Information/ Background

We present a rare case of Herpes Simplex Virus (HSV) laryngitis resistant to standard antiviral treatment in an immunocompromised patient individual with HyperIgM Syndrome. He presented with progressive laryngeal papillomatous disease (voice and airway symptoms) requiring unplanned tracheostomy. Histopathology was consistent with Herpes. Disease progression occurred despite acyclovir therapy and ultimately tracheostomy was required. The patient was treated with foscarnet with good clinical response and was successfully decannulated.

Case Report

A 44 year old man with a background of primary immunodeficiency of HyperIgM Syndrome presented with hoarseness/dyspnea on a background of previous treatment for recurrent respiratory papillomatosis (RRP). Flexible laryngoscopy revealed bilateral vocal fold thickening and inflammation with interarytenoid involvement and a narrowed glottic airway. Intraop findings were papillomatous, proliferative lesions localized to the larynx with interarytenoid scar tissue which was resected. Biopsies sent for histopathology and tissue culture returned as ulcerated, inflamed mucosa with papilliform squamous hyperplasia. Cells at the margins of the ulcer displayed marked viral cytopathic effect consistent with a herpetic infection. Immunohistochemical staining using polyclonal antisera to Herpes Simplex Virus types I and II demonstrated strong nuclear and cytoplasmic immunoreactivity within a subset of epithelial cells. He was commenced on IV acyclovir then oral valacyclovir but his symptoms progressed over time.

Repeat microlaryngoscopy was performed with a view for debulking his RRP and further specimens were sent for histology and culture. Increased disease bulk with extension of inflammation into the trachea and a 4mm airway was identified. With inability to establish a safe airway endoscopically - unplanned tracheostomy was performed. This time, his specimens returned as positive for HSV I and II but negative for neoplasia and papillomatosis.

The patient was treated with IV acyclovir for one week with minimal improvement of laryngeal findings, raising the suspicion of resistant HSV. He was then switched to IV foscarnet. He received 3 weeks of induction IV foscarnet at 6mg twice a day, followed by another 2 weeks of maintenance foscarnet at 6mg daily. Follow up laryngoscopy 2 weeks after the new treatment commenced revealed a dramatically improved larynx with resolution of exudative tissue. The patient also reported a marked improvement in voice and breathing and he was decannulated successfully. Voice and airway were within normal limits at clinic visit 6 weeks later.

Discussion

15 cases of HSV laryngitis have been reported in the literature. The clinical presentation and duration of symptoms for patients is highly variable. The most common presenting symptom is dysphonia (present in 70%), followed by odynophagia, dyspnea and lastly, stridor. Typical oropharyngeal ulcerative lesions may not be a prominent feature. Findings on direct nasoendoscopy may reveal granular mucosal changes, exudative lesions or marked edema. In the majority of most cases, HSV infection was confirmed by biopsy and immunohistochemical staining. A consistent theme in our literature review is the variable presentation and appearance of this disease. This can lead to unnecessary airway manipulation and a delay in diagnosis. For this reason, we advocate early diagnostic biopsy of unusual or poorly responsive laryngeal lesions.

All cases reported in the literature showed significant improvement with standard antiviral treatment (acyclovir). But this was not the case in our patient, who exhibited resistance to standard acyclovir treatment and required IV foscarnet therapy. Hence, acyclovir resistant HSV laryngitis should be considered in immunocompromised patients if there is failure of response to acyclovir.

Conclusion

This case illustrates the importance of keeping HSV laryngitis on the list of differentials when patients present with unusual ulcerative, proliferative or polypoid laryngeal lesions which may mimic a malignancy. An early diagnostic microlaryngoscopy with tissue for culture and histopathology is crucial for proper treatment to be implemented. Failure of response to standard antiviral treatment should raise the consideration of acyclovir resistant HSV. This is especially so in immunocompromised patients who may have a variable presentation and response to treatment.