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The Filum Disease and the Neuro-Cranio-Vertebral Syndrome: Definition, Clinical Picture and Imaging Features

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BACKGROUND

This study summarizes and culminates the endeavors of various researchers who have been pursuing so far three convergent lines of research: the tethered cord syndrome;the etiopathogenic relationship between Arnold Chiari Syndrome Type I (ACSI), Idiopathic Syringomyelia (ISM) and Idiopathic Scoliosis (IS) and other associated pathologies; and finally, the role of spinal cord tethering in the development of Idiopathic Scoliosis.

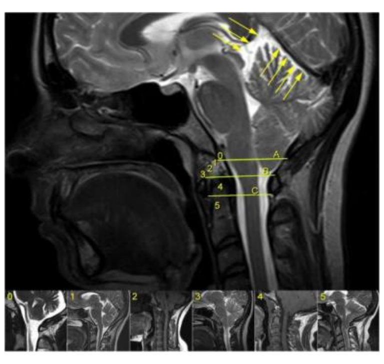
Based on the arguments outlined in the doctoral thesis "*Contribution to the etiology of syringomyelia*" [1], thetraction of the spinal cord and brain is proposed as themain mechanism involved in the etiopathogenesis of ISM, ACSI, IS and other diseases also considered idiopathic,such as Platybasia, Basilar Impression, RetroflexedOdontoid and Brainstem Kinking [2,3].

The objective of this study is to introduce the concept Neuro-Cranio-Vertebral Syndrome (NCVS) to define the set of clinical and imaging manifestations that affect the nervous system, the skull and the spine in the form of known diseases like Arnold-Chiari Syndrome Type I, Idiopathic Syringomyelia, Idiopathic Scoliosis and other anomalies like Platybasia, Basilar Impression, Retroflexed Odontoid and Brainstem Kinking. The Filum Disease (FD) is the most frequent congenital form of the Neuro-CranioVertebral Syndrome.

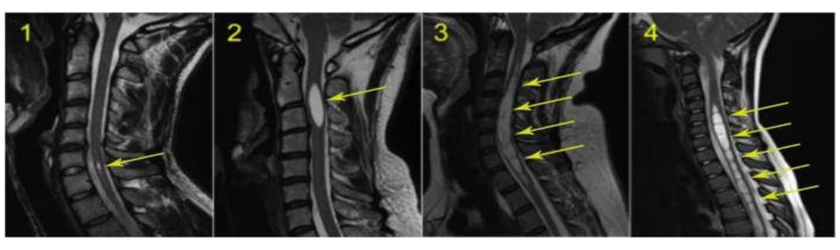
METHODS

Between April 14th 2009 and December 16th 2015, 1285 patients with one or several of the diagnoses of Arnold-Chiari Syndrome Type I, Idiopathic Syringomyelia, Idiopathic Scoliosis, Platybasia, Basilar Impression, Brainstem Kinking, low-lying conus medullaris and related pathologies were seen at the Institut Chiari & Siringomielia & Escoliosis de Barcelona out of whom, we present the clinical and imaging features in a sample of 373 patients, selected because they presented complete data registered for the purposes of this investigation, after excluding cases with significant neurological or neurosurgical antecedents that could interfere with their clinical or imaging presentation: procedures such as suboccipital craniectomy, syringostomy, ventriculo-peritoneal shunting, instrumentation for scoliosis, discectomies, laminectomies for spinal stenosis,as well as demyelinating, inflammatory, tumorous or traumatic diseases of the central and peripheral nervous system.

