Epistaxis Severity Score in Pediatric Patients with Hereditary Hemorrhagic Telangiectasia

Matthew G Petersen, BS[1]; Cristian D Gonzalez, BS, BA[1]; Jamie C McDonald, MS[2,3]; David A Stevenson, MD[4]; Kevin J Whitehead, MD[5]; Angela Presson, PhD[6]; Qian Ding, BS[6]; Kevin F Wilson, MD[7]

[1]University of Utah School of Medicine, [2]Department of Pathology, University of Utah, [3]Department of Radiology, University of Utah, [4]Department of Pediatrics, Division of Medical Genetics, Stanford University, [5]Division of Cardiovascular Medicine, Pediatric Cardiology, University of Utah, [6]Division of Epidemiology, University of Utah, [7]Division of Otolaryngology, University of Utah

Abstract

Epistaxis is one of the hallmark features of Hereditary Hemorrhagic Telangiectasia (HHT). Epistaxis severity in pediatric patients with HHT has not been well described. This study evaluates the relationship between epistaxis severity, gender, age and genotype in pediatric patients with HHT.

Statistical analyses were conducted on 69 subjects grouped according to identified HHT proband: ACVRL1, ENG, and SMAD4. Median Epistaxis Severity Score (ESS) was higher among ENG group vs ACVRL1 group. Age of epistaxis onset was also earlier in the ENG cohort when compared to the ACVRL1 cohort. No statistical significance was seen in regards to age or gender.

Introduction

Hereditary Hemorrhagic Telangiectasia (HHT) is an autosomal dominant disorder of vascular malformation causing multiple telangiectasia and arteriovenous malformations (AVMs). While potentially fatal AVMs can occur in cerebral, hepatic and pulmonary circulation, they are most often clinically heralded by epistaxis in pediatric patients[1].

HHT demonstrates an age-dependent penetrance with progression of symptoms occurring over a lifetime. Recurrent, spontaneous epistaxis has been reported in 63%-66%[2,3,4] of pediatric HHT patients and up to 96%[5] of adult HHT patients. Epistaxis had median age of onset at 12 years old[6,7]. In a study that evaluated symptomatic children with HHT, all subjects presented with epistaxis during their follow-up visit[8].

There has been increasing interest in the prevalence and character of HHT vascular malformations; however, understanding of epistaxis as a marker of disease severity in pediatric patients is lacking. Additionally, there is a paucity of genotype-phenotype data in children and adolescents with HHT. This study aims to address the following: 1) to describe epistaxis severity based on genetic proband, age and gender; 2) grade epistaxis severity; 3) to elucidate patterns of epistaxis in pediatric patients with HHT.

Methods and Materials

A retrospective chart review of all pediatric patients (0-18 years old) with clinically suspected HHT at a multidisciplinary HHT clinic from January 2010 to April 2016 was performed. The cohort consisted mostly of children from the Mountain West (Utah, Wyoming, Montana, Idaho, Nevada) who were referred to the University of Utah HHT Clinic in Salt lake City, UT for suspected or known HHT.

For each patient, demographic information, clinical presentation, a molecular diagnosis, age of epistaxis onset and Epistaxis Severity Score[9] were recorded. ESS was administered in clinic using a 3-month recall survey. Statistical analyses were conducted for groups of patients according to HHT proband: ACVRL1, ENG, and SMAD4. Statistical analyses were performed with SAS 9.4 (SAS Institute Inc.) All p-values were 2-sided and were evaluated at a 0.05 significance level.

