Diagnostic differences for older adults with dermatologic disease: considering paradigm changes

Shreya A Sreekantaswamy[1,2] BS, Bina Kassamali[3,4] BA, Avery LaChance[3,4] MD MPH, Daniel C Butler[1] MD

Affiliations: [1]Department of Dermatology, University of California San Francisco, San Francisco, California, USA, [2]School of Medicine, University of Utah, Salt Lake City, Utah, USA, [3]Harvard Medical School, Boston, Massachusetts, USA, [4]Department of Dermatology, Brigham and Women's Hospital, Boston, Massachusetts, USA

Corresponding Author: Daniel Butler MD, 1701 Divisadero Street, San Francisco, CA, 94115, Tel: 415-353-7800, Email: Daniel.Butler@UCSF.edu

Keywords: dermatomyositis, granuloma annulare, geriatric dermatology, older adult, pruritus, pyoderma gangrenosum, urticarial eruptions

To the Editor:

Disease schematics often neglect nuanced presentations in adults aged 65 or older. There is, however, a growing body of evidence that for many conditions, older adults may require unique diagnostic and workup considerations. This perspective shares five dermatologic diseases that require distinct approaches in older adults, aiming to ignite discussion and research on how dermatology can change current paradigms to meet these patients' needs.

Paraneoplastic granuloma annulare (GA) is rare but may be more likely in older adults [1]. Paraneoplastic GA typically presents as generalized disease, [1] and in older patients generalized GA tends to have a more chronic course [2]. Although the relationship between GA and cancer is controversial, malignancies that have been found with paraneoplastic GA include lymphoproliferative disease and solid organ tumors of the colon, lung, breast, and cervix [1,3,4]. Classically, individuals with disseminated GA are counseled to complete age-appropriate malignancy screening and are evaluated for cancer recurrence [4]. This guidance, however, may cause providers to omit key aspects of malignancy work-up in older adults. For instance, cervical cancer screening and mammograms are not included after ages 65 and 75, respectively, and lung cancer screening is limited to those with a smoking history. Providers should therefore have a low threshold to thoroughly evaluate older adults with generalized GA for a symptom-based malignancy workup in addition to standard screening [3].

Expanded malignancy screening should also be considered for older adults with dermatomyositis (DM). Although DM is commonly associated with ovarian and lung cancer, 50% of malignancies in patients older than 65 have been found to be colorectal [5]. As with GA, all patients should undergo age-appropriate malignancy screening, be evaluated for cancer recurrence, and undergo targeted work-up triggered by abnormalities identified on examination. Although no consensus has been reached surrounding guidelines for malignancy screening, studies have suggested that blind CT or PET CT scans (abdominal-thoracic for men and chest-abdomen-pelvis for women) should be included in the diagnostic workup of DM, particularly in the three years following diagnosis, given their high positive rates for detecting malignancy in asymptomatic individuals [5,6]. It is also important to note that in older adults, deconditioning can mimic the weakness characteristic of DM. In these cases, a bilateral thigh MRI with myositis protocol can be used to confirm active muscle disease.

Similarly, solid-organ and hematologic malignancies have been found to be more common in older adults with pyoderma gangrenosum (PG), [7]. Older adults with PG were also more likely to have rheumatoid arthritis, ankylosing spondylitis, and hematologic disorders than younger patients [7]. In addition to a

standard PG workup and symptom-based workup for arthritis and autoimmune conditions, older adults with PG should receive age-appropriate cancer screening for solid organ malignancies and a blood smear and monoclonal gammopathy evaluation with a low threshold for hematology-oncology referral for bone marrow biopsy [7].

Urticarial eruptions and pruritus are common in older adults and may be an initial manifestation of bullous pemphigoid (BP), [8]. Providers should consider a BP enzyme linked immunosorbent assay and biopsy with diffuse immunofluorescence for further evaluation. Older adults are also particularly susceptible to urticaria secondary to polypharmacy and their medications should be reviewed to find implicated drugs such as diuretics and penicillin antibiotics [9]. Pruritus in older adults is considered to be multifactorial due to loss of barrier function, immunosenescence, or neurological pathology [10]. Workup should be conducted based on diagnostic clues: itch with a rash is likely immunological in nature, itch in a fixed location is likely neurological, and itch in tandem with dry skin is likely related to loss of barrier function [10].

