Top Ten Things Rheumatologists Should (And Might Not) Know About Dermatologic Disorders

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Rheumatologists can positively impact patients beyond diagnosing and treating musculoskeletal disorders. All patients suffer dermatologic conditions at some time; the first organ we see during a physical examination is the skin. Cutaneous malignancies affect nearly one third of the population; a rheumatologist's examination may be the first opportunity to diagnose skin cancer. Common inflammatory disorders may be mistaken for infectious processes. With an increasing number of patients on immunosuppressive therapies, distinguishing dermatitis from cellulitis is important. Moreover, dermatologic assessments may assist in the diagnosis of rheumatologic diseases, for example, connective tissue diatheses and psoriatic arthritis (PsA). Rheumatologists have additional opportunities to reduce morbidity and mortality by recognizing certain dermatologic conditions.

1. Malignant Melanoma[1-4]

With a lifetime risk of 1%, melanomas have a relatively high incidence and prevalence in the adult population. Worldwide, melanomas are responsible for 48,000 deaths annually. Primary malignant melanomas occur in tissues seeded with melanocytes, which include eyes, brain, gut, and skin. Cutaneous melanomas are by far the most common. The frequent diagnosis, and ready detection, of cutaneous melanomas undoubtedly reflects the relative abundance of melanocytes in the skin, which is exposed to the most common inducer of melanomas: ultraviolet radiation. Early diagnosis and treatment should reduce morbidity and mortality.

The hallmarks of a classic, cutaneous melanoma include hyperpigmentation and an irregular border. The "ABCD" guidelines (Asymmetry, Border irregularity, Colouration variegate or unusual, and Diameter greater than 6 mm) serve as quick and easy indicators despite lack of validation. A differential diagnosis need include seborrheic keratosis, congenital nevi, Clark's nevi, and lentigines.

Seborrheic keratosis are most often elevated, pigmented (tan to black) hyperkeratotic papules having a stuck-on, wart-like appearance and texture. Everyone eventually develops one or more seborrheic keratoses. As the name suggests, congenital nevi are collections of melanocytes evident at or soon after birth. Congenital nevi range from isolated, small papules or patches with the appearance of regular nevi, to widespread pigmented patches or papules scattered or contiguous over large segments of the body. Regular nevi most often appear between the ages of five and 50 but develop throughout life in many individuals. Clark first described Clark's nevi as multiple, atypically pigmented large nevi occurring in family members predisposed to developing malignant melanomas. Clark's nevi appear as "fried eggs" with lighter coloured, irregular boarders surrounding a central, more darkly pigmented macule. Clark's nevi can be difficult to distinguish from early malignant melanomas. Having a few Clark's nevi is not associated with an increased risk of melanoma; on the other hand, having dozens to hundreds of Clark's nevi is clearly associated with an increased risk for the development of melanoma. Lentigines are irregularly shaped, hyper-pigmented macules most often the result of excessive sun exposure. Given the irregular borders and hyperpigmentation, melanomas, Clark's nevi, and lentigines may be visually indistinguishable.

2. Non-melanoma Skin Cancer[5]

Basal cell carcinoma is the most common cutaneous malignancy with a nearly 30% lifetime risk. Basal cell carcinomas are typically slow growing, pink papules or macules possessing a scant degree of translucency.

Though basal cell carcinomas may occur on any part of the body, they are most frequently noted on sun-exposed areas such as the face, upper trunk, and arms. The risk of basal cell carcinomas metastasizing is extremely low; nonetheless, early diagnosis is important in reducing morbidity and disfigurement resulting from excision or therapeutic radiation.

Squamous cell carcinomas present with a broad, clinical spectrum. The textbook presentation is that of a rapidly growing, indurated, keratotic papule or nodule. Like basal cell carcinomas, squamous cell carcinomas are far more common on sun-exposed skin than non-exposed skin. It is not uncommon for squamous cell carcinomas to present in a more indolent fashion with slow growing patches or papules. Unlike basal cell carcinomas, however, the risk of squamous cell carcinomas metastasizing can be significant depending upon anatomical location, inherent tumour aggression (rapidly growing tumours tend to be more aggressive), and perineural invasion. Early detection and intervention is important in reducing morbidity and mortality.

