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Tree Man Syndrome

By George Qiao

Imagine a condition in which lesions that grow on your appendages are so severe that you cannot use your hands and feet properly. Moreover, these lesions are large and painful, and prevent you from being able to perform daily activities. Surgery, a common answer for this condition, can temporarily control the growths, but the lesions continue to grow back after each surgical operation. Currently, there is no cure, and the treatments only offer a temporary fix. Therefore, you are faced with a lifelong condition that severely limits your ability to live a normal life. Though there are many debilitating diseases, few of them are not given much attention. For example, one extremely rare disease is Epidermodysplasia verruciformis (EV), or tree man syndrome, characterized by bark-like warts growing on the body.[1] Although the exact number of cases of EV is uncertain, about 200 cases in the world have been reported thus far.[2]

Discovered in 1922, EV is an autosomal recessive disorder that increases one's susceptibility to the human papilloma virus (HPV) and is characterized by lesions that resemble wood. Furthermore, EV increases one's risk of developing skin cancer.[3] HPVs are non-enveloped, double-stranded DNA viruses responsible for many lesions and cancers, and are often sexually transmitted.[4] They infect the stratified epithelium of the epidermis, and do not lead to symptoms for most individuals, although some cases can involve development of warts. For infected individuals who show symptoms but are not suffering from EV, the warts are not as vast in number as those in patients with the mutations associated with EV.[5]

Researchers have generally attributed EV to mutations in the EVER1 and EVER2 genes, also called TMC6 and TMC8, respectively. These genes code for transmembrane proteins of keratinocytes, which are epidermal cells targeted by HPV. The proteins bind to and form a complex with a zinc transporter protein called zinc transporter 1 (ZnT-1). The EVER-ZnT complex transports zinc from the cytoplasm into the endoplasmic reticulum of the cell, directly decreasing the amount of zinc in the cytoplasm and indirectly decreasing the amount of zinc in the nucleus.[5,6] Zinc is an ion vital for the function of AP-1 transcription factors which promote expression of the HPV genome. The EVER-ZnT complex limits the activity of AP-1 transcription factors by decreasing the concentration of zinc in the nucleus, thereby limiting the ability of HPV to replicate.[7] A mutation in either of the genes EVER1 or EVER2 would prevent the proper functioning of the EVER-ZnT complex and allow the proliferation of HPV. With the mutation, HPV infection can lead to uncontrolled division of keratinocytes, resulting in bark-like warts, especially on the hands and feet.[1] Immunohistochemistry with antibodies specific for HPV can detect HPV infection in keratinocytes and is used to diagnose patients with EV.[2]

Several treatments exist to combat EV, although there still remains no cure. The condition can be treated with surgery, which can remove the growths. However, surgery only offers a temporary solution to the condition, as the warts often return after surgery. One man in Bangladesh suffering from EV underwent multiple surgical operations to remove his warts in 2016. Although the surgeries granted him the ability to use his hands and feet for a period of time, the warts returned. Since 2016, he has had 25 surgeries, and has not found a permanent solution to the condition.[8,9] Other treatments include cryotherapy, interferons, and

retinoids, all of which also offer temporary solutions to the problem.[9, 10]

Further research on EV should be conducted so that the scientific community can come closer to a cure for this debilitating disease. One path to take is to determine different possible causes of EV. Despite the experiments performed to determine the role of the EVER genes, it is not certain that a mutation in these genes is the sole cause of EV. In a particular study involving 41 EV patients, mutations in the EVER genes were present in 75 percent of the patients but absent in the remaining 25 percent, suggesting that there are other possible causes of EV.[6] Thus, more research should be conducted to identify alternative causes of the condition. If we can determine the different mechanisms of action of this disease, we can come closer to a cure by directly targeting those mechanisms. Hopefully, in the future, we can find a solution that can help end the suffering of those affected by the disease.

References

1. Uddin, K., Amin, R., Majumder, S. N., Aleem, M. A., Rahaman, A., Dity, N. J., Baqui, M., Akter, H., Rahman, M. M., Woodbury-Smith, M., Scherer, S., & Uddin, M. (2018). An *ANKRD26* nonsense somatic mutation in a female with epidermodysplasia verruciformis (Tree Man Syndrome). *Clinical case reports*, *6* (8), 1426–1430.

2. Epidermodysplasia verruciformis. (n.d.). Retrieved from https://rarediseases.info.nih.gov/diseases/6357/epidermodysplasia-verruciformis

3. de Jong, S. J., Imahorn, E., Itin, P., Uitto, J., Orth, G., Jouanguy, E., Casanova, J. L., & Burger, B. (2018). Epidermodysplasia Verruciformis: Inborn Errors of Immunity to Human Beta-Papillomaviruses. *Frontiers in microbiology*, *9*, 1222.

4. Wang, C. J., & Palefsky, J. M. (2015). Human Papillomavirus (HPV) Infections and the Importance of HPV Vaccination. *Current epidemiology reports*, *2*(2), 101–109.

5. Patel, T., Morrison, L. K., Rady, P., & Tyring, S. (2010). Epidermodysplasia verruciformis and susceptibility to HPV. *Disease markers*, *29*(3-4), 199–206.

6. Kalińska-Bienias, A., Kowalewski, C., & Majewski, S. (2016). The EVER genes - the genetic etiology of carcinogenesis in epidermodysplasia verruciformis and a possible role in non-epidermodysplasia verruciformis patients. *Postepy dermatologii i alergologii*, *33*(2), 75–80.

7. Lazarczyk, M., Pons, C., Mendoza, J. A., Cassonnet, P., Jacob, Y., & Favre, M. (2008). Regulation of cellular zinc balance as a potential mechanism of EVER-mediated protection against pathogenesis by cutaneous oncogenic human papillomaviruses. *The Journal of experimental medicine*, *205*(1), 35–42.

8. Pokharel, S., & Regan, H. (2019, January 21). Bangladesh's 'tree man' is back in hospital and needs more surgery. Retrieved from https://www.cnn.com/2019/01/21/health/tree-man-bangladesh-surgery-intl/index.html

9. (n.d.). Retrieved from https://abcnews.go.com/Health/tree-man-syndrome/story?id=60686709

10. Dash, M. (2018). Tree man Syndrome. *Madridge Journal of Internal and Emergency Medicine*, *2*(2), 78–79.

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