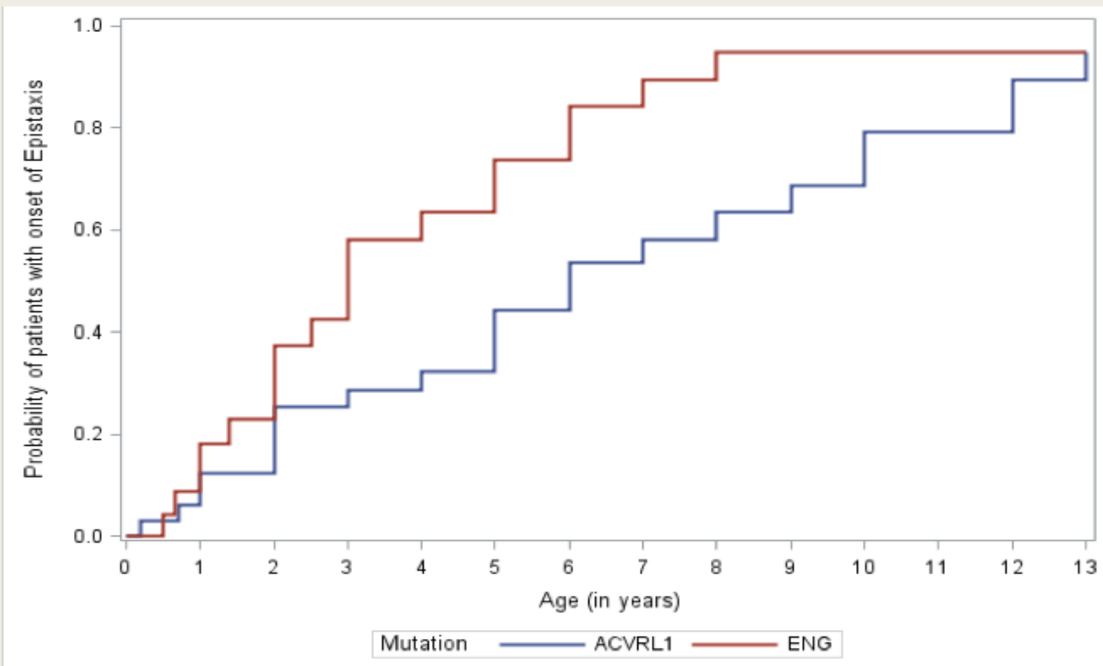


Chart 1. Age of Onset in Pediatric HHT Patients: Stratification by Mutation (ACVRL1 vs ENG)

Results

Sixty-nine subjects were identified; 60 had HHT confirmed by genetic testing, 9 met clinical diagnostic criteria. Median ESS was higher among the ENG group versus ACVRL group (2.3 years vs 1.1 years, p=0.003).

Age of epistaxis onset was earlier in ENG cohort compared to their counterparts in the ACVRL1 cohort (3.0 years versus 6.0 years; p=0.041). There were no statistically significant differences in ESS when patients were stratified by age or sex. Of the 69 subjects, three sought interventions to control epistaxis while anemia was noted in only two patients.

Figure 1. Epistaxis Frequency by Proband

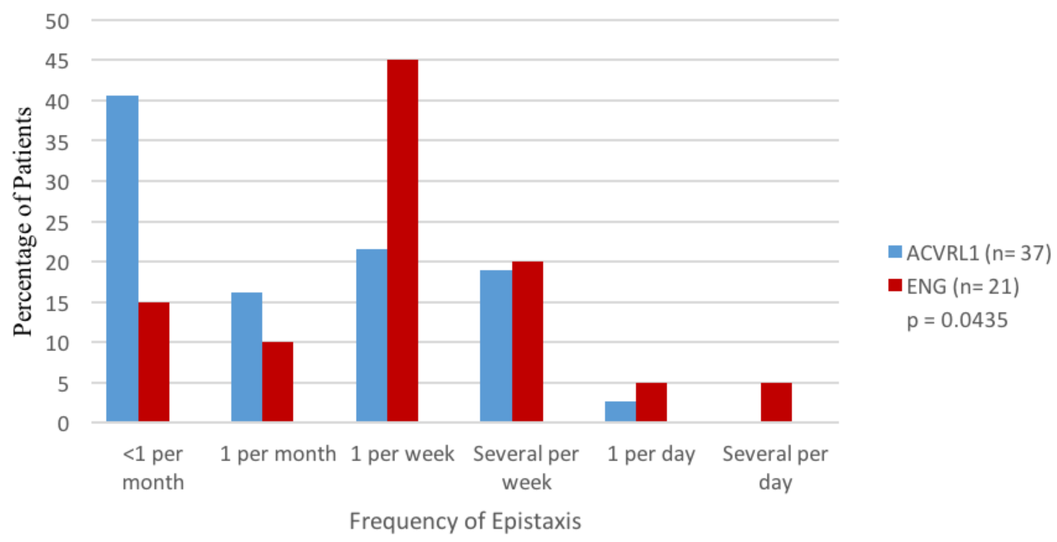
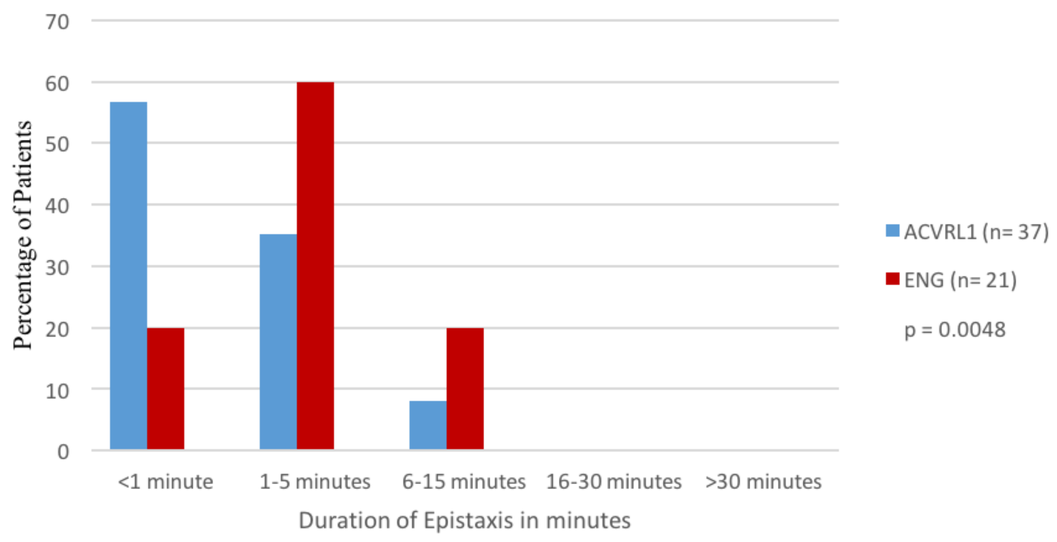