3. Cutaneous Infections[6,7]

Cutaneous infections are extremely common and range from near trivial folliculitis to life-threatening cellulitis caused by common, as well as exotic and opportunistic, organisms. Of the common and noteworthy infections, cellulitis and erysipelas are the most frequent; Strep. pyogenes and less frequently Staph. aureus are the responsible organisms. Generally, cellulitis and erysipelas are readily diagnosed with warm, inflamed, tender expanding patches of skin associated with constitutional symptoms. In some instances, cellulitis is confused with other inflammatory dermatoses, venous stasis dermatitis (SD) being the most common. An additional confounder is the mild suppression of the typical signs of cutaneous infections: redness, warmth, and tenderness by systemic anti-inflammatory agents with tumor necrosis factor (TNF)-antagonists possibly being the most prominent. The latter may result in delayed diagnosis.

Prudence, rather than evidence, suggests dosing of biologic agents should be held until resolution of the cellulitis.

4. Stasis Dermatitis[8]

Because it is common and readily misdiagnosed as cellulitis, it is important for rheumatologists to recognize and confidently diagnose SD. Superficial varices on the legs are principal in the development of the condition; back pressure resulting from incompetent deep venous structures causes dilation of superficial venous plexes. Dilated venous plexes, in turn, produce edema of the skin and soft tissue as well as deposition of hemosiderin near the epidermal junction and in the underlying tissues. Hemosiderin may be absorbed by keratinocytes resulting in a rust-brown discoloration of skin; however, hemosiderin may also serve as an irritant causing further edema and inflammation of the skin and subcutaneous tissues.

Inflammation of skin is associated with rubor and calor. One helpful distinction between SD and cellulitis is that stasis may be pruritic whereas cellulitis is not. Unfortunately, tenderness or pain does not always distinguish cellulitis from SD.

Three factors may be helpful in making a diagnosis of stasis dermatitis over cellulitis. First is the history. SD tends to be chronic, with several days to weeks of persistent inflammation over the same area, whereas cellulitis, caused by common organisms, is acute and rapidly spreads from its nidus over hours. Moreover, patients

with cellulitis often experience constitutional signs and symptoms, including fever, chills, and malaise, all of which are uncommonly associated with SD. Finally, a heightened clinical awareness of SD in patients with dependent edema and varicosity, or erythema confined to those regions overlying dilated venous plexes, would prove beneficial.

5. Allergic Contact Dermatitis[9]

Allergic contact dermatitis (ACD) presents as pruritic, well demarcated, erythematous and sometimes bullous plaques. Lines of demarcation reflect the area of contact with an allergen. Nickel remains the most common allergen; however, topical antibiotics and topical corticosteroids are frequently administered, and are common allergens as well. Untreated, allergic contact reactions will persist for several days to a few weeks. There are several reasons ACD is important to a rheumatologist. Like SD, ACD may be confused with cellulitis; however, ACD is often pruritic while cellulitis is not. ACD is fixed and well defined where as cellulitis tends to be diffuse with poorly defined expanding edges. Additionally, ACD is not associated with constitutional signs and symptoms, while chills and malaise are often associated with cellulitis. Of course, ACD is very common in the population, suggesting that rheumatologists are prone to ACD themselves, being yet another reason ACD is important to a rheumatologist.

6. Pyoderma Gangrenosum[10]

One of the more dramatic cutaneous disorders is pyoderma gangrenosum (PG). Sometime indolent in nature, PG more often than not develops from a small erythematous papule that rapidly expands into a plaque with central ulceration and undermined, elevated, erythematous, crenate edges. Rapid spread is measured in hours to days, with ulcers exposing underlying subcutaneous fat and muscle measuring a few to several tens of centimeters in diameter. PG appears to be an epiphenomenon driven by underlying inflammatory disorders, including inflammatory bowel disease (IBD) and rheumatoid arthritis (RA). Cases of PG have also been associated with psoriasis, PsA, and ankylosing spondylitis (AS).

