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CASE REPORT

Trichodysplasia Spinulosa

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ABSTRACT: Trichodysplasia spinulosa (TS) is a unique, rare clinical and histological dermatologic entity described mainly in a setting of immunosuppression. It is caused by a novel human polymoavirus, TS-associated polyomavirus. Reduction of immunosuppression and/or anti-viral therapy is the main therapeutic strategies used to treat such cases. We report a biopsy-proven case of TS in a male renal transplant patient who presented to a dermatology outpatient clinic in Montreal, Canada, in 2015. He was managed with valgancyclovir with no obvious response. Subsequently, a trial of topical imiquimod was commenced. Awareness of TS can prompt early diagnosis and management to prevent possible complications.

Keywords: Immunosuppression; Organ Transplant; Human Polyomavirus; Case Report; Canada.

Trichodysplasia spinulosa (TS) is a rare cutaneous manifestation due to a viral infection affecting mainly immunosuppressed hosts. The majority of patients are solid organ recipients or patients diagnosed with haematological malignancies.[1]

Given its rarity, in most cases there is a potential delay in diagnosis. Moreover, the pathogenesis of TS is not completely understood. Few therapeutic options are suggested by published case reports and no standard therapies are approved yet.[2]

We present a case of TS in a renal transplant recipient and review the main characteristic features of this entity.

Case Report

A male in his 60s presented to a dermatology outpatient clinic in Montreal, Canada, in 2015 for evaluation of facial papules. These were of 2-month duration and progressively increasing in number, affecting the whole face but were more concentrated on the nose. There was mild facial pruritus. The patient was a kidney transplant recipient since July 2014 for hypertensive nephropathy. He was on therapy with mycophenolic acid and tacrolimus. Medical history was positive for osteoarthritis, gout and IgA gammopathy (monoclonal gammopathy of undetermined significance). His other medications included amlodipine, phosphate, magnesium, pantoprazole and acetylsalicylic acid.

Skin examination revealed follicular flesh-coloured to pinkish monomorphic papules mainly on the central face involving the forehead and nose with central white protruding spines. Scalp, mucosal membranes, palms and soles were not affected [Figure 1].

Considering his immunosuppressive status, the differential diagnosis included mainly infectious aetiologies such as molluscum contagiosum, filiform verrucae and TS of immunosuppression. In addition, idiopathic follicular hyperkeratotic spicules or other adnexal pathologies such as sebaceous hyperplasias, trichoepitheliomas, fibrofolliculomas, trichodiscomas and facial fibrous papules (angiofibromas) were also considered as possibilities.

Histopathological examination of one of the papules showed dilated follicular infundibulae with keratin plugs and viral-like changes with large irregular eosinophilic/basophilic trichohyalin-like granules within the inner root sheath cells consistent with TS [Figure 2]. Additional tests such as electron microscopy or polymerase chain reaction (PCR) were not performed.

Based on typical clinical findings in the setting of renal transplantation and suggestive histologic features, the patient was diagnosed with TS. He was managed initially with oral valganciclovir without adequate response. Subsequently, a trial of topical imiquimod was commenced. Unfortunately, he was lost to follow-up.

Verbal informed consent was obtained from the patient for publication purposes.

Discussion

TS is a rare clinicopathologic skin entity primarily described in immunosuppressed individuals and is caused by TS-associated polyomavirus (TSPyV).[2]

The first case of TS was reported in 1995 by Izakovic *et al.* who describing a new entity with spiny follicular hyperkeratosis thought to be related to cyclosporine treatment.[3]

