Hypermobiliteetti - Ylitaipuisuusoireyhtymät Meilahti sisät. meeting. 190912

Seppo Villanen fysiatri, yl.el.
kivunhoidon ja kuntoutuksen erit.pät.
Mehiläinen, Vantaan Lääkärikeskus.
Orton, SatKS, TELK

diagnooseja

- M24.2 nivelsiteen sairaus, tarkemmin määrittämätön nivelsiteiden löysyys
- M35.7 hypermobiliteettioireyhtymä (HMS tai HS) tai BJHS (benign joint hypermobility syndrom) = GHJ (General Joint Hypermobility Syndrome)
- Q79.6 Ehlers-Danlos oireyhtymät (EDS)I-X, diagnoosi viivästyy eniten , tarvitaan 20 erikoislääkäriä ennen kuin oikea diagnoosi saadaan (Castori 2009).
- Q82.88 cutis laxa,L57.4 cutis laxa senilis
- Marfan oireyhtymä (MFS)
- Osteogenesis imperfecta (OI)
- Kontrakturaali oireryhtymä, epidermolysis bullosa, pseudoxanthoma elasticum, silvermans syndrome

Epidemiology of General Joint Hypermobility and Basis for the Proposed Criteria for Benign Joint Hypermobility Syndrome: Review of the Literature

LARS REMVIG, DORTE V. JENSEN, and ROBERT C. WARD

ABSTRACT. ***Objective.*** This literature review of generalized joint hypermobility (GJH) syndromes discusses information regarding sex-, age-, and race-related factors from publications that specifically document validated GJH criteria.

Methods. We present an analysis of criterion-referenced connections that identify similarities among major and minor clinical criteria that identify both GJH and benign joint hypermobility syndrome (BJHS). In our search, we found considerable empirical evidence that supports an increased prevalence of hypermobility among children, women, and certain racial groups. Two commonly used clinical assessment tools, the Carter and Wilkinson criteria (≥ 3 positive tests out of 5) and the Beighton method (≥ 4 positive tests out of 9), are the sources of these data. BJHS is diagnosed through a set of major and minor criteria — a combination of symptoms and objective findings — that include arthralgia, back pain, spondylosis, spondylolysis/spondylolisthesis, joint dislocation/subluxation, soft tissue rheumatism, marfanoid habitus, abnormal skin, eye signs, varicose veins or hernia or uterine/rectal prolapse.

Results. Clinically, there is some evidence that arthralgia, the proposed BJHS major criterion, is a major component of alleged hypermobility-related problems. In contrasting, there is no clear evidence that proposed BJHS minor diagnostic criteria are associated with hypermobility-related problems. An empirical correlation between hypermobility and osteoarthritis is possible, but so far unproven. There are no randomized controlled studies regarding effects of existing treatments.

Conclusion. Generalized hypermobility is both sex- and age-related. Racial differences are also identifiable. The existence of BJHS can be accepted using present criteria. (First Release Jan 15 2007; J Rheumatol 2007;34:804–9)

Key Indexing Terms:
JOINT LAXITY HYPERMOBILITY EPIDEMIOLOGY SYNDROME CRITERIA

Musculoskeletal complaints in association with general joint hypermobility (GJH) were, in 1967, labelled as hypermobility syndrome (HS)[1], which now is called benign joint hypermobility syndrome (BJHS)[2]. In a previous article[3] focusing on reproducibility and validity of tests and criteria for GJH and BJHS, we concluded that future syndrome-related validity studies will have to be developed on the basis of construct validity using criteria presumed to be part of the syndrome. In this article we focus on 4 items: (1) The epidemiology of GJH, looking for documentation of age, sex, and racial variations in the prevalence of GJH. (2) Are the major and minor diagnostic criteria for BJHS well enough documented? (3) Is there sufficient evidence to suggest that BJHS leads to an increased prevalence of osteoarthritis (OA)? (4) What scientifically documented prevention and treatment strategies and algorithms are available?

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MATERIALS AND METHODS

We searched PubMed, Cochrane Library, and PEDro using the following: joint instability, hypermobility, joint dislocation, back pain, shoulder injuries, sprain, children, age, sports injuries, marfanoid habitus, eye signs, and pregnancy. From the results, we reviewed GJH-related articles that used validated tests and standards synonymous with Carter and Wilkinson's criteria[4] and Beighton's method[5]. Other publications using limited modifications of the validated tests and criteria are also incorporated.

RESULTS

Epidemiology

Age, sex, and race. Beighton, *et al* demonstrated that the number of positive hypermobility tests was age- and sex-related[5]; the younger the children, the higher the score. Women had higher scores than age-matched men. The findings were confirmed by some authors[6-10], but not all[4,11,12].

Hypermobiliteetin prevalenssi eri väestöryhmissä, ikä ja sukupuoli vaikuttavat myös

Table 1. Prevalence of hypermobility among non-Caucasian women and men in various age groups using validated hypermobility tests and criteria.

Study	Race, Age, yrs	Prevalence of Hypermobility Female, % (N)	Male, % (N)
Walker[13]	Amerindians, 0–19	18 (212)	12 (184)
	Inuit 0–19	32 (165)	29 (133)
Klemp[14], New Zealanders	Caucasian > 5	6 (195)	2 (159)
	Maori > 5	9 (256)	2 (182)
El-Garf[21], Egyptians	Arabic 6–15	18 (498)	14 (499)
Pountain[61], Oman inhabitants	Mixed Arabic 16–25	29 (178)	9 (131)
Al-Rawi[62] Iraqis	Arabic 20–24	39 (1187)	25 (587)
Al-Rawi[50], Iraqis	Arabic 23–65	18 (76)	—
Birrell[6], Yoruba Africans	Negroid 6–66	57 (116)	35 (88)
Beighton[5]*, Tswana Africans	Negoid ≥ 20	20	6

* Beighton did not define any criterion, but mentioned that 80% of females and 94% of males had 0–2 positive tests.