The most effective means of treating PG is to treat the associated inflammatory disease. In those instances which prove recalcitrant, or for which no underlying disease is found, urgent dermatological referral is imperative.

7. Drug Eruptions[11]

Cutaneous drug eruptions are common and not usually difficult to diagnose. The difficulty is in determining causality. Nonsteroidal anti-inflammatory drugs (NSAIDs) are common causes of cutaneous drug reactions; these are frequently prescribed by rheumatologists. Cutaneous drug reactions are an important aspect of rheumatologic practice, but, unfortunately, many of the rheumatologist's patients are on multiple drugs, many of which are over-the-counter products, making causal attribution difficult.

The diagnosis of a drug reaction is based upon two aspects of the presentation, namely, the distribution of the reaction and the contemporaneous development of a reaction associated with the introduction of a drug. Most reactions occur within the first seven to 10 days of therapy. A typical reaction consists of scattered, erythematous, and sometimes pruritic macules or patches. Urticarial eruptions are likewise very common, with the urticaria being widespread and variable in location and intensity. A less frequent, but immunologically interesting, phenomenon is a fixed drug reaction. Typically, fixed drug reactions consist of a single, erythematous patch which recurs on exactly the same location with each exposure. Withdrawal of the drug will typically see the eruption resolve within 14 days; protracted reactions are uncommon. Cross-reactions among certain classes of drugs (*e.g.*, penicillins and NSAIDs), suggest the prescribing physician should take precautions to prescribe outside of class and acknowledge the potential for reactions occurring, even though the drug class is very different from that causing the initial reaction.

8. Psoriasis[12]

Affecting 2% to 5% of the population, the accurate and rapid diagnosis of psoriasis can play an important role in establishing the diagnosis of PsA, with upwards of 30% of these psoriasis patients going on to develop PsA.

Classically, psoriasis presents as erythematous patches or elevated plaques covered with varying degrees of scale from nearly scale-free to oyster shell keratosis. Those areas most commonly affected are the scalp, elbows, knees, and gluteal cleft. A great deal of scientific noise has been made regarding the association of disease location and development of arthritis, but given the high prevalence of disease in the classic regions, such associations are of no predictive value.

Difficulty in making the diagnosis of cutaneous disease may be the result of treatment, or mild or atypical morphological characteristics of cutaneous signs; for example, scale in intertriginous regions and on the genitals will be minimal or absent. Treatment with emollients or topical antibiotics containing active ingredients may significantly alter the clinical presentation. Occasionally, biopsies are necessary to make definitive diagnoses. It is important to have the specimens evaluated by a dermatopathologist, as making the distinction between psoriasis and other inflammatory dermatoses can be challenging.

9. Nail Pitting[13]

Though most dermatologists and rheumatologists associate nail pits with psoriasis, nail pits are associated with several cutaneous disorders. Certainly, nail pitting is common in patients with psoriasis, but it may be equally common in patients with alopecia areata. Alopecia areata is an autoimmune disorder characterized by localized and sometimes widespread hair loss. Rare cases of nail shedding are seen with both alopecia areata and psoriais. Nail pitting may likewise occur in the normal population. Other suggested causes of nail pitting include lichen planus, dermatitis, chronic renal failure, reactive arthritis, vitiligo, hemodialysis, pemphigus, sarcoidosis, connective tissues diatheses, and secondary syphilis.

Nail pitting in the presence of a sero-negative, inflammatory arthropathy may be very suggestive of PsA, but nail pitting alone is insufficient to make a firm diagnosis.

10. Psoriasis is the Best Disease for Assessing Drug Safety[14]

Evaluating safety signals is fraught with confounders: co-morbidities, concomitant medications, and the impact of the underlying condition. While co-morbidities are common in psoriatics, the underlying disease tends to be more indolent than RA. Additionally, psoriatics are usually treated using a monotherapy paradigm. For the most part, psoriasis patients resemble a normal population, making them an ideal population in which to ascertain potential risks associated with a given therapy.

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