Editorial Comment

Of mites and men: scabies in patients with kidney disease

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Introduction

In this issue of the journal, Yates et al. [1] describe the interesting case of a 54-year-old renal transplant recipient with enigmatic pruritus. Many diagnostic considerations were entertained and drugs stopped, switched and changed again to the point where even stopping the immunosuppression altogether and sacrificing the graft were considered by the desperate patient. Eventually, scabies was diagnosed and the patient made an uneventful recovery with appropriate treatment. Here, we aim to provide some context for their report and discuss scabies and its relevance in renal patients.

Scabies

The word scabies is derived from the Latin word 'scabere' (to scratch) [2]. The disease is caused by Sarcoptes Scabiei var. hominis, an eight-legged parasitic arthropod without animal reservoir. Scabies has clearly blighted mankind since times immemorial [3] and its signs and symptoms were well known to Greek and Roman investigators. The pathophysiology of scabies still remains poorly misunderstood, not least because the mite is only 0.3–0.4 mm, i.e. at the limit of visibility. Italian naval physician Giovanni Cosimo Bonomo was the first to describe (and draw) S. Scabiei var. hominis in patients at the spa of 17th century Livorno in Italy [4]. His findings remained forgotten until 1834 when medical student Simon Francois Rennucci, prompted by habits he had seen in his native Corsica, 'rediscovered' the mite in skin lesions [3]. Later, Ferdinand von Hebra in Vienna described the life cycle and stages of infection [3]. We now know that four stages (egg, larva, nymph and adult) culminate in the female mite burrowing into the stratum corneum and depositing eggs along her burrow. The pruritus is the result of a type IV reaction to the mite and its products.

Today, scabies is believed to affect up to 300 million people worldwide. The incidence of the disease fluctuates with poverty, migration and wars (Figure 1) [3]. Outbreaks in developed countries usually occur in institutions and care homes; dialysis centres have been affected as well [5]. It is still widely assumed that transmission is through clothes. However, during World War II, entomologist Kenneth Mellanby performed transmission studies in volunteers' made up of conscientious objectors [6] and disproved the widely held belief that towels, clothing and bedding are involved in transmission.

Elevated, intensely pruritic lesions on hands and feet particularly affecting the inter-digit webbing are highly suspicious of scabies. The symptoms are often worse during the night. Secondary bacterial infections can occur and complicate the picture. Most patients eventually control the mite count as a function of their cellular immunity. Proof of the diagnosis requires demonstration of mites or their products in skin scrapings or by applying adhesive tape to the lesion and examining the tape under a microscope. The latter is simple and can be performed by a non-specialist, possibly even by a nephrologist: all that is required is the trusted microscope already used for urine microscopy and some clear adhesive tape. Other tests include administering ink to the skin (burrow ink test) and dermoscopy [7]. The differential diagnosis is broad and includes eczema, tinea, atopic dermatitis, Langerhans cell histiocytosis, bullous pemphigoid and papular urticaria [8].

There are relatively few well-designed trials to guide treatment of scabies, although recent European guidelines have been formulated [9]. Topical permethrin 5% cream and malathion are widely regarded as first-line treatment [10]. The important point to remember in prescribing this therapy is to use two treatments 1 week apart, as this is necessary to kill mites that have hatched out from eggs after the first application. One has to also ensure that all close contacts apply the treatment at the same time as the patient as re-infection is common. Oral ivermectin is often used for crusted scabies in immunocompromised patients or during outbreaks where topical treatment is seen as impractical. Post-scabetic nodules, which occur as discrete and itchy papules, persist without the presence of the scabies mite and cause recalcitrant eczema and pruritus. Treatment of these conditions requires an additional use of topical steroids and emollients.

Scabies and pruritus in chronic kidney disease (CKD)

Intractable pruritus worsening at night is the diagnostic hallmark of scabies, but pruritus is also a common and
bothersome symptom among many uninfected patients with advanced CKD [11]. The pathogenesis of uraemic pruritus remains poorly understood but hyperparathyroidism, inadequate dialysis and sweat gland atrophy are well-described risk factors. Incidence and prevalence may be decreasing, perhaps as a result of better dialysis provision, improved management of hyperparathyroidism, or both [12]. However, prevalence rates as high as 42% in patients on maintenance dialysis are still being reported in contemporary studies [13]. Renal physicians may be tempted to ascribe all itching in their patients to uraemic pruritus, although it is difficult to uphold that assumption in the case under discussion, i.e. in a patient 9 months after successful renal transplantation: in our experience, uraemic pruritus settles quite quickly after transplant, as long as the graft function is good.