Das Ehlers-Danlons syndrom
S.Böhm ym Orthopäde 2002:31;108-121

- Jo muinaiset skyytit…
- Janszoon van Meekeren 1668, kirurgi Amsterdam
- Tschernogubovs 1891, (ihot.l. Venäjä)
- Ehlers Edvard ihot prof, Tanska 1901
- Danlos Henri sisät.l., Ranska 1908
- Von Pommeau und Soulie; nimi: EDS syndrooma - nimitys (aika ?)
- Parkes Weber 1.nosologia Ehlers-Danlosin syndroomille 1933
- Hypermobiliteettisyndrooma 1932

EDS-prevalenssi

- Saman suuntainen eri väestöryhmissä (ei rotuvaikutusta), naisilla yleisempi
- Suomessa prevalanssi on auki sekä hypermobiliteetin että EDS:n suhteen
- Eri lähteiden mukaan 1/5000-1/10000-/1/25000 (Dominique, Germain 2007), tästä esim. EDS IV 5-10%.

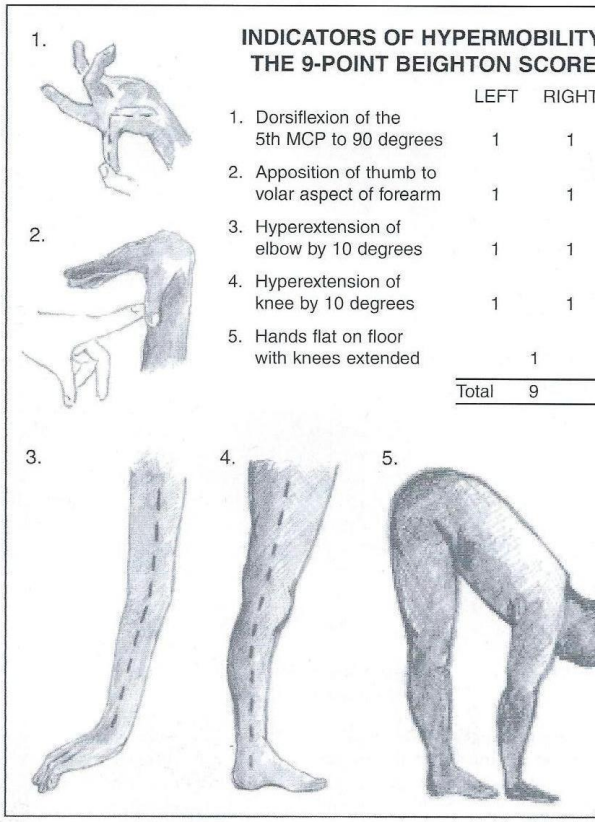
The man behind the syndrome. P. et G. Beighton Spinger Verlag 1986

Edward Lauritz Ehlers 1863-1937 Tanska

Henri Alexandre Danlos 1844-1912. Pariisi

Cutis laxa?

Beightonin kriteerit: käsipainoitteinen (yläraajoista 6.). Posit. on 5/9 -9/9



INDICATORS OF HYPERMOBILITY
THE 9-POINT BEIGHTON SCORE

	LEFT	RIGHT
1. Dorsiflexion of the 5th MCP to 90 degrees	1	1
2. Apposition of thumb to volar aspect of forearm	1	1
3. Hyperextension of elbow by 10 degrees	1	1
4. Hyperextension of knee by 10 degrees	1	1
5. Hands flat on floor with knees extended	1	
Total	9	

HMS

- Hypermobility syndrome, Kirk, Ansell; Bywaters 1967
- BHJS-normaalin ääripää (Jessee 1980)
- Benign Joint Hypermobility Syndrome (BHJS) Berliinin kokous 1986, Brighton 1988.
- British Society of Rheumatology 1991: HMS kriteerit, spesifiteetti 93 %, sensiviteetti 93%, ikäryhmä 16-85, huom. ei voi käyttää lapsilla
- Joint Hypermobility – tärkeä tunnistaa (Hakim ja Grahame 2003)

M35.7 HMS kriteerit

- Major:
- beighton 4/9 tai enemmän, nivelkivut yli 3 kk 4 tai useammasa nivelessä
- Minor criteria: beighton ikätasoitus
- nivelkipu 1-3 nivelessä tai selkäkipu yli 3kk, spondylolyysi tai listeesi,
- diskolaatio tai subluksaatio yhdessä tai useammassa nivelessä,
- Pehmytkudosoireet: epikondyliitti, tenosynoviitti, bursiitti yli 3 kohdassa
- Marfanoidi habitus
- Poikkeava iho , striiat, papapyrusiho, arvet
- Silmät, silmaluomet putovat, myopia, ihopoimu
- Suonikohjut , kohtuprolapsi, tyrät
- Jos on EDS 1. asteen sukulaisilla niin riittää 2 min krit, muuten 2 maj tai 1 maj +2 min tai 4 min. krit.

EDS alaryhmät

- Villafranche 1997 nosologia Am J Med Genet, 77;31-37, 1998
- Klassinen; EDS I ja II, (COL5A1 ja COL5A2 90%, kollageeni V (Symoens 2012)
- Hypermobiili EDS (III), EDS-HT (COL 3CA1??)
- Vaskulaarinen EDS IV, (COL3A1) (voi olla uusi mutaatio Sadakata 2010, Rebelo 2011 – molemmat kuvanneet eri mutaation), elinikä alle 50 v.
- Kyfoskolioottinen EDS VI, lysyloksidaasi, PLOD1
- Artrokalaattinen EDS VIIA ja EDS VIIB
- Dermatosparaktinen EDS VIIC, prokollageeni-N-proteaasin puutos, ADAMTS2
- Muut EDS V, EDS X, EDS ja tenaskiini-X-puutos
- Uusi EDS syndrooma (Kosho 2010) ,