Figure 2. Epistaxis Duration by Proband



Discussion

Epistaxis presents early in HHT and patients with the ENG proband tend to present with more severe epistaxis than those with ACVRL1 proband. Our cohort contained only two patients with a SMAD4 proband, this cohort was dropped from further analysis.

While statistically significant differences existed between cohorts with different probands, no such difference in presentation exists between male and female patients nor children and adolescent patients.

It should be noted that of those patients with ACVRL or ENG probands who presented with nosebleeds, the average age of presentation was 5 years. This is, on average, much younger than has been found in previous literature.

Conclusions

Epistaxis may present early in HHT. Severity in the pediatric population appears to be worse in patients with the ENG proband. Generally, epistaxis associated with HHT presents mildly in pediatric patients and can be easily missed in the community setting.

By understanding and recognizing the clinical presentation of epistaxis in pediatric patients with HHT, community providers can assist in the early detection of such patients and refer them to specialty care.

Contact

Matthew G Petersen
University of Utah School of Medicine
Email: matthew.petersen@hsc.utah.edu
Phone: (801) 898-8307

References

1. Sekarski LA, Spangenberg LA. Hereditary hemorrhagic telangiectasia: children need screening too. *Pediatr Nurs.* 2011 Jul-Aug;37(4):163-8
2. Folz BJ, Zoll B, Alfke H, Toussaint A, Maier RF, Werner JA. Manifestations of Hereditary Hemorrhagic Telangiectasia in Children and Adolescents. *Eur Arch Otohinolaryngol.* 2006 Jan;263(1):53-61
3. Giordano P, Lenato GM, et al. Hereditary hemorrhagic telangiectasia: arteriovenous malformations in children. *J Pediatr.* 2013 Jul:163(1):179-86.e1-3
4. GiordanoP, Nigro A, Del Vecchio GC, Sabba C, De Mattia D. HHT in Childhood: Screening for Special Patients. *Curr Pharm Des.* 2006;12(10):122-5.
5. Plauchu H, de Chadarevian JP, Bideau A, Robert JM. Age-related Clinical Profile of Hereditary Hemorrhagic Telangiectasia in a Epidemiology Recruited Population. *Am J Med Genet.* 1989 Mar;32(3):291-7.
6. Faughnan ME, Palda VA, et al. International Guidelines for the Diagnosis and Management of Hereditary Haemorrhagic Telangiectasia. *J Med Genet.* 2011 Feb;48(2):73-87.
7. McDonald J, Bayrak-Toydemir P, Pyeritz RE. Hereditary Hemorrhagic Telangiectasia: An Overview of Diagnosis, Management and Pathogenesis. *Genet Med*. 2011 Jul;12(7):607-16.
8. Mei-Zahav M, Letarte M, Faughnan ME, Abdalla SA, Cymerman U, MacLusky IB. Symptomatic Children with Hereditary Hemorrhagic Telangiectasia: A Pediatric Center Experience. *Arch Pediatr Adolesc Med.* 2006 Jun;160(6):596-601.
9. Hoag JB, Terry P, Mitchell S, Reh D, Merlo CA. An Epistaxis Severity Score for Hereditary Hemorrhagic Telangiectasia. *Laryngoscope.* 2010 Apr; 120(4):838-43.