There is a remarkable lack of published evidence regarding scabies and CKD, and there may also be a considerable degree of under-diagnosis, under-reporting, or both. Anecdotal reports [14] and personal experience suggest that scabies is not uncommon in advanced CKD and many clinicians recall cases on dialysis units. Some small outbreaks in dialysis centres have also been reported [5, 15]. It is easy to see how such an outbreak could have a major impact on a dialysis unit: considerable resources will have to be put in place for screening patients, prescribing treatment and monitoring of therapeutic efficacy. Household contacts need to be tracked down and carers and ambulance drivers, and one would have to liaise with public health authorities. Nephrologists affected by such outbreaks may take consolation from the fact that numbers of patients exposed in a dialysis unit are still relatively small compared with other facilities, such as intensive care units with many hundreds of potential patients [16]. The fact that treatment is relatively straightforward is also reassuring: neither topical permethrin nor oral treatment with ivermectin requires special precautions or dose reductions in patients with CKD or those on dialysis, although it should be borne in mind that the latter increases the anti-coagulant effect of warfarin.

Rather than being a secondary diagnosis, scabies can also cause kidney disease as mentioned by Yates et al. Studies by Hoy et al. [17] suggested that post-streptococcal glomerulonephritis (PSGN) caused by super-infected scabies contributes markedly to the burden of CKD in the Aboriginal community in Australia. Whether, and if so to what degree, scabies contributes to the global burden of CKD remains difficult to gauge given that large studies are lacking. We believe that such an effect is rather unlikely, given that PSGN, associated with scabies remains very rare or unheard of in many large European centres. Nonetheless, nephrologists need to remain vigilant in patients with PSGN, and the association underscores once more that scabies is not always a diagnosis made in primary care where expertise in dealing with scabies is probably strongest.

Crusted scabies in renal transplant recipients

Crusted or Norwegian scabies denotes a variant of the disease seen in immunocompromised hosts including renal transplant recipients [7]. Crusted scabies may also occur in the absence of a well-defined immune deficiency, for example in the elderly or patients with Down syndrome. Yates et al. describe the clinical features (Figure 2) in some detail [1]. It is worthwhile to emphasize that pruritus may be absent or minimal. In the immunocompromised, the papular pruritic eruption of the classical pattern affecting the web spaces of the fingers, flexor wrists, peri-umbilical area and genitals may not

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Fig. 1. Scabies in early 19th century France. Cartoon by Hippolyte Bellangé. Image in the public domain [28]. Throughout history, scabies is often reported during war and the author of the cartoon may have observed cases in returning soldiers of Napoleon’s armies.

Fig. 2. Crusted scabies in a patient with advanced CKD. Reproduced from [29], with permission.
occurred, and the picture can be more of a widespread eczematous eruption. Very high levels of serum IgE and eosinophilia in peripheral blood are further clues to the diagnosis. Compared with patients with an intact immune system, patients with crusted scabies may have a mite burden in the order of thousands to millions compared with immunocompetent patients who only have a mite burden of up to fifteen [18]. Treatment of crusted scabies also differs from classical scabies. The use of topical scabicide, e.g. permethrin, is again recommended together with a keratolytic which facilitates the breakdown of crusts and improves penetration of the topical agent. Multiple doses of oral ivermectin are also recommended depending on the severity of the disease [19]. As far as we could ascertain, the drugs do not interact with the metabolism of calcineurine inhibitors.

Renal transplant patients are perfect hosts to the mite as Yates et al. [1] and others have demonstrated [20–25]. Yates et al. [1] also discuss in detail the differential diagnosis of pruritus in renal transplant patients. In hindsight, one may wonder why the diagnosis was not considered earlier and why a dermatologist first saw the patient 13 weeks after the onset of pruritus. Yates et al. [1] argue, and rightly so, that one of the reasons that the diagnosis was missed for so long is the diagnostic method of availability heuristics. This approach describes a mental short cut that leads to making judgements about the probability of events by how easy it is to think of examples. This form of error is more common with pattern recognition than with inductive or deductive strategies of diagnostic reasoning. It is often combined with a willingness to accept new evidence only if it fits the original diagnosis [26]. In the case under discussion, the fact that the pruritus became uncontrollable not long after steroid bolus treatment should have rang alarm bells and an infectious aetiology should have been re-considered. Yates et al. may take solace in reading the reports of other seasoned nephrologists and transplant physicians who missed the diagnosis of scabies [27], resulting in scabies transmission to 21 other patients and staff in two different institutions.

Conclusion

Yates et al. delightful article provides a timely reminder of scabies as an important differential diagnosis of pruritus in renal patients. Like syphilis, scabies is an age-old imitator and often misdiagnosed. We speculate that undiagnosed cases still lurk among our many patients with CKD and those populating our transplant outpatient clinics. It is hoped that Yates’ paper may increase the vigilance within the renal community, and perhaps discourage renal physicians from all too easily available heuristics.

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References


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