EDS nosologia

TYPE	CLINICAL FEATURES	INHERITANCE	BASIC DEFECT
CLASSICAL (formerly EDS I & II gravis and mitis type)	**MAJOR:** Skin hyperextensibility; widened thin scars; joint hypermobility. **MINOR:** Smooth velvety skin; molluscoid pseudotumours; complications of loose joints; muscle hypotonia; easy bruising; manifestations of tissue extensibility (hernia, cervical insufficiency etc); positive family history.	Autosomal dominant.	Abnormality of the pro alpha 1 (V) or pro alpha 2 (V) chain of the type V collagen encoded by COL5A1 and COL5A2 genes (in some but not all families)
HYPERMOBILITY (formerly EDS III hypermobile type)	**MAJOR:** Generalised joint hypermobility; skin hyperextensible and smooth or velvety. **MINOR:** Recurrent joint dislocations; chronic limb and joint pains; positive family history.	Autosomal dominant.	Unknown
VASCULAR (formerly EDS IV arterial or ecchymotic type).	**MAJOR:** Arterial/intestinal/uterine fragility or rupture; easy bruising; characteristic facial appearance. **MINOR:** Hypermobility of small joints; tendon and muscle rupture; clubfeet; varicose veins; positive family history; sudden death in close relative.	Autosomal dominant.	Structural defects in the pro alpha 1 (III) chain of collagen type III, encoded by the COL3A1 gene.
KYPHOSCOLIOSIS (formerly EDS VI ocular or scoliosis type)	**MAJOR:** Generalised joint laxity; severe muscle hypotonia in infancy; scoliosis present at birth and progressive fragility of the sclera of the eye. **MINOR:** Tissue fragility; easy bruising; arterial rupture; Marfanoid body shape; microcornea; skeletal osteopenia on X-ray; positive family history of affected siblings.	Autosomal recessive.	Deficiency of lysyl hydroxylase, a collagen modifying enzyme.
ARTHROCHALASIA (formerly included in EDS VII)	**MAJOR:** Severe generalised joint hypermobility with dislocations; congenital bilaterial hip dislocations. **MINOR:** Skin hyperextensibility; tissue fragility and scarring; easy bruising; muscle hypotonia; kyphoscoliosis; skeletal osteopenia on X-ray; positive family history.	Autosomal dominant.	Deficiencies of the pro alpha (1) or pro alpha 2 (I) chains of collagen type 1 due to skipping of exon 6 in the COL1A1 or COL1A2 gene.
DERMATOSPARAXIS (formerly included in EDS VII)	**MAJOR:** Severe skin fragility; sagging, redundant skin. **MINOR:** Soft, doughy skin texture; easy bruising; premature rupture of foetal membranes; hernias.	Autosomal recessive.	Deficiency of procollagen 1 N-terminal peptidase in collagen type 1.

Other rare forms of EDS

EDS V: X-linked type resembles the Classical type, in mild to moderate severity. Delineated in a single large family in the UK.

EDS VIII: Periodontal type resembles the Classical type with the addition of fragility of the gums. Very rare. Syndromic status uncertain. Autosomal Dominant.

EDS X: Resembles the Classical type, in mild degree, with the additional feature of abnormal platelet aggregation. Syndromic status uncertain. Autosomal Recessive?

Entries now removed from the EDS Classification

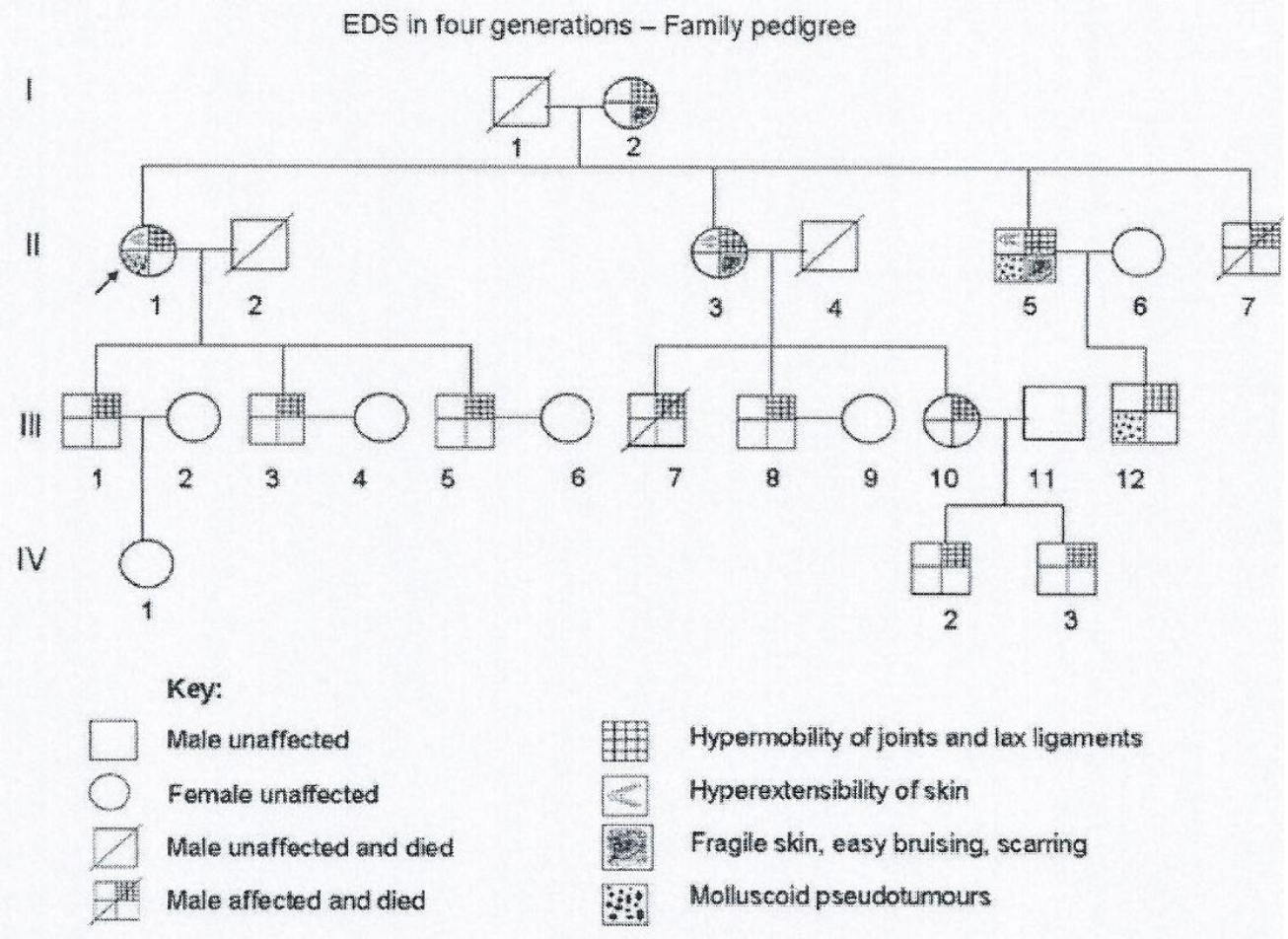
EDS IX: Now termed 'occipital horn syndrome'. X-linked disorder of copper metabolism, which is allelic to Menkes syndrome.