These five conditions exemplify how disease schematics can neglect older adults, demonstrating that older patients with these conditions often require a more involved workup than younger patients (**Table 1**). Dermatologists need to explicitly include older adults in research and discussion of these diseases so that we can better understand how to diagnose and care for this vulnerable population.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Mangold AR, Cumsky HJL, Costello CM, et al. Clinical and histopathologic features of paraneoplastic granuloma annulare in association with solid organ malignancies: A case–control study. *J Am Acad Dermatol*. 2018;79:913-20.e1. [PMID: 29920319].
2. Heymann WR. Granuloma annulare's triangular association with malignancy. *J Am Acad Dermatol*. 2018;79:822-3. [PMID: 30179637].
3. Nordmann TM, Kim J-R, Dummer R, Anzengruber F. A Monocentric, Retrospective Analysis of 61 Patients with Generalized Granuloma Annulare. *Dermatology*. 2020;236:369-74. [PMID: 32403113].
4. Keimig EL. Granuloma Annulare. *Dermatol Clin*. 2015;33:315-29. [PMID: 26143416].
5. Sparsa A, Liozon E, Herrmann F, et al. Routine versus Extensive Malignancy Search for Adult Dermatomyositis and Polymyositis: A Study of 40 Patients. *Arch Dermatol*. 2002;138:885-90. [PMID: 12071815].
6. Li X, Tan H. Value of (18)F-FDG PET/CT in the detection of occult malignancy in patients with dermatomyositis. *Heliyon*. 2020;6:e03707-e. [PMID: 32274435].
7. Ashchyan HJ, Butler DC, Nelson CA, et al. The Association of Age With Clinical Presentation and Comorbidities of Pyoderma Gangrenosum. *JAMA Dermatol*. 2018;154:409-13. [PMID: 29450453].
8. Bakker CV, Terra JB, Pas HH, Jonkman MF. Bullous Pemphigoid as Pruritus in the Elderly: A Common Presentation. *JAMA Dermatol*. 2013;149:950-3. [PMID: 23804286].
9. Verheyden MJ, Bilgic A, Murrell DF. A Systematic Review of Drug-Induced Pemphigoid. *Acta Derm Venereol*. 2020;100. [PMID: 32176310].
10. Berger TG, Shive M, Harper GM. Pruritus in the Older Patient: A Clinical Review. *JAMA*. 2013;310:2443-50. [PMID: 24327039].

Table 1. *Work-up considerations for flagship diagnoses in older adults.*

Paraneoplastic granuloma annulare	Presentation	Disseminated [1] Chronic
	Associations	Lymphoproliferative disease [1,3,4] Solid organ malignancy [1,3,4] Colon Lung Breast Cervical
	Workup	Age-appropriate cancer screening[a] [1] Symptom-directed cervical and lung cancer screening
Dermatomyositis	Presentation	No significant difference in clinical presentation, but consider that muscle weakness could be from deconditioning
	Associations	Solid-organ malignancy [5] Ovarian Lung Colorectal: most common in older adults
	Workup	Age-appropriate cancer screening[a] Blind CT scan [2] or PET CT [6] Men: abdominal-thoracic Women: pelvic-abdominal-thoracic In older adults presenting with weakness that mimics weakness associated with DM, rule out deconditioning with a bilateral thigh MRI with myositis protocol
Pyoderma gangrenosum	Presentation	Higher rate of pathergy compared to younger adults [7]
	Associations	Inflammatory arthritides [7] Solid organ and hematologic malignancy [7] Hematologic disorders (especially monoclonal gammopathy of undetermined significance, myelodysplastic syndrome, polycythemia vera) [7]
	Workup	Age-appropriate cancer screening[a] Blood smear [7] Monoclonal gammopathy evaluation (serum protein electrophoresis, urine protein electrophoresis, immunofixation) [7] Referral to hematology oncology for consideration of bone marrow biopsy [7]
Urticarial eruptions	Presentation	Higher rates of bullous pemphigoid (BP) presenting as urticaria [8]
	Associations	Drug-induced BP (loop diuretics, penicillin antibiotics, gliptins, PD1/PDL1 inhibitors), [9]
	Workup	Bullous pemphigoid enzyme linked immunosorbent assay (ELISA) + diffuse immunofluorescence (DIF) + biopsy Medication review for polypharmacy
Pruritus	Presentation	Itch with dry skin [10] Itch with a rash [10] Itch in fixed location [10]
	Associations	Loss of barrier function [10] Immunosenescence [10] Neuropathy [10]
	Workup	Older adults have certain conditions (e.g. scabies, bullous pemphigoid) that predominantly present as itch more so than rash, workup should include exclusion of these conditions: Empiric treatment for scabies if high suspicion BP ELISA + DIF

[a]Age-appropriate cancer screening for adults over age 65 includes: 1) Colon cancer: up to age 75, 2) Lung cancer: if active or former smoker (quit within 15 years) with 20-pack year smoking history, 3) Breast cancer: up to age 75
Other than these specific evaluations, a thorough review of systems, history, and physical examination should be conducted to look for signs of other underlying malignancy or recurrence in patients with a cancer history.