Bleeding risks associated with tonsillectomy in patients with Ehlers-Danlos syndrome

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INTRODUCTION

Ehlers-Danlos syndrome (EDS) is an inherited collagen disorder that, based on the subtype, comes with varying risks of life-threatening hemorrhage. The risk of post-operative adenotonsillectomy (T&A)/tonsillectomy hemorrhage should be scrutinized in patients with EDS. Better risk assessment will aid in medical optimization before surgery, counseling families of surgical risks, and may decrease admission costs in lower-risk EDS patients.

BACKGROUND

https://www.compleowaco.com/ehlers-danlos-syndrome/

- EDS is characterized by joint hypermobility, skin hyperextensibility, easy bruising, and abnormal scarring(1).
- Caused by a COL5A1, COL5A2 mutation, or COL1A1 mutation in the arthrochalasia type, or COL3A1 mutation in the in vascular specific subtype. These affect type V collagen production leading to decreased tissue tensile strength(2).
- Sources of bleeding in EDS include GI bleeding, menorrhagia, intracranial hemorrhage, aneurism ruptures, and aortic dissection secondary to aortic root dilation(3).
- Von Willebrand (VWb) factor binds to type V collagen to induce clotting; hence, EDS patients may experience increased bleeding similar to VWb disorder, due to the inability of normal VWb factor to bind to abnormal collagen binding sites(4).
- There is a paucity of data on post-op bleeding complication rates for EDS patients during routine surgical procedures, such as T&A.
- Assessing the risk of bleeding in EDS patients following T&A can lead to informed decision-making around admitting this patient population following any surgical procedure, which could save families unnecessary costs(5).

HYPOTHESIS

Children with EDS experience increased rates of post adenotonsillectomy bleeding when compared to children who have no increased post-operative T&A hemorrhage risk factors

METHODOLOGY

- A retrospective chart review/case-control study was completed on all children receiving a T&A with a diagnosis of EDS and a random selection of over 25,000 patients without a diagnosis of EDS who received a T&A in the past 10 years at Children's Hospital of Colorado.
- Controls were excluded if they had a bleeding disorder or warranted admission after T&A based on the 2019 ENT clinical practice guidelines criteria(5).

METHODOLOGY

- Children undergoing a T&A for a diagnosis of periodic fever, aphthous stomatitis, pharyngitis and adenitis syndrome were also excluded.
- Bleeding risk in children with EDS was assessed by EDS subtype, prior echocardiograms, electrocardiograms, and laboratory data.

RESULTS

Variables	Ehlers-Danlos syndrome		Control		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	9.02	5.5	7.29	4.6	8.076	5.070	0.051
BMI	17.9	4.7	20.5	7.8	19.3	6.6	0.035*
BMI Percentile	46.4	36	57.5	39	54.4	37.9	0.106
AHI	5.2	5.2	20.3	26.5	14.9	22.4	0.061
Nadir in sleep study	80.30%	7.10%	82.60%	7.70%	81.00%	7.40%	42.40%
LOS after post-op bleed	1.56	1.1	1.17	0.983	1.4	1.1	0.505
POD bleed	6	4.7	8	4	6.7	4.4	0.392
PT level	13.8	0.8	13.2	1.1	13.8	0.9	0.364
PTT level	34	6.4	32.4	3.5	33.7	6.4	0.755
INR level	1.1	0.1	1	0.1	1.1	0.1	0.304
Factor V assay level	78.1	27.6	0	0	73.8	24.6	0.719
Hemoglobin level	13.4	1.6	13.2	1	133	1.5	0.779
Hematocrit level	40	38.4	38.4	3.1	40	4.7	0.431
Platelet level	310	87.5	360.6	83.7	319.7	87.9	0.178

