there are conditions and therapeutic considerations that continue to be challenging—hence, great imitators.

The most widespread and historically known of these great masqueraders were discussed in part I,[1] including syphilis,[2] leprosy,[3] tuberculosis,[4] sarcoidosis,[5] mycosis fungoides,[6] viral exanthems,[7] Behçet's disease,[8] Mal de Meleda,[9] and self-induced dermatosis.[10] With this in mind, I have continued to explore those entities that remain great imitators.

Additional great imitators

Apart from the illnesses discussed in the preceding section, leishmaniasis, nocardiosis, cutaneous metastases, Langerhans cell histiocytosis, and scleroderma-like syndromes qualify for being "great imitators." Some are uncommon in various parts of the world, whereas others may have such varied manifestations that the diagnosis presents a quandary. These "great imitators" make up part II.

Leishmaniasis and nocardiosis

Two infectious diseases that can be considered *great imitators* are leishmaniasis and nocardiosis. Leishmaniasis was known in ancient Egypt as the "Balkh Sore," which was described by Avicenna (930-1037). Various presentations have been known, such as the Aleppo boil or the Baghdad boil. A Scottish pathologist, William Boog Leishman (1865-1926), eventually found the pathogen while serving in India.[11,12] The World Health Organization considers leishmaniasis as one of the neglected tropical diseases.[13] Gurel et al. emphasizes that it may be characterized by various atypical lesions, although cutaneous leishmaniasis often appears as typical papulonodular or plaque lesions.[14] Some of these atypical clinical manifestations are acneiform, chancriform, eczematous, erysipeloid, fissured, lupoid, nodulo-ulcerative, panniculitis, paronychial, psoriasiform, sporotrichoid, and verrucous.

Primary cutaneous nocardiosis is a relatively rare infectious disease. Cutaneous nocardiosis presents either as a part of disseminated infection or as a primary infection resulting from inoculation. Nocardia was first described by a French veterinarian, Edmond Nocard (1850-1903) in 1888 in relation to bovine farcy, and 2 years later, the human infection was identified by Hans Eppinger (1879-1946) as a systemic infection.[15] The isolation of active bacteria is very difficult and often can be identified only by experienced microbiologists; Ramos-e-Silva et al. states that the deep fungal infection can be readily confused with any number of presentations, including sporotrichosis, tuberculosis, atypical mycobacteria dermatitis, leishmaniosis, syphilis, cutaneous malignancy, or lupus erythematosus.[16]

HIV infections and skin findings

Human immunodeficiency virus (HIV), needless to say, causes or aggravates untold numbers of diseases. Sometimes, the initial diagnosis of this infection is simply a facial flush. Karadag et al. emphasizes the unexpected of an HIV infection: age, location, rare etiologic agents, and/or poor therapeutic response or severe presentation.[17]

Contact dermatitis

Contact dermatitis is a commonly seen group of diseases that have the ability to mimic a wide variety of dermatologic conditions, including inflammatory dermatoses, infectious conditions, cutaneous lymphomas, drug eruptions, and nutritional deficiencies. Elmas et al. emphasizes the diagnostic clues and the differential diagnosis of contact dermatitis as a great mimicker.[18]

Drug eruptions

Drug eruptions are one of the primary imitators. The effects of drug eruptions on the skin were presented in *Drug Eruptions: A Clinical Study of Irritant Effects of Drugs upon Skin,* by Prince A. Morrow (1846-1913), who introduced the

concept.[19] Chia-Yu Chu categorizes reactions caused by pharmacologic agents into two main groups as drug-induced skin diseases and dermatosis-like drug eruptions.[20] Both types are great imitators in dermatologic practice and can be easily misdiagnosed as other diseases or lead to unrecognized causative agents. Some of the imitator drug reactions discussed in this part include acneiform, alopecia-like, burn-like, cellulitis-like, eczematoid, erythema-nodosum-like, erythroderma-like, ichthyosis-like, lichen-planus-like, lupus-erythematous-like, measles-like, pellagra, pemphigus, pityriasis-rosea-like, psoriasis-like, seborrheic-dermatitis-like, vasculitis, vitiligo-like drug eruptions.[20]

Imitating skin reactions induced by antitumor agents

Cutaneous reactions caused by antitumor drugs are diverse, and they create difficulty in diagnosis if the link cannot be determined. Ludwig et al. groups antitumor drugs as antimetabolite, chemotherapeutics, genotoxic agents, spindle inhibitors, signal transduction inhibitors, and immunotherapies for explaining the side effects they cause.[21] Although some of these are common untoward events (ie, maculopapular eruptions, which almost all drugs may cause and can imitate), some can create easily diagnosed lesions such as bleomycin-induced flagellate erythema.[21]

Cutaneous metastasis

56Cutaneous metastasis caused by tumors may also imitate many diseases. These metastases occur in a variety of presentations, including dermal subcutaneous nodules, inflammatory carcinoma, alopecia, mammary Paget's disease, carcinoma encuirasse, carcinoma telangiectoides, or sclerodermoid. Jaros et al. groups these imitator lesions according to the organs that are the primary cause.[22]

Langerhans cell histiocytosis

Some inflammatory neoplasia, such as Langerhans cell histiocytosis, might also be great imitators. Claire et al. emphasizes that this uncommon entity should remain high on a clinician's differential diagnosis in treatment resistant cases of conditions, such as seborrheic dermatitis, diaper dermatitis, or arthropod bites.[23] Histopathologic examination and specific immunohistochemical stains will assist in making an appropriate diagnosis.