EDS XI: Now termed 'familial joint hypermobility'. Resembles hypermobility form of EDS.

EDS ja perimä

- Periytyvät mendeliaanisesti
- EDS I-IV, EDS VIIA ja VIIB-VIII periytyvät autosomeissa vallitsevasti
- EDS VI, EDAS VIIC ja EDS X periytyvät autosomeissa peittyvästi
- EDS V periytyy X –kromosomaalisesti
- suku, lapset, huom. beightonin kriteerit eivät ole luotettavia alle 15 v.

EDS perimä; 4 sukupolvea



EDS, diagnoosi

- Perinnöllisyys, oireet, synnytys, lapsuus, muut sairaudet
- Beightonin kriteerit, ihon kosketustuntuma (pehmeä samettimainen), mustelmat, arvet (piranhan purema), nivelten subluksaatiot olat, sormet, sydämen auskultaatio, jalkapohjat, niskat
- Rtg tutkimukset, syd. UÄ, DXA, niskan MRI
- Muiden sairauksien selvittäminen
- Hypermobiliteetti ryhmässä diagnoosi on kliininen: ”sormituntuma”

EDS jalkaterä

- Pitkittäinern holvi ja poikittainen holvi funktionaalisesti matalia, jalkaterä leviää huomattavasti kuormituksessa eli kengän numero kasvaa…
- Avojaloin jalkapohja imeytyy lattiaan kiinni; ”plop, plop” –ääni, vrt imukupit
- Jalkapohjan rasva on paksua ja liikkuvaa, vrt kävely tennispallon päällä
- Jalkapohjan rasva ei yleensä atrofioidu iän myötä

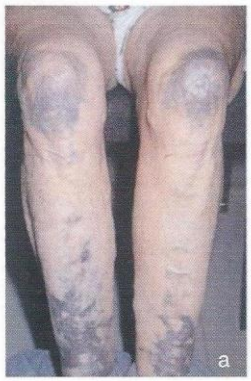
EDS käsi

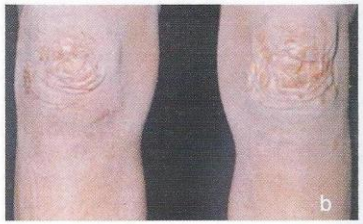
- PIP ja DIP nivelet luksoituvat, dorsaalisesti 10-40 astetta
- CMCI nivelet luksoituvat.
- Ranteet luksoituvat ja ranneluut eivät liiku lineaarisesti, ranteissa nivellukkoja
- Vaikea kirjoittaa, avata purkkeja, ovia, käyttää hakaneulaa, nappeja
- Kestovoimaa ei ole; sormikoukkutesti

EDS olka

- subluksoituvat, esim. yöllä tai bussin nykäisystä, joskus esim. tanssiessa tai kliinisen tutkimuksen yhteydessä, kliinisessa tutkimuksessa helppo todeta olan löysyys
- vaikeita kipuja, ilman degen. löydöksiä
- kinesioteippaus, elastiset olkatuet (tosin niitä ei saa päälle)

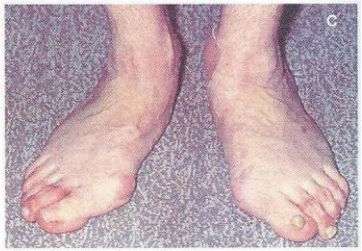
EDS klassinen



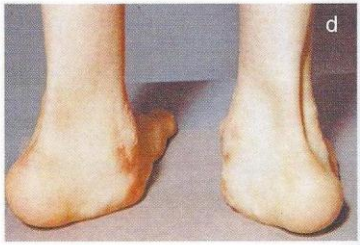


(a) Black haemosiderin deposits from old bruising of the shins. Similar changes occur in Classical, Vascular and type VIII families

(b) Wrinkled and scarred knees typical of Classical type EDS.

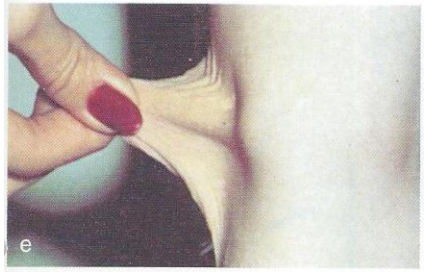


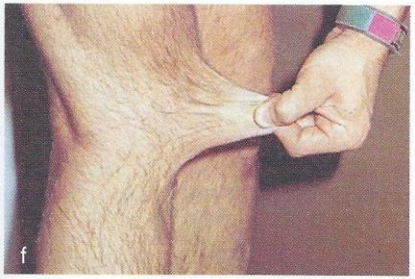
(c) "Diamond shaped" feet with bilateral hallus valgus (twisted big toe). This is typical of Classical, Hypermobility and Arthrochalactic type EDS.



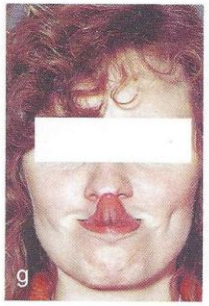
(d) Extreme pes planus (flat feet) as looked at from the rear. This patient with Kyphoscoliotic type EDS actually weight bears on the inside of the flattened arches. As seen from behind, the ankle is rotated clockwise on the left and anticlockwise on the right. Milder pes planus is also seen in Classical and Hypermobility type EDS.

EDS diagnoosia

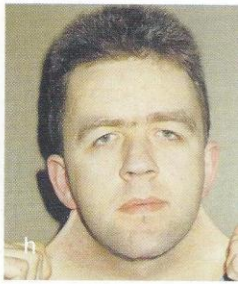




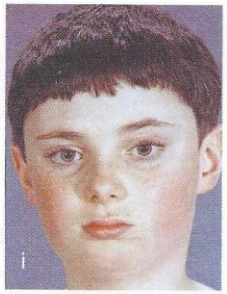
(e & f) Hyperexensibility of the skin of the elbow and knee respectively. This strongly suggests Classical, Hypermobility or Arthrochalactic type EDS.



