Abstract _

PERIANAL CROHN'S DISEASE IN A LARGE MULTICENTER PEDIATRIC COLLABORATIVE

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Background: Perianal fistulas are a common complication of Crohn's disease (CD). The epidemiology of perianal CD among children is virtually unknown. The objective of this study was to characterize the prevalence of perianal CD using in a large population of pediatric CD patients. **Methods:** We used the ImproveCareNow (ICN) Network registry of prospectively collected visit-level data to identify CD patients (May 2006-October 2014). ICN is a multicenter (65 sites) pediatric inflammatory bowel disease (IBD) quality improvement collaborative. Clinicians prospectively document physical examination and phenotype classification at each outpatient IBD visit. Perianal exam findings and concomitant phenotype change were used to corroborate time of new-onset perianal disease. Period prevalence of perianal disease was determined by first occurrence of perianal findings and was stratified by age, gender and race and was compared across groups (chi square). Cumulative risk of perianal disease was estimated using Kaplan-Meier survival analysis and compared between groups with Cox proportional hazard regression models. **Results:** The ICN registry included a total of 10,969 IBD patients (44% female); 7,076 (65%) were classified as having CD; 397 (6%) could not be classified due to missing/conflicting entries and were excluded. Among the remaining CD cases (n=6,679) 1,399 (21%) developed perianal disease. Perianal disease was more common among males (22% vs. 20%; p=0.017). Perianal disease was also more common among African Americans (26%) and Asians (24%) compared to Whites (20%; p=0.029). Asians and African Americans also developed perianal disease earlier in their disease course than Whites (Figure 1; p=0.004).

Conclusions: In this large multicenter collaborative, we found that perianal disease is common among children with CD. Differences in the development of perianal disease were found across race groups. Treatment strategies are needed to prevent fistula development. In addition, racial disparities should be characterized to better understand and develop effective mitigation strategies.

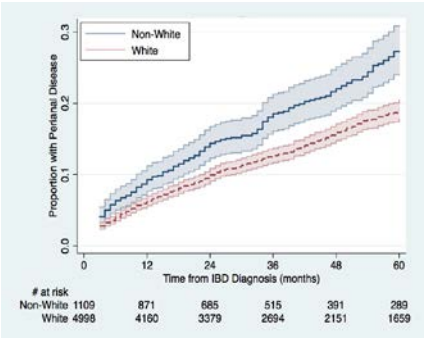

Figure 1.

Abstract _

TARGETING CLINICALLY INTEGRATED SEQUENCING RESULTS IN PEDIATRIC HIGH-GRADE GLIOMA

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Background: Pediatric high-grade glioma (WHO Grade III and IV) is a devastating brain tumor with a median survival of less than two years. Novel therapies based on the distinct biology of pediatric high-grade glioma (HGG) are urgently needed. Here, we describe a strategy for validating targets identified from clinical integrated sequencing using a newly established pediatric HGG primary cell culture with *PDGFRA*/*FGF2* amplification as a representative example.
Methods: Paired whole exome sequencing of tumor and germline DNA and tumor transcriptome sequencing was performed on a pediatric thalamic HGG sample through Pediatric MI-ONCOSEQ Study. Primary cell culture was created by harvesting tumor cells at the time of tumor resection. Additionally, data was integrated from multiple human datasets and sequencing platforms to analyze the impact of PDGFR pathway amplifications and mutations on survival in one of the largest ever surveys of pediatric high-grade glioma patients (n=293).
Results: Integrative clinical sequencing of patient tumor sample revealed somatic tumor gene amplifications and outlier increased expression of *PDGFRA* and *FGF2*. Based on these amplifications, cells were treated with tyrosine kinase inhibitors known to target PDGFR and FGF signaling. Dasatinib inhibited proliferation most effectively, which was specific to this primary HGG cell culture. Integration of multiple human datasets shows that *PDGFRA* amplification, but not mutation, is associated with decreased survival in pediatric high-grade glioma patients ($P = 0.0026$).
Conclusion: We present a method for *in vitro* validation of molecular targets in pediatric high-grade glioma to provide personalized pre-clinical data which can be immediately implemented in the clinic. This approach could provide alternative treatment strategies for children bearing malignant brain tumors. We are now developing a pilot trial to treat pediatric patients with HGG with the addition of promising personalized targets using this method.