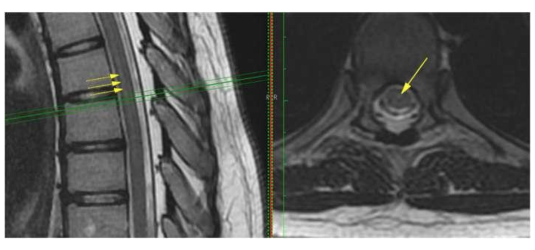
We performed an initial descriptive analysis of the general data (gender, age, type and duration of clinical course), dividing the variables into three main categories: clinical symptoms, clinical signs and imaging features. The variables followed in this study were analyzed looking for associations between components of the three categories mentioned above, taking into account topographical criteria. We used Pearson's chi-squared test and Kendall's test for ordinal data and Mantel-Haenszel chi-square test for stratified data, considering $p < 0.05$ as significance threshold. Finally, we created continuous variables by grouping symptoms and signs according to topographical criteria and these variables, as well as the different kinds of imaging features were analyzed together, first through comparison of the means and Student's t-test for independent samples and then through the creation of dispersion diagrams and computing Pearson's correlation coefficient.



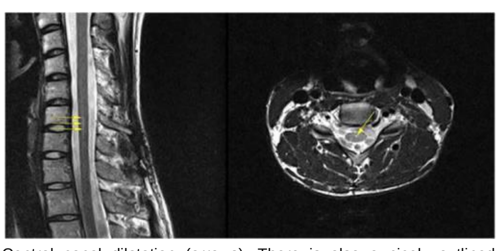
Classification of the magnitude of DCT with examples for each degree. A=McRae's line (FM); B=Upper border of atlas (C1); C=Lower border of atlas (C1). The interval A-B has been divided into an upper (grade 1), middle (grade 2) and lower (grade 3). They are followed by grade 4 (between the upper and lower borders of C1), and finally grade 5 (Underneath the lower border of C1). When the tonsil reaches exactly line A, it is considered grade 0, that we call Impaction of Cerebellar Tonsils. The arrows indicate another relevant parameter often associated to DCT, the Increase of the Supracerebellar Space



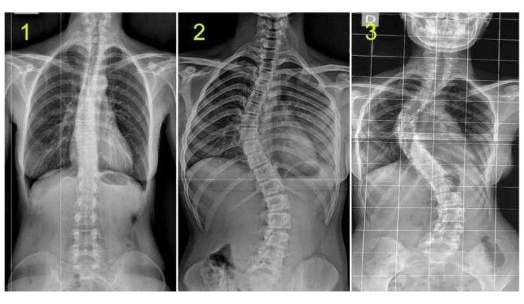
Classification of the extension of syringomyelic cavities Grade 1 (less than one vertebral segment); grade 2 (between 1 and 5 vertebral segments); grade 3 (between 6 and 10 vertebral segments); grade 4 (more than 10 vertebral segments).



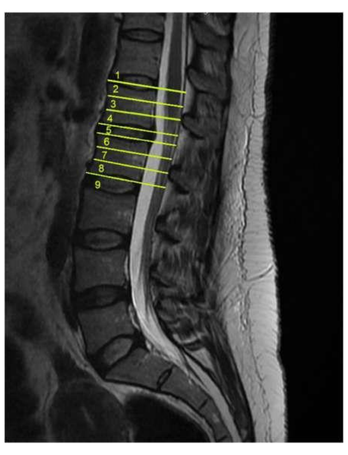
Spinal Cord Ischemia-Edema visible in a portion of the thoracic spinal cord on the sagittal cut (left, arrows), corresponding with an image of centro-medullary edema on the axial cut (right, arrow)



Central canal dilatation (arrows). There is also a nicely outlined Tense Spinal Cord on the sagittal cut (left)



Classification of Idiopathic Scoliosis. 1 = mild; 2 = modrate; 3 = severe



Levels used in the classification of the depth of the conus medullaris position with regard to vertebral segments: 1 (up to the D12L1 intervertebral disc); 2 (upper third of L1 vertebral body); 3 (middle third of L1 body); 4 (lower third of L1 body); 5 (L1L2 intervertebral disc); 6 (upper third of L2 body); 7 (middle third of L2 body); 8 (lower third of L2 body); 9 (lower than L2 body).