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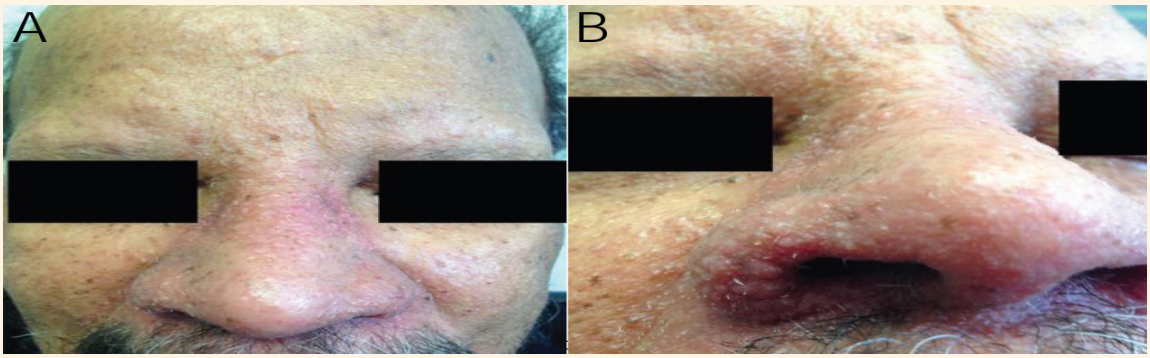

Figure 1: Photographs of the face of a male patient in his 60s. **A:** Skin-coloured monomorphic papules on central face, forehead and nose with protruding central whitish spines. **B:** A close-up image of the papules with white central spines.

Four years later, Haycox *et al.* described a possible polyomavirus association with TS; electron microscopy findings of lesional skin were consistent with polyomavirus-induced changes and the condition was termed trichodysplasia spinulosa.[4] This was confirmed only in 2010 when a novel double-stranded DNA virus was isolated from the hyperkeratotic lesions using a rolling-circle amplification detection method.[5] The presence of 1 million viral load in lesional skin compared to non-lesional skin further reinforced the causal relationship.[6]

TSPyV is a member of Polyomaviridae family. BKPyV and JCPyV are the first members discovered in 1970s known to infect humans.[7] These are linked to transplant-related kidney disease and progressive multifocal leukoencephalopathy, respectively.[8]

There are four novel members from the same family linked to cutaneous conditions mainly in association with immunosuppression including TSPyV. Merkel cell PolyomaVirus (MCPyV) is linked to a rare neuroendocrine tumour of the skin; Merkel cell carcinoma (MCC) has an overall viral prevalence of 80% of the cases. Human PolyomaVirus 6 (HPyV6) and 7 (HPyV7) are associated with unique pruritic dyskeratotic dermatoses in immunosuppressed individuals.[7]

Exposure to TSPyV occurs at a very young age and usually follows an asymptomatic latent course. Seroprevalence of TSPyV in immunocompetent adults is high (up to 80%). Moreover, seroprevalence increases even more in immunocompromised individuals and more in patients with TS.[1,6] Interestingly, only a minority of immunosuppressed hosts will develop TS clinically.[1] van der Meijden *et al.* proposed that the cause of TS is primary polyomavirus infection in immunocompromised hosts rather than reactivation of a latent viral infection which can explain the rarity of this condition.[9] Further studies are required to determine other variables that cause the disease in specific patient populations. The only evidenced dermatologic clinical phenotype of TSPyV is TS.[1]

Clinically, TS appears as flesh-coloured to erythematous follicular-based papules concentrated on the central face with white spicules protruding from the papules. It can progress to alopecia especially of the eyebrows and thickening of the skin leading to leonine faces.[10] TS can also affect the trunk, extremities and neck.[6]

The distinctive histopathological features of TS involve acanthosis of the epidermis, aberrant large, distended follicles with dilated infundibulum and presence of large eosinophilic, trichohyaline granules