(g) Positive Gorlins sign with the ability to extend the tongue forwards and upwards to touch the tip of the nose. It is typical of certain EDS subtypes, but not confined to this disorder.

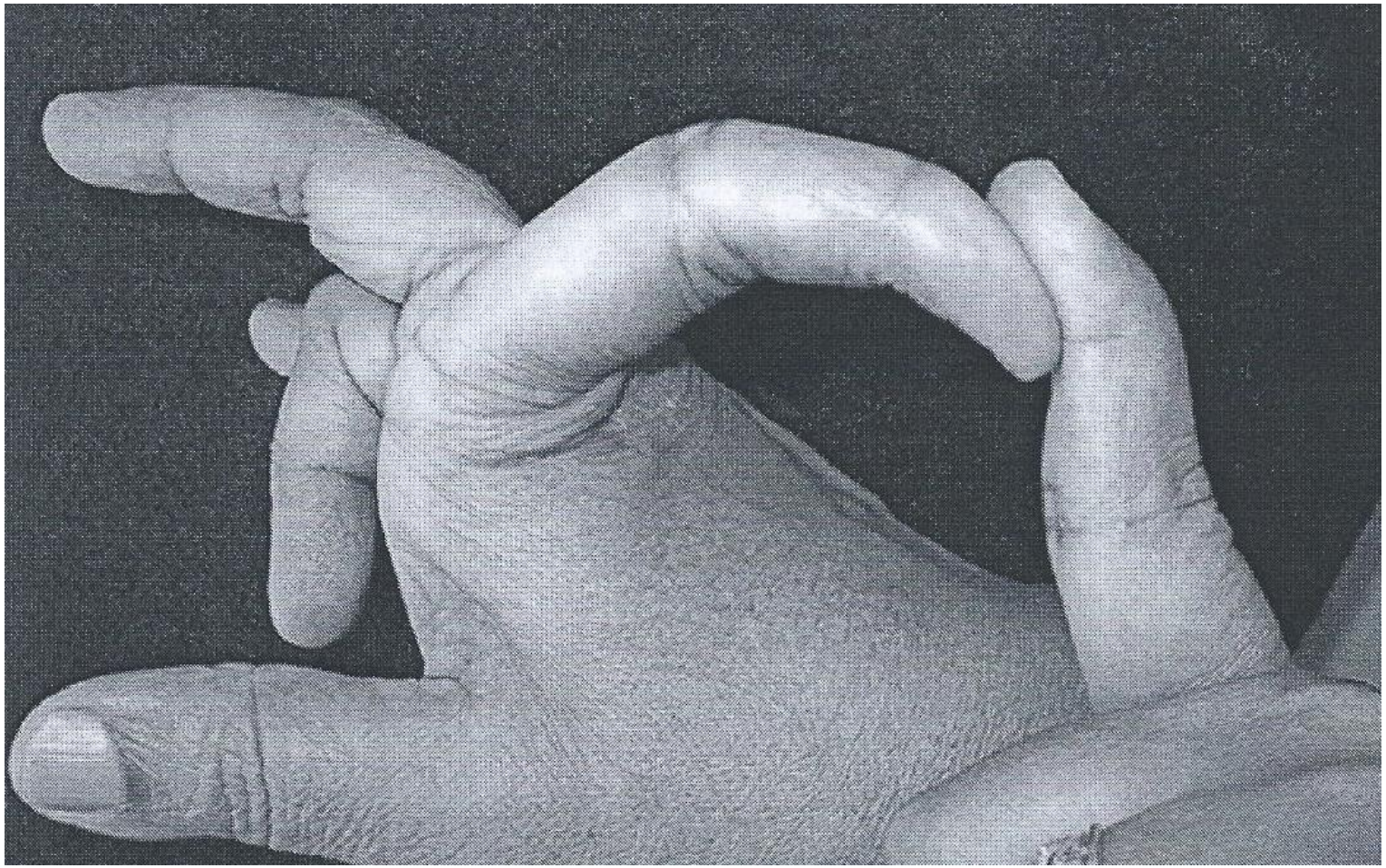


(h) Facial features of Classical type EDS. The eyes slant downwards and outwards which is common in some families. Note the hyperextensible neck skin and the scarred forehead.

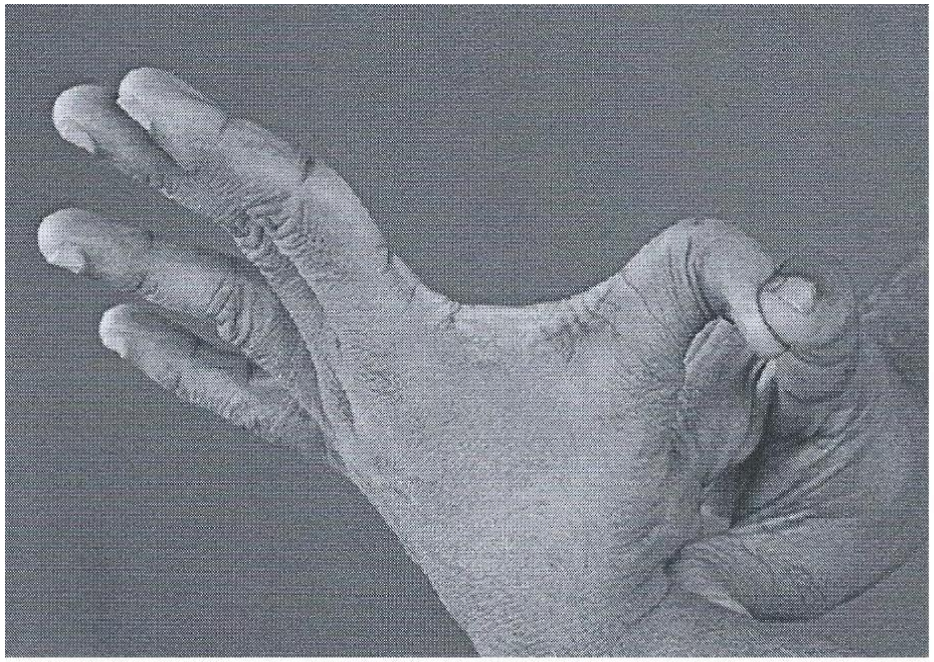


(i) Typical facial features of Vascular type EDS. The widely spaced eyes and lobeless ears are typical of this subset.