RESULTS

CLINICAL SIGNS ASSOCIATED WITH CRANIAL OR GENERAL SYMPTOMS:

Deviation of the uvula and/or tongue with:Headache (p = 0.011) and Nausea and/or vomiting (p =0.014); **Spontaneous nystagmus with**: Balance alterations (p = 0.020 Kendall), Tinnitus (p = 0.000) and Cognitive deterioration (p = 0.011 Kendall). **Positive Romberg test with**: Balance alterations(p = 0.002);**Decreased grip strength with**: Cognitive deterioration (p = 0.021 Kendall);**Altered sensibility to temperature with**: Mood alterations (p = 0.000).

CLINICAL SIGNS ASSOCIATED WITH MEDULLARY SYMPTOMS:

Altered sensibility to temperature with: Cervical pain (p = 0.004), Upper extremity pain (p = 0.000), Upper extremity numbness (p = 0.000), Upper extremity weakness (p = 0.000), Lower extremity pain (p = 0.045 Kendall) and Alterations of temperature perception (p =0.000). **Altered sensibility to touch with**: Cervical pain (p = 0.044 Kendall), Upper extremity pain (p = 0.000), Upper extremity numbness (p = 0.000), Upper extremity weakness (p = 0.001) and Lower extremity. **Alterations of deep tendon reflexes in upper extremities with**: Upper extremity weakness (p = 0.042) and Sphincter alterations (p = 0.024 Kendall). **Decreased grip strength with**: Upper extremity weakness (p = 0.000). **Alterations of deep tendon reflexes in lower extremities with**: Lower extremity weakness (p = 0.002) and Gait alteration (p = 0.046 Kendall). **Positive Mingazzini's test with**: Lower extremity weakness (p = 0.001).

RELATIONSHIPS BETWEEN CLINICAL VARIABLES (SYMPTOMS AND SIGNS) AND IMAGING FEATURES:

Clinical variables associated with Descent of cerebellar tonsils: Headache (p = 0.018), Deviation of the uvula and/or tongue (p = 0.013) and Decrease of grip strength (p = 0.042).
Clinical variables associated with Intramedullary cyst: Nauseas and/or vomiting (p = 0.000), Visual alterations (p = 0.001), Tinnitus (p = 0.007), Cognitive deterioration (p = 0.001), Insomnia (p = 0.021), Fatigue (p = 0.000), Upper extremity numbness (p = 0.014), Alterations of temperature perception (p = 0.019), Upper extremity weakness (p = 0.006), Deviation of the uvula and/or tongue (p = 0.027), Altered sensibility to temperature (p = 0.001) Altered cutaneous abdominal reflexes (p = 0.002), Upper extremity pain (p = 0.003), Lower extremity numbness (p = 0.045), Altered sensibility to touch (p = 0.000) and Altered cutaneous plantar reflexes (p = 0.010).
Clinical variables associated with Deviation the vertebral column (Idiopathic scoliosis): Thoracic back pain (p = 0.034), Spontaneous nystagmus (p = 0.038 Kendall), Altered sensibility to touch (p = 0.013), Altered cutaneous abdominal reflexes (p = 0.044 Kendall) and Altered cutaneous plantar reflexes (p = 0.001).

RELATIONSHIPS AMONG VARIOUS IMAGING FEATURES:

Descent of cerebellar tonsils with: Occipitocervical junction malformations (p = 0.015 Kendall), Syringomyelia with cervical component (p = 0.003), Level of conus medullaris (p = 0.008) and Deviation of the vertebral column (p = 0.014 Kendall);
Level of conus medullaris with Deviation Spine (p = 0.045 Kendall).

