Psoriasis in an HIV-Infected Woman on Antiretroviral Therapy

Maitseo K. Nwako-Mohamadi MBChB BAO MSc[1], Vidushi Madan MD[2], Matthew N. Tanko MBBS FMCPath (Nig)[3] and Sandro Vento MD[4]

Departments of [1]Medicine and [2]Pathology, Nyangabgwe Referral Hospital, Francistown, Botswana
Departments of [3]Pathology and [4]Internal Medicine, University of Botswana, Gaborone, Botswana

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A 66 year old HIV-infected black African woman presented in April 2013 at the Dermatology Clinic of Nyangabgwe Referral Hospital in Francistown, Botswana, with a generalized rash of 1 year duration that had started as itchy blisters (exacerbated by sweating) scattered all over her body. Scratching led to the appearance of scaly plaques that bled easily. The patient also reported painful swelling of the lower legs and pain in the right knee. She did not smoke or drink alcohol and there was no history of skin disease in her family. The patient had been on tenofovir-emtricitabine-efavirenz antiretroviral therapy for 11 months; she had also received another treatment she could not recall that had not led to amelioration of the skin lesions. Examination showed widespread bilateral scaly plaques, some with an annular shape; a few plaques were crusted [Figure 1]. Her face was spared, and the body surface area affected was 20%. The right knee was mildly edematous and tender on palpation with normal range of motion. Bilateral mild pitting edema was present, including the shins. A diagnosis of possible superinfected linear IgA bullous dermatosis was made and the patient was started on prednisolone, promethazine, erythromycin, 10% sulphur ointment and hydrocortisone ointment.

HIV = human immunodeficiency virus

One month later she reported some improvement, with flaring of the condition on tapering of the steroids. Examination revealed pustules on the edges of some of the annular plaques; CD4 cells were 187/µl and HIV-RNA level was below 400 copies/ml. The patient was prescribed a 1 month course of methotrexate in addition to prednisolone, cloxacillin and promethazine. After a further month she was still complaining of itching. Psoriasis was suspected, a biopsy was done, and 6% coal tar, prednisolone, promethazine, doxycycline, tetmosol soap and 10% sulphur ointment were prescribed. Histology showed hyperkeratosis, parakeratosis, acanthosis, bulbous elongation of rete ridges and chronic dermal inflammation, in addition to thinning of the suprapapillary epidermis. Munro's micro-abscesses were also focally observed, consistent with a diagnosis of psoriasis.

The patient defaulted follow-up and presented again in October 2013 complaining of severely itchy bleeding plaques and swelling of the feet; she could not put on shoes due to the edema. Examination showed discrete papules in the neck region, multiple discrete to confluent scaly plaques with some occasional pustules on the lower limbs [Figure 2], nail horizontal ridges and subungual hyperkeratosis. The body surface

Figure 1. Multiple discrete to confluent bilateral scaly plaques on extensor surfaces of the lower limbs. Some lesions look annular especially on the thighs. Occasional pustules are also noted as well as bilateral knee edema (Note: the patient wrapped her right knee with a scarf because of pain)

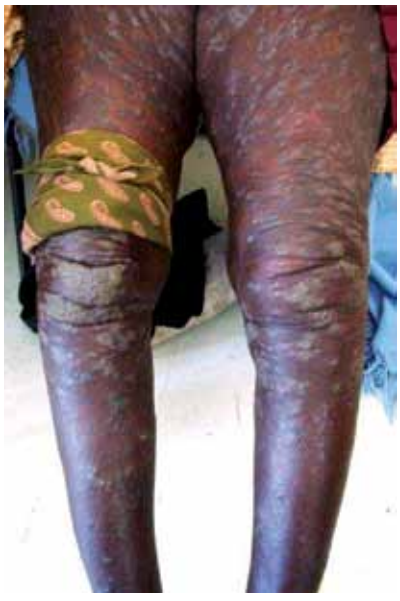
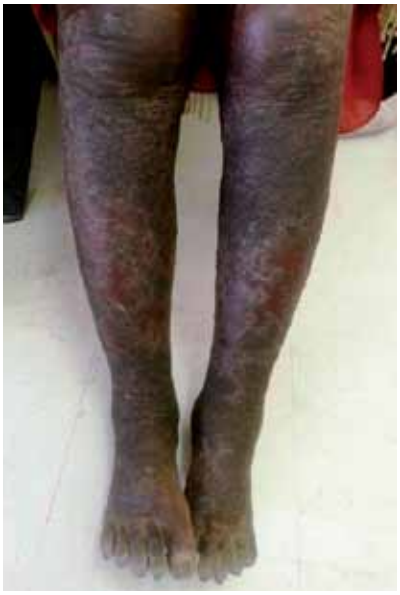


