

Introduction

Chiari malformation type I (CM-I) is an anatomical abnormality characterized by the inferior displacement of cerebellar tonsils through the foramen magnum into the upper cervical spine.^{1,2} Symptoms include headache, neck pain, dizziness, diplopia, swallowing difficulty, and unsteady gait. The surgical treatment consists of posterior fossa decompression, with or without duraplasty and C1 laminectomy. Connective tissue disorder is associated with increased risk of poor wound healing, progressive scoliosis, and other delayed complications. However, published data about the prevalence of connective tissue disorders in familial chiari malformation remains limited.

Aims and Objectives

1) To determine the prevalence of connective tissue disorders in familial CM-I

To determine the prevalence of other comorbidities in familial CM-I

Methods

- An Institutional Review Board (IRB) was obtained prior to the start of the study
- **Inclusion criteria:**
 - Individuals of all ages diagnosed with CM-I between January 2012 and December 2022
 - Individuals who have been under the care of the senior author between January 2012 and December 2022 at Michigan Head and Spine Institute (MHSI)
- Eligible participants were recruited via email.
- Eligible participants were asked to complete an online survey, composed of 10 questions.
- For eligible participants aged 17 years or older, a parent or legal guardian was asked to complete the survey
- Data variables were assessed using the Chi-square test.

Results

382 participants (54 males, 382 females) completed the survey (response rate = 42.9%). Due to some incomplete responses, 354 responses were analyzed. Data was divided into two groups. Compared to families with only one person affected, families with two or more people with CM-I were more likely to have a history of joint replacements (39.5% vs. 59.1%, p=0.0162), joint dislocations (15.2% vs 51.3%, p<0.0001), easy bruising (52.2% vs 75.3%, p=0.0038), and connective tissue disorders (15.2% vs 41.2%, p=0.0004).(Table 1). They were also more likely to have a history of carotid dissection, brain or aortic aneurysm. However, these findings were not statistically significant. (Table 1)

Ehlers-Danlos syndrome (EDS) was the most prevalent diagnosed connective tissue disorder in both groups (42.8% vs 67.7%).

The prevalence of comorbidities was higher in familial CM-I (76 vs 4 for POTS, 54 vs 9 for tethered spinal cord, and 29 vs 0 for mast cells activation disorder). (Table 2)

Table 1: Participants' responses to the health-related questionnaire.				
	Family history of two or more people with chiari malformation type I?			
	No (N=46)	Yes (N=308)	Total (N=354)	P-value
Family history of brain aneurysm or aneurysm rupture, n (%)				
0.2310 ¹				
No	39 (88.6%)	198 (81.1%)	237 (82.3%)	
Yes	5 (11.4%)	46 (18.9%)	51 (17.7%)	
Unknown	2	64	66	
Family history of aortic aneurysm or aneurysm rupture, n (%)				
0.3454 ¹				
No	39 (90.7%)	197 (85.3%)	236 (86.1%)	
Yes	4 (9.3%)	34 (14.7%)	38 (13.9%)	
Unknown	3	77	80	
Family history of carotid dissection, n (%)				
0.1676 ¹				
No	38 (100.0%)	198 (95.2%)	236 (95.9%)	
Yes	0 (0.0%)	10 (4.8%)	10 (4.1%)	
Unknown	8	100	108	
Family history of joint replacement or other surgery, n (%)				
0.0162 ¹				
No	26 (60.5%)	110 (40.9%)	136 (49.6%)	
Yes	17 (39.5%)	159 (59.1%)	176 (56.6%)	
Unknown	3	39	42	
Family history of frequent joint dislocation or injuries, n (%)				
<.0001 ¹				
No	35 (76.1%)	112 (36.4%)	147 (41.5%)	
Yes	7 (15.2%)	158 (51.3%)	165 (46.6%)	
Unknown	4 (8.7%)	38 (12.3%)	42 (11.9%)	
Family history of easy bruising, n (%)				
0.0038 ¹				
No	18 (39.1%)	58 (18.8%)	76 (21.5%)	
Yes	24 (52.2%)	232 (75.3%)	256 (72.3%)	
Unknown	4 (8.7%)	18 (5.8%)	22 (6.2%)	
Family history of connective tissue disorder, n (%)				
0.0004 ¹				
No	30 (65.2%)	111 (36.0%)	141 (39.8%)	
Yes	7 (15.2%)	127 (41.2%)	134 (37.9%)	
Unknown	9 (19.6%)	70 (22.7%)	79 (22.3%)	

¹Chi-Square p-value

Table 2: Proportion of participants with comorbidities			
	Does anyone in the family have scoliosis or chiari malformation?		
	NO (N=46)	YES (N=308)	Total (N=354)
Do you have any of the following comorbidities? (n)			
Postural orthostatic tachycardia syndrome (POTS),	6	74	80
Mast cells activation disorder	0	29	29
Tethered spinal cord	9	54	63

Conclusions

Previous studies have shown that Chiari patients with co-morbidities have a higher risk of treatment failure. Our data suggests that connective tissue disorder may be ubiquitous in patients with familial CM-1. Pre-operative identification of connective tissue disorders and other comorbidities in CM-I patients may help contribute to strategies to help mitigate this risk

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