Concerning the Pearson correlation coefficient applied to the new continuous variables, formed by grouping symptoms and signs according to topographic criteria reveals good correlations within the group of clinical symptoms and signs. The strongest ones between General symptoms & Cranial symptoms (r = 0.531, p = 0.000), Medullary symptoms & Medullary signs (r = 0.523, p = 0.000), Cervical symptoms & Medullary symptoms (r = 0.513, p = 0.000), Cranial symptoms & Medullary symptoms (r = 0.420, p = 0.000) and General symptoms & Medullary symptoms (r = 0.414, p = 0.000).

DICUSSION

Epidemiology
There is a predominance of the female gender (72%), the most frequent age to be diagnosed is 33 years (average 33.66 years, with standard deviation 15.87 years) and the time interval lapsed from onset until diagnosis is most often longer than 10 years, in 48% of cases.

Symptoms (Table 3)
The following principal symptoms define the clinical picture of Filum Disease in decreasing order of frequency: headache 84%, lumbosacral pain 72%, cervical pain 72%, balance alteration 72%, paresthesias 70%, thoracic back pain 65%, visual alterations 57%, lower extremity pain 56%, nervousness 53%, sphincter alterations 52%, fatigue 49%, upper extremity weakness 49%, nausea and/or vomiting 49%.

Table 3 Frequency of clinical symptoms in the selected 373 patients. [1]Instability, dizziness, vertigo, etc. [2]Blurred vision, phosphenes, scotomata, etc. [3]Sensation of cold hands and/or feet, intolerance/unawareness of coldness/warmth. [4]Incontinence/retention, urgency, frequency, etc. [A]Later during the analysis, grouped together as "Cognitive deterioration". [B]Later during the analysis, grouped together as "Mood alterations"

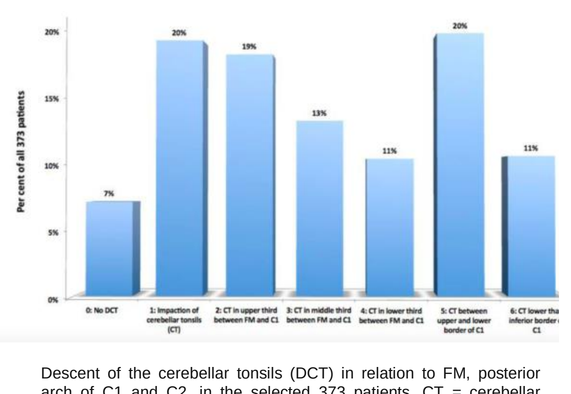
Symptom		Frequency	Percentage
1.	Headache	312	84
2.	Nausea and/or vomiting	182	49
3.	Balance alterations[1]	268	72
4.	Difficulty swallowing	141	38
5.	Visual alterations[2]	212	57
6.	Double vision	58	16
7.	Tinnitus	171	46
8.	Speech disorders[A]	92	25
9.	Memory deterioration[A]	162	43
10.	Attention alteration[A]	143	38
11.	Sadness[B]	100	27
12.	Anxiety[B]	45	12
13.	Nervousness[B]	196	53
14.	Sleeplessness	181	49
15.	Fatigue	183	49
16.	Upper extremity pain	167	45
17.	Lower extremity pain	208	56
18.	Thoracic pain	81	22
19.	Cervical pain	268	72
20.	Thoracic back pain	243	65
21.	Lumbosacral pain	270	72
22.	Upper extremity numbness	110	30
23.	Lower extremity numbness	76	20
24.	Paresthesias	262	70
25.	Alterations of temperature perception[3]	146	39
26.	Cramps	44	12
27.	Upper extremity weakness	182	49
28.	Lower extremity weakness	175	47
29.	Sphincter alterations[4]	192	52
30.	Gait alteration	170	46