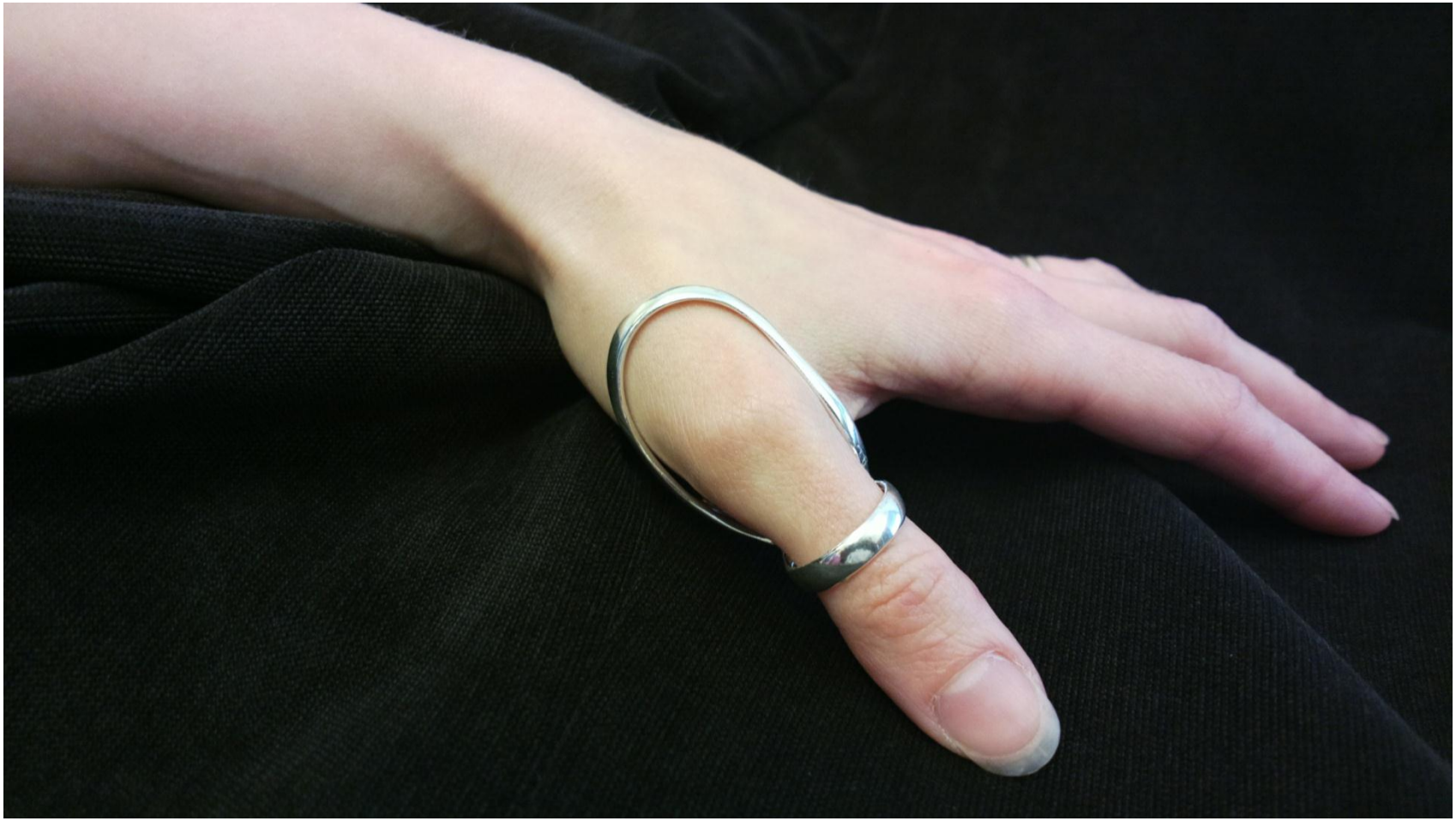
EDS sormi



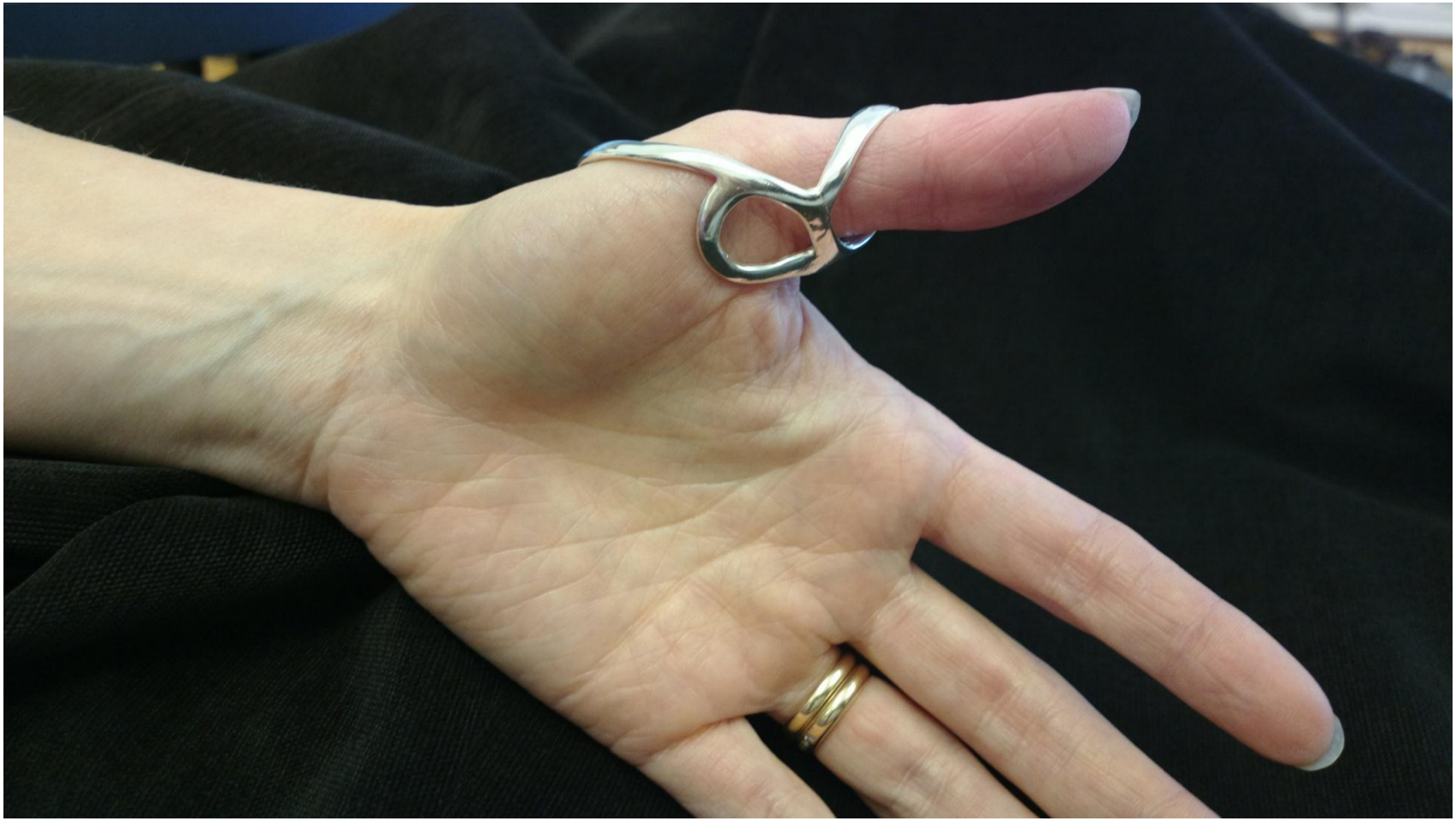
