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Erlotinib Therapy For Recurrent Respiratory Paillomatosis And Extralaryngeal Spread In Pediatrics

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ERLOTINIB THERAPY FOR RECURRENT RESPIRATORY PAILLOMATOSIS AND EXTRALARYNGEAL SPREAD IN PEDIATRICS

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Background

Recurrent respiratory papillomatosis (RRP) can be a potentially life-threatening condition and a treatment challenge. There is currently no cure for this disease, and treatment is primarily concerned with control of lesions with local surgical therapies. Surgical interventions are associated with significant scarring and detrimental effects on patient voice and respiratory status.

More attention is being placed on finding alternative therapies to decrease the need for frequent surgeries. Epidermal growth factor receptors (EGFR) have increased expression in respiratory papillomas making them a potential pharmacologic target. EGFR inhibitors have been reported to be an effective adjunctive therapy in patients with RRP

Objectives

•To report our institutional experience with **Erlotinib**, an EGFR inhibitor, in two pediatric patients with severe RRP.

Methods

• Retrospective chart review of 2 pediatric patients with severe RRP

Results

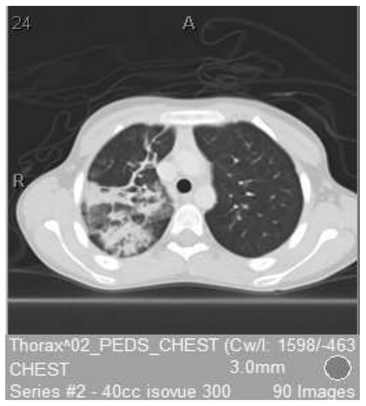
•**Patient 1** is a 19y/o F referred to us at age 11.Diagnosed with RRP at birth. Since age 1.5yrs, underwent micro-laryngoscopy, bronchoscopy with laser or surgical excision of the lesions, on a 1-2 monthly basis.

•**O/E** no skin lesions. Her voice was only a whisper. No difficulty breathing or stridor. Pre-pubertal. Endoscopic exam 3 weeks prior to starting therapy showed severely scarred larynx, no obvious laryngeal disease, diffuse subglottic and tracheal papillomatosis with extension into the left main bronchus. **Biopsy of the lesion showed squamous papilloma, EGFR positive.**

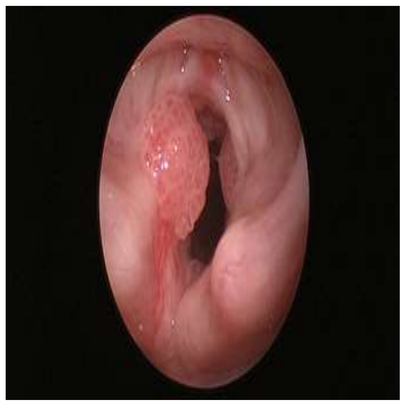
Patient 2 is 14y/o M referred to us at age 12. Diagnosed at 5 months with RP of the larynx. Underwent micro-laryngoscopy, bronchoscopy with laser or surgical excision of the lesions, on a 1-2 monthly basis. He developed respiratory distress post laryngoscopy and found to have 3 pulmonary lesions confirmed as papillomatosis post thoracotomy with wedge resections.

•Both patients were started on an EGFR inhibitor, Erlotinib at a dose of 85mg/m2 daily and DIM (diindolylmethane) 150mg twice daily. The skin care regimen included regular moisturizers and sunscreen; topical steroids and antibiotics as needed. Therapy was well tolerated except for grade 1 skin rash in both patients and grade 1 diarrhea as well, in Patient 1.

•For patient 1, within a month of therapy there was significant decrease in the lesions and by 6mo complete resolution of papillomatosis. She had 15mo of therapy. She is in remission 6 years off therapy. For patient 2, there has been decrease in lesions and the interval between laryngoscopy since start of therapy. CTs of chest confirm no recurrence of pulmonary lesions since starting Erlotinib.



Patient 2: CT chest



Patient 2: Respiratory papilloma on laryngoscope

Discussion

In our two patient cohort, a regimen of erlotinib and DIM resulted in decreased disease burden and an increase in intervals for required MLB and surgical excisions. In both patients studied. Both patients tolerated this therapy regimen well with minimal dermatologic and gastrointestinal side effects. Of note, it is interesting that patient 2 had an EGFR negative biopsy sample while having positive outcomes on treatment. The sample in question was from a metastatic site other than the primary laryngeal site. Positive results could be for a number of reasons including primary site expression of EGFR or unknown down-stream effects of erlotinib as described by Ishii et al in EGFR negative non small cell lung cancer.[3] Our sample size described was small and a larger population is needed to study this treatment regimen against a control to better understand the possible potential benefits versus surgical excision as monotherapy.

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