Variables	Ehlers-Danlos syndrome (n=60)		Control (n=72)		All Patients (n=132)		p-value
	Total (n)	Prop (%)	Total (n)	Prop (%)	Total (n)	Prop (%)	
EDS subtype:							
Gravis (1)	1	2.10%	-	-	-	-	-
Mitis (2)	1	2.10%	-	-	-	-	-
Hypermobile (3)	42	89.40%	-	-	-	-	-
Vascular (4)	2	4.30%	-	-	-	-	-
Unknown	1	2.10%	-	-	-	-	-
Sex:							
Male	19	31.70%	35	48.60%	56	57.60%	
Female	41	68.30%	37	51.40%	76	42.40%	.033*
Race:							
White	56	93.30%	53	73.60%	109	82.60%	
Black	4	6.70%	4	6.90%	9	1.50%	
Asian/AP	0	0%	2	2.80%	2	0.80%	
NA/AN	0	0%	1	1.40%	1	8.30%	
Other	0	0%	11	15.30%	11	6.90%	0.010**
Ethnicity:							
Non-Hispanic	54	90%	45	62.50%	99	75%	
Hispanic	6	10%	27	37.50%	33	25%	<0.001*
Adenotonsillar hypertrophy	45	75%	57	79.20%	102	77.30%	0.677
Halitosis	22	36.70%	23	31.90%	45	34.10%	0.585
Chronic Tonsilitis	27	45%	24	33.30%	51	38.60%	0.21
History of >/= PTA	1	1.70%	2	2.80%	3	2.30%	1
PFAPA diagnosis	2	3.40%	0	0%	2	1.50%	0.201
Sleep disordered breathing	44	73.30%	58	80.6	102	77.30%	0.405
Sleepy study performed	18	30%	24	33.30%	42	31.80%	0.711
OSA diagnosis	16	26.70%	23	32.40%	39	29.80%	0.566
OSA severity:							
Mild	6	40%	5	23.80%	11	30.60%	
Moderate	4	26.70%	7	33.30%	11	30.60%	
Severe	5	33.30%	9	42.90%	14	38.90%	0.582
Echo performed	34	56.70%	7	9.70%	41	31.10%	<0.001*
Abnormal echo results	4	11.40%	3	25.00%	7	14.90%	0.35
Aortic root dilation	1	2.90%	0	0%	1	2.40%	1
ECG performed	39	65%	9	12.50%	48	36.40%	<0.001*
Abnormal ECG	5	12.80%	3	30%	8	16.30%	0.33
Hx of bleeding problems	17	28.30%	1	1.40%	18	13.6	<0.001*
Bleeding disorder/Anticoagulation use	9	15%	0	0%	9	6.80%	<0.001*
Family history of bleeding	9	15%	2	2.80%	11	8.30%	0.023*
EBL >5cc	18	30%	19	26.40%	37	28%	0.699

RESULTS

Variables	Ehlers-Danlos syndrome (n=60)		Control (n=72)		All Patients (n=132)		p-value
Post T&A admission	31	51.70%	40	55.60%	71	53.80%	0.727
PT high level	0	0%	0	0%	0%	0	1
PTT high level	3	27.30%	0	0%	3	23.10%	1
INR high level	3	25%	0	0%	3	21.40%	1
Abnormal factor V	4	50%	0	0%	4	44.40%	1
Fibrinogen high level	0	40%	0	0%	2	40%	-
EPI - platelet aggregation abnormalities	0	-	0	-	-	100%	-
Von Willebrand abnormal level	0	-	0	-	-		
Low hematocrit post T&A	12	37.50%	1	14.30%	13	33.30%	0.388*
Low hemoglobin post T&A	3	9.40%	0	0%	3	2.60%	0.614
Low platelets post T&A	1	2.90%	0	0%	1	2.40%	1
Post T&A hemorrhage	11	18.30%	8	8.30%	17	12.90%	0.118
ED observation after hemorrhage	3	27.30%	0	0%	3	17.60%	0.515
Admission after hemorrhage	7	63.60%	5	83.30%	12	70.60%	0.6
OR for post T&A bleed control	4	36.40%	4	66.70%	8	41.10%	0.355
TXA use	1	11.10%	0	0%	1	7.10%	1
Amicar use**	2	28.60%	0	0%	2	16.70%	0.47
DDAVP use	2	22.20%	0	0%	2	14.30%	0.505
Hematology consulted	3	33.30%	0	0%	3	21.4%	0.258
Vitamin C use	1	11.10%	0	0%	1	7.10%	1
Factor replacement***	1	10%	0	0%	1	6.70%	1
Transfusion needed	0	0%	0	0%	0	0%	-

* P-value <0.05

** noted that these patients were pre-emptively given amicar prior to T&A to use post operation to prevent a bleed.

*** patient with factor replacement use had vWB disease

- Of 62 patients with EDS and 72 controls, those with EDS were more likely to be female (p=0.033), younger (p=0.051), and non-Hispanic white (p<0.001, p=0.01).
- Post-operative hemorrhage rates were unaffected by post-operative admission in both controls and EDS patients (p=0.609).
- EDS patients had no differences in blood loss during the T&A (p=0.669) and no significant risk of a post-operative hemorrhage (p=0.118).
- Isolated bleeding disorders did not increase postoperative hemorrhage (p=0.092); however, EDS patients had more comorbid bleeding disorders (p<0.001).
- When controlling the differences in the exposure and control population, there was no difference in bleeding risk.

DISCUSSION

- Patients with EDS showed no significant increase in the risk of a post-tonsillectomy hemorrhage when compared to children without EDS.
- The combination of EDS, prior hemorrhage events, and comorbid bleeding disorders may elevate the risk of post-tonsillectomy hemorrhage.
- Pre-operative optimization should be taken on a case-by-case basis.
  - If low risk pre-operatively, patients with EDS may not pose a significant risk of hemorrhage.

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