Figure 2. Bilateral, confluent, hyperpigmented scaly plaques on extensor surfaces of lower limbs with nail hyperkeratosis



area affected was 18%. The patient was diagnosed with psoriasis and likely psoriatic arthritis, started on isotretinoin, betamethasone ointment and promethazine, and was encouraged to moisturize intensively. Isotretinoin rather than metrotrexate was used due to the low CD4 cell number.

Psoriasis might worsen or it might be detected for the first time following HIV infection [1]. It is particularly severe (usually affecting more than 50% of the body) [2], and generally presents late in the course of the infection when CD4 cell counts are less than 200/μl [3] and the patient is not on antiretroviral therapy [2]. Antiretrovirals can be beneficial and the eventual clearing of psoriasis is concomitant with a decrease in the HIV load [4]; stopping antiretrovirals can lead to psoriasis exacerbation [5].

Our case indicates that psoriasis treatment can be problematic also in patients on antiretrovirals and with undetectable viral load if the CD4 cell count does not increase above 200/μl.

Corresponding author:
Dr. S. Vento
School of Medicine, University of Botswana, Private Bag 00713, Gaborone, Botswana
Phone: (267) 355-4190
Fax: (267) 310-5979
email: ventosandro@yahoo.it

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Capsule

Regulating DNA repair

Chromosomes carry the intricate code that makes and organizes cells and organisms. But chromosomes can break, causing a serious potential threat to cell and organismal survival. Repairing such breaks is vital, but repair can come with its own dangers, as certain repair pathways are necessarily error-prone – restoring chromosome integrity at the cost of introducing mutations into the genome. Microhomology-mediated end joining (MMEJ) is an error-prone form of repair that relies on very small (~5 to 25 base pairs) fortuitous homologies near the broken ends of chromosomes, which allow them to come together and be rejoined. A microhomology signature is often seen in breakpoints in chromosome arrangements in cancers and other diseases, suggesting that MMEJ is commonly involved in such genome derangement. Deng and collaborators investigated MMEJ in the budding yeast *Saccharomyces cerevisiae*. They found that although resection [the trimming back of one of the DNA stands to generate a single-stranded DNA (ssDNA) tail] at the ends of the breaks is important to expose regions of microhomology internal to the break, it is not rate-limiting for repair. On the other hand, replication protein A, which binds ssDNA, actively prevents spontaneous annealing between the microhomologies and suppresses MMEJ.

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Eitan Israeli

Capsule

REST and stress resistance in aging and Alzheimer's disease

Human neurons are functional over an entire lifetime, yet the mechanisms that preserve function and protect against neurodegeneration during aging are unknown. Lu and colleagues show that induction of the repressor element 1-silencing transcription factor (REST, also known as neuron-restrictive silencer factor, NRSF) is a universal feature of normal aging in human cortical and hippocampal neurons. REST is lost, however, in mild cognitive impairment and Alzheimer's disease. Chromatin immunoprecipitation with deep sequencing and expression analysis show that REST represses genes that promote cell death and Alzheimer's disease pathology, and induces the expression of stress response genes. Moreover, REST potently protects neurons from oxidative stress and amyloid β-protein toxicity, and conditional deletion of REST in the mouse brain leads to age-related neurodegeneration. A functional orthologue of REST, *Caenorhabditis elegans* SPR-4, also protects against oxidative stress and amyloid β-protein toxicity. During normal aging, REST is induced in part by cell non-autonomous Wnt signaling. However, in Alzheimer's disease, frontotemporal dementia and dementia with Lewy bodies, REST is lost from the nucleus and appears in autophagosomes together with pathological misfolded proteins. Finally, REST levels during aging are closely correlated with cognitive preservation and longevity. Thus, the activation state of REST may distinguish neuroprotection from neurodegeneration in the aging brain.

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Eitan Israeli