Sclerodermoid skin diseases

Many skin diseases may have a scleroderma-like appearance, making the diagnosis a difficult one. Varju et al. discusses several of these diseases, including endocrinologic diseases (POEMS syndrome, hypothyroidism), metabolic/biochemical abnormalities (nephrogenic systemic fibrosis), and diseases with mucin deposition (scleromyxedema, scleredema).[24] Additional ones with such presentations are genetic diseases (Werner's syndrome and acrogeria) or storage diseases, and they are highlighted separately in the paper.[24]

Conclusions

Although I have selected entities that are worthy of the appellation "great imitator," I recognize that there are many more diseases and syndromes that may mimic one another. With the rapid strides that contemporary medicine continues to make, I hope that our diagnostic skills and therapeutic choices will be able to keep pace.

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References

1. Karadağ AS, Chen W. Great imitators in dermatology: part I. *Clin Dermatol* 2019;37:173-174.
2. Çakmak SK, Tamer E, Karadağ AS, et al. Syphilis: a great imitator. *Clin Dermatol* 2019;37:182-191.
3. Kundakci N, Erdem C. Leprosy: a great imitator. *Clin Dermatol* 2019;37:200-212.
4. Chen Q, Chen W, Hao F. Cutaneous tuberculosis: a great imitator. *Clin Dermatol* 2019;37:192-199.
5. Karadağ AS, Parish LC. Sarcoidosis: a great imitator. *Clin Dermatol* 2019;37:240-254.
6. Hodak E, Amitay-Laish I. Mycosis fungoides: a great imitator. *Clin Dermatol* 2019;37:255-267.
7. Knöpfel N, Nogueira-Morel L, Latour I, et al. Viral exanthems in children: a great imitator. *Clin Dermatol* 2019;37:213-226.
8. Akdeniz N, Elmas ÖF, Karadağ AS. Behçet syndrome: a great imitator. *Clin Dermatol* 2019;37:227-239.
9. Bakija-Konsuo A, Zitinski M, Fatovic-Ferencic S. Mal de Meleda: a great imitator. *Clin Dermatol* 2019;37:175-181.
10. Gupta MA, Gupta AK. Self-induced dermatoses: a great imitator. *Clin Dermatol* 2019;37:268-277.
11. Oumeish OY. Cutaneous leishmaniasis: a historical perspective. *Clin Dermatol* 1999;17:249-254.
12. Nazzaro G, Rovaris M, Veraldi S. Leishmaniasis: a disease with many names. *JAMA Dermatol* 2014;150:1204.
13. WHO. Neglected tropical diseases. Leishmaniasis belongs to the list of 20 neglected tropical diseases according to the WHO. Available at: https://www.who.int/neglected_diseases/diseases/en/. Accessed January 4, 2018.
14. Gurel MS, Tekin B, Uzun S. Leshmaniasis: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
15. McNeil MM, Brown JM. The medically important aerobic actinomycetes: epidemiology and microbiology. *Clin Microbiol Rev* 1994;7:357-417.
16. Ramos-e-Silva M, Lopes RS, Trope BM. Cutaneous nocardiosis: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
17. Karadag AS, Elmas OF, Altunay IK. Cutaneous manifestations associated with HIV infections: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
18. Elmas OF, Akdeniz N, Atasoy M, et al. Contact dermatitis: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
19. Morrow PA. *Drug Eruptions: A Clinical Study of Irritant Effects of Drugs upon the Skin.* New York: William Wood & Company. 1887:iii-iv.
20. Chu CY. Drug eruptions: a great imitators. *Clin Dermatol* 2020;38 xxx-xxx.

21. Ludwig C, Goh V, Rajkumar J, et al. Drug eruptions associated with tumor therapy: a great imitators. *Clin Dermatol* 2020;38 xxx-xxx.
22. Jaros J, Hunt S, Mose E, et al. Contact dermatitis: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
23. Claire KS, Bunney R, Ashack KA, et al. Langerhans cell histiocytosis: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.
24. Varjú C, Kumánovics K, Czirják L, et al. Scleroderma-like syndromes: a great imitator. *Clin Dermatol* 2020;38 xxx-xxx.