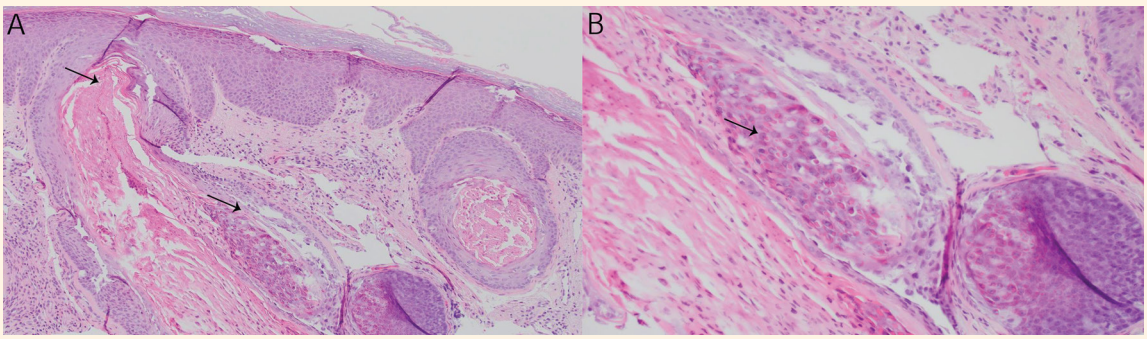

Figure 2: A: Haematoxylin and eosin stain at × 10 magnification showing dilated follicular infundibulae with keratin plugs (black arrow) and viral epithelial changes (arrowhead) consistent with trichodysplasia spinulosa.
B: Haematoxylin and eosin stain at × 20 magnification showing the irregular outer root sheath with TS-associated polyomavirus viral epithelial perinuclear eosinophilic/basophilic changes (arrow).

within excessive proliferating inner root sheath cells of the hair bulb.[8,10]

The classic clinical setting and characteristic histologic findings are usually sufficient to make the diagnosis. Further testing with PCR detection of the virus from the lesions and electron microscopy studies can also be used to confirm the diagnosis.[10]

In a recent review article, Curman *et al.* reported data of all published cases of TS; a total of 60 cases were reviewed.[1] Almost all patients were immunosuppressed. The main associated conditions were haematolymphoid malignancies (including multiple myeloma, acute and chronic lymphocytic leukemia, acute myelocytic leukemia, non-Hodgkin's lymphoma, B-cell lymphoma and myelodysplastic syndrome) or solid organ transplant recipients (including kidney, kidney/pancreatic, heart, lung, liver, intestinal and multivisceral transplant). Other associations include systemic lupus erythematosus on immunosuppressive therapy, Gorlin's syndrome on vismodegib treatment, HIV and B- cell lymphoma and myocarditis.[1]

Interestingly, TS was reported in the setting of remission of lymphoma with a new diagnosis of colon cancer and in the setting of lymphoma relapse.[11,12] This adds to our limited understanding of the pathogenesis of the disease.

Jose *et al.* reviewed TS cases associated with solid organ transplant and emphasised that it appears during the first year after transplant with the highest level of immunosuppression.[2] The current patient developed TS within the first year following his renal transplant. He was diagnosed promptly with characteristic morphology, location of the eruption and histology features.

Managing TS is challenging. However, reduction of immunosuppression is the mainstay of treatment. This might not be always feasible given the risk of organ rejection or flare of the underlying disease. Next line of management is antiviral treatment including topical cidofovir 1–3% or oral valganciclovir.[2] Particularly, 3% topical cidofovir might be the most efficient.[1] Topical tazarotene and manual extraction were reported useful in single case reports.[13,14] Oral leflunomide was reported to dramatically improve the condition in two organ transplant patients.[15] Spontaneous regression has also been described but this took longer.[2]

Conclusion

TS is an emerging folliculocentric viral infection that occurs predominantly in immune-altered individuals. Since the rate of organ transplantation and relative immunosuppression are increasing globally, TS may become more prevalent. We present this case to increase awareness of this unique dermatosis to healthcare providers for early diagnosis and prompt treatment to prevent facial disfigurement. The current state of knowledge is still inadequate to explain many aspects of TS.

AUTHORS' CONTRIBUTION

AAK performed the literature review and primary manuscript construction. EM reviewed the case details and edited the manuscript. KN did a general review and edited the entire manuscript. KAW reviewed the histopathology slides, literature review on the pathology section and did a general review and grammatical editing of the manuscript. All authors approved the final version of the manuscript.

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