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Current Trends in the Management of Recurrent Respiratory Papillomatosis

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Editorial

Recurrent respiratory papillomatosis (RRP) has prevailed as an enigma to Otolaryngologists worldwide from time immemorial. It has been a nemesis to manage with no clear drug of choice or surgical procedure devised till date. RRP is characterized by human papilloma virus (HPV) induced exophytic papillomas in respiratory mucosa, extending along the airway anywhere from supraglottis onto the terminal bronchioles. This condition occurs more commonly in children, sometimes of juvenile onset and in adults to a lesser extent. Although it is benign, its virulent spread and aggressive recurrence deem it to be confronted like a malignant process [1].

The disease is known to be caused by HPV subtypes 6, 11, 16 and 18. Surgical excision of lesions to open up the obstructed airway and improve voice remains the gold standard for management [1]. In recent times, modality of surgery has shifted from cold instruments to the use of powered instruments like laser and microdebrider. Microdebrider is the best preferred tool today, due to its dual ability for fast debulking and suction simultaneously, without the potential risk of generating plumes as in laser which can disseminate viral prions onto the surgical team [2]. Overzealous removal of lesions especially those not interfering in airway passage or in voice impairment, result in excessive mucosal injury and over expression of HPV in diseased and surrounding cells, along with the morbid sequelae of laryngotracheal stenosis, which is even more difficult to handle in cases of RRP, wherein tracheostomy is best to be avoided [3].

Adjuvant therapy has come into vogue as a valuable tool to suppress the virulence of RRP along with the scope of developing immunity to the pathological virus strains over time. The current indications for adjuvant therapy are when there is need for more than four surgical procedures per year, rapid regrowth of papilloma with airway compromise or distal multi-site spread of disease and also for extra-respiratory lesions occurring in the oral cavity and esophagus [4]. This adjuvant therapy most commonly includes Cidofovir (Antiviral), HPV vaccine (Gardasil), Bevacizumab/ Avastin (Monoclonal Antibody), Interferon Alpha (Immunomodulator) and Photodynamic therapy but none have achieved universal acceptance [2-5].

Interferons are proteins released from leukocytes in response to viral infection which help to activate immune cells and down regulate antigen production. Today recombinant pegylated - IFN - alpha - 2a (peg - IFN - alpha - 2a / shanferon) has replaced the earlier available IFN - alpha which had more side-effects [6]. Shanferon is being used in the tapering dosage of once a week for 4 weeks initially, followed by one injection per 2 weeks for 2 months, then as one injection per month for next 4 months while sequential assessment of airway is done with fibreoptic tracheo-bronchoscopy.

The quadrivalent HPV vaccine Gardasil, given intramuscularly at 0, 1 and 6 months has activity against both low - risk HPV types 6 and 11 and high - risk HPV types 16 and 18. Studies have shown that quadrivalent vaccination in RRP patients with HPV DNA - positivity, increased anti - HPV antibodies thereby reducing the recurrence rates. By combining viral capsid proteins with adjuvants such as aluminium, a much higher antibody titre could be achieved after vaccination than with a natural infection. Thereby, HPV vaccination in the general population can provide better immunity against development of disease and it has now been incorporated into the national vaccination programme for both girls and boys in the UK and USA.

Current trends indicate that wide - spread vaccination of pre - adolescent females will also markedly decrease HPV genital wart acquisition and will further reduce the incidence of secondary laryngeal infections via vertical HPV transmission. This shall lead to reduction in overall RRP incidence in the near future [7]. The Centre for Disease Control and Prevention (CDC) at Atlanta, USA recommends the novel nonavalent vaccine - Gardasil - 9 covering a wider range of HPV variants. The restricted availability and expense of such adjuvant therapies, currently limit their clinical utility especially among the developing and under-developed countries. Therefore there is no universal recommendation advocated for the management of RRP till date [2- 8].

A combination of medical and surgical tools need to be well equipped in the armamentorium of the ENT surgeons who are actively engaged in the battle against this challenging entity. While the principle of surgery is to maintain the airway and voice, medical therapy focuses on reducing the viral load, boosting host immunity and reducing the recurrence rates over time. Hope prevails in the horizon as current research focuses on advanced molecular genetic manipulation, nano-particle technology and stem cell therapy in order to find a miracle cure for this elusive sinister viral disease.

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