EDS peukalo



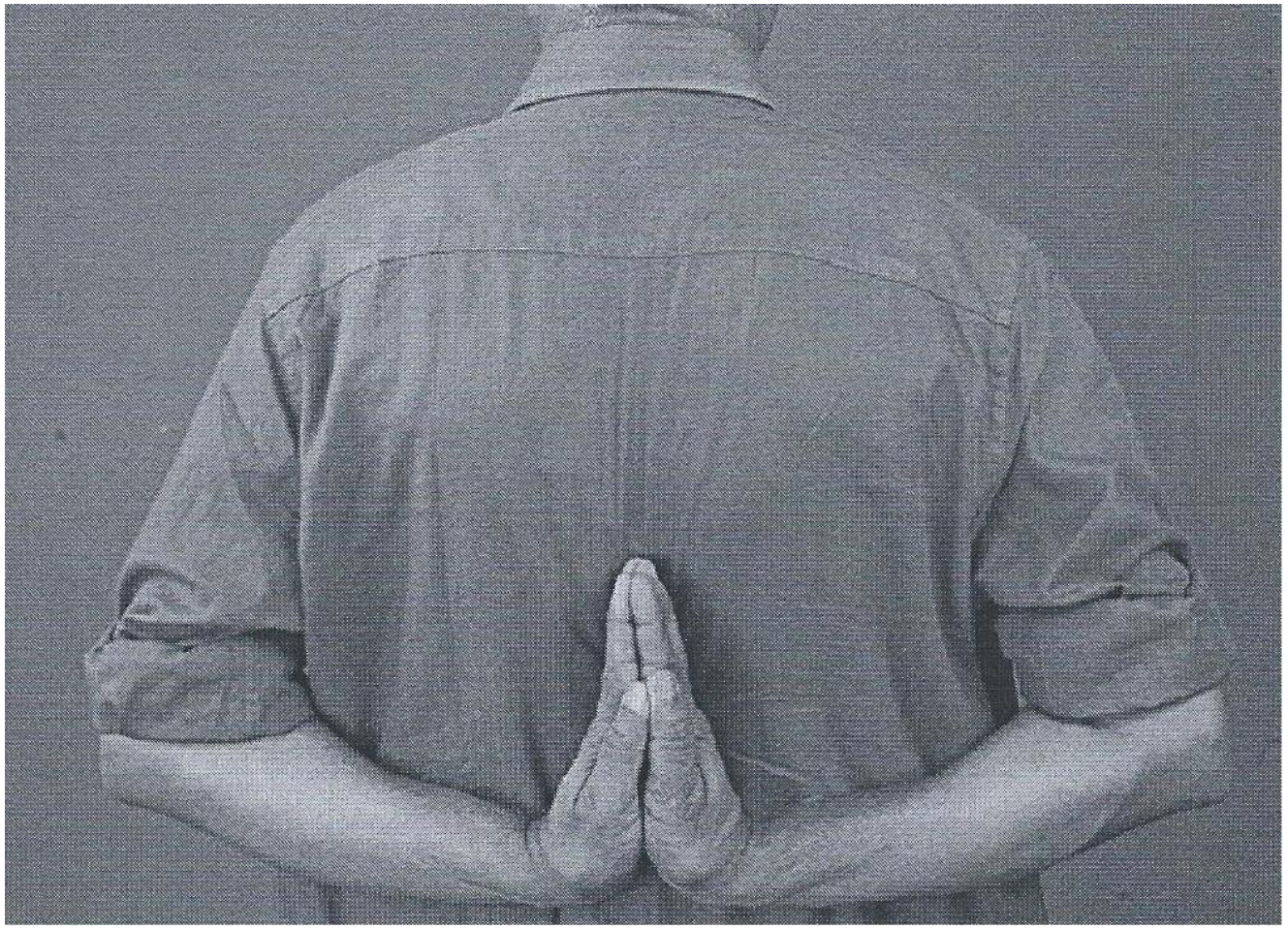
EDS ja peukalotuki (Villa Manus)