Signs (Table 4)
The most frequent signs in Filum Disease, in decreasing order of frequency, are: altered deep tendon reflexes in upper extremities 86%, altered deep tendon reflexes in lower extremities 82%, altered plantar reflexes 73%, decreased grip strength 70%, altered sensibility to temperature 69%, altered abdominal reflexes 68%, positive Mingazzini's test 66%, altered sensibility to touch 65%, deviation of the uvula and/or tongue 64%, spontaneous nystagmus 55%, positive Romberg's test 50%, positive straight leg-raising test 44%. Significantly, the statistical analysis confirms the presence of correlations between Conus Medullaris level and Descent of cerebellar tonsils (p = 0.008) and between Conus Medullaris level and Deviation of the vertebral column (p = 0.045). It also confirms the existence of a correlation between Descent of cerebellar tonsils and Syringomyelia with cervical component (p = 0.003), coexisting with an interestingly inverse, that is, negative association between Descent of cerebellar and "low" Syringomyelia (without cervical component, i.e. thoracic or thoracolumbar) (p = 0.001). We also detected a positive correlation between Descent of cerebellar tonsils and Deviation of the vertebral column (p = 0.014). Out of all symptoms and clinical signs, only the unilaterally or bilaterally positive straight leg-raising test (p = 0.048) and the unilaterally or bilaterally decreased grip strength (Kendall p = 0.019) have correlations with the level of conus medullaris. Altered deep tendon reflexes have correlations with Syringomyelia with cervical component (p = 0.005) and with Deviation of the vertebral column (p = 0.000).

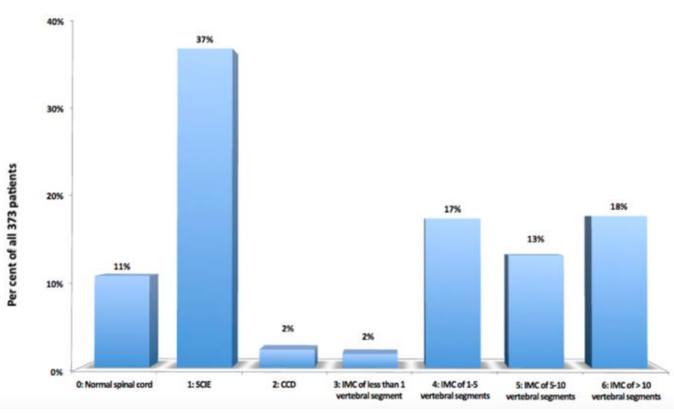
Table 4 Frequency of clinical signs in the selected 373 patients

Signs		Frequency	Percentage
1.	Spontaneous nystagmus	204	55
2.	Deviation of uvula and/or tongue	237	64
3.	Altered sensibility to temperature	257	69
4.	Altered sensibility to touch	242	65
5.	Altered deep tendon reflexes in upper extremities	322	86
6.	Altered deep tendon reflexes in lower extremities	309	83
7.	Altered cutaneous abdominal reflexes	254	68
8.	Altered cutaneous plantar reflexes[1]	274	73
9.	Positive straight leg-raising test	165	44
10.	Positive Mingazzini's test	245	66
11.	Positive Romberg's test	188	50
12.	Decreased grip strength	259	70

[1]Babinski's sign was present on one or both sides in 109 patients (29%)

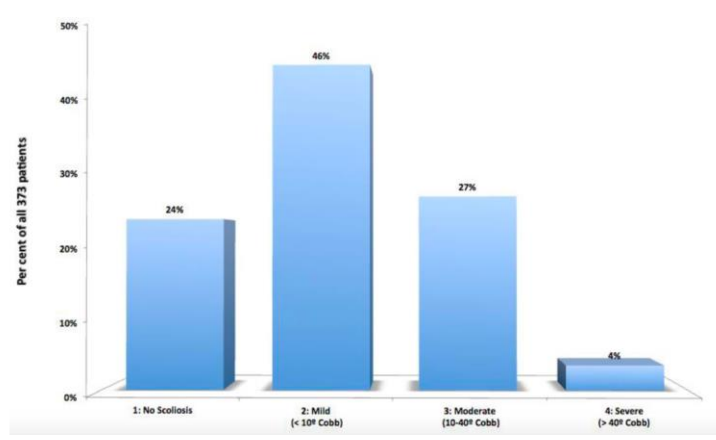


Descent of the cerebellar tonsils (DCT) in relation to FM, posterior arch of C1 and C2, in the selected 373 patients. CT = cerebellar tonsils; FM = foramen magnum; C1 = first cervical vertebra

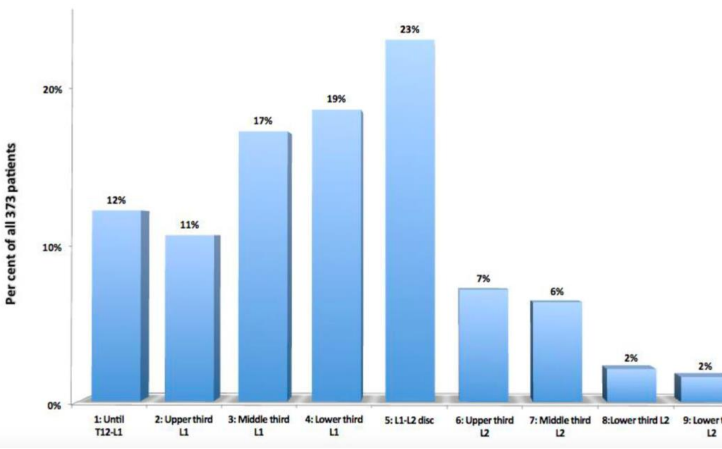


Frequency of presyringomyelic lesions and of the various degrees of longitudinal extension of syringomyelic cavities (Grade 0 corresponds to normal spinal cord), in the selected 373 patients. SCIE = Spinal Cord Ischemia-Edema; CCD = Central Canal Dilatation; IMC=Intramedullary Cyst

Imaging
Relevant imaging features in decreasing order of frequency are: altered position of cerebellar tonsils 93% (Descent of cerebellar tonsils 73% and impaction Cerebellar Tonsils 20%); Low Conus Medullaris below T12-L1 88%; Deviation of the vertebral column in 76%; multiple disc disease 72%; syringomyelic cavity 52%.



Presence of DVC (IS), classified by its severity measured according to Cobb's method, in the selected 373 patients



Height of the tip of the conus medullaris according to the corresponding vertebral levels (D12, L1, L2), from cranial to caudal, in theselected 373 patient

CONCLUSIONS

These observations are compatible with the conclusions of the thesis: the caudal traction force applied to the nervous system by means of the filum terminale is expressed in the form of Descent of cerebellar tonsils as the entire encephalon, including its lower most part, the cerebellar tonsils, shift through the foramen magnum; the spine, seeking to minimize trauma on the spinal cord, bends and creates abnormal spinal curvatures such as scoliosis, kyphosis, hyperlordosis, rotoscoliosis, straightening; the central spinal cord tissue suffers ischemia and necrosis with production of a cavity filled with interstitial fluid or serum, the syringomyelic cavity; by acting on the skull and brainstem at the beginning of bone maturation, Platybasia, Basilar Impression, Retroflexed Odontoid and Brainstem Kinking develop. The course of the syringomyelic cavity is toward fistulization and mixing of the intracavitary fluid with cerebrospinal fluid, towards redilatation when there is a valvular mechanism or toward collapse and spinal cord atrophy.

Concluding a doctoral thesis and resulting published papers [1-3,4,5], we have proceeded thus to the description of a new nosological and etiopathogenic concept, proposing the pathological conditions of Filum Disease, when its origin is congenital, and Neuro-Cranio-Vertebral Syndrome, when the nature of the mechanical conflict between neuraxis and spine is acquired. It is important for future studies to help understand better the origin of the axial caudal force, in order to assess the impact of the Filum Disease in the individual and in the population in general, which will help to comprehend the magnitude, consequences and anomalies of the asynchronic growth between neuraxis and spine on the central nervous system, skull and spine, as well as the rest of the organism.

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