EDS tuki, jatkoa



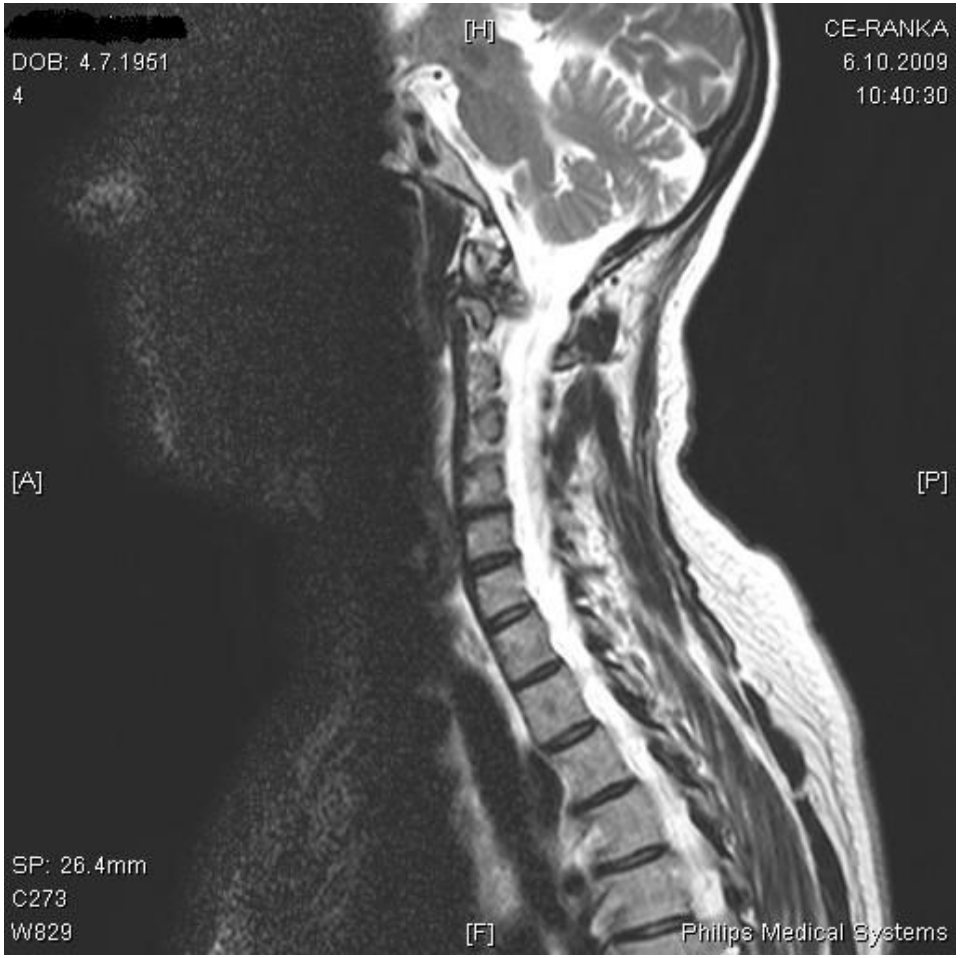
reverse namaskar



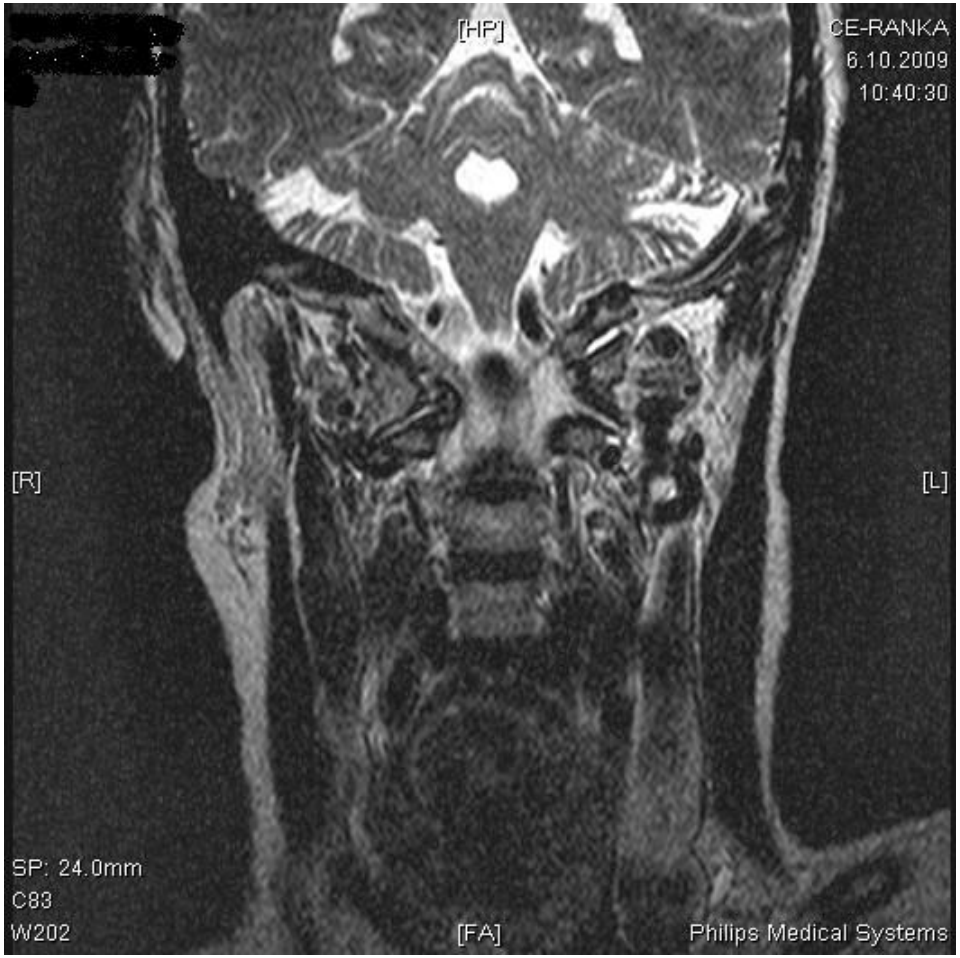
EDS niska

- Avara foramen magnum, instabiili yläniska
- Chiari I, huom mri on tehty maaten !
- Emme tiedä mikä on tilanne kuormitettuna!!
- Yhdellä potilaalla tonsillaherniaatio muuttui niskan taivutuksen mukana.
- pään mri yleensä normaali, aivojen konsistenssi?
- Muut anomaliat.
- Intubaatio voi olla vaarallinen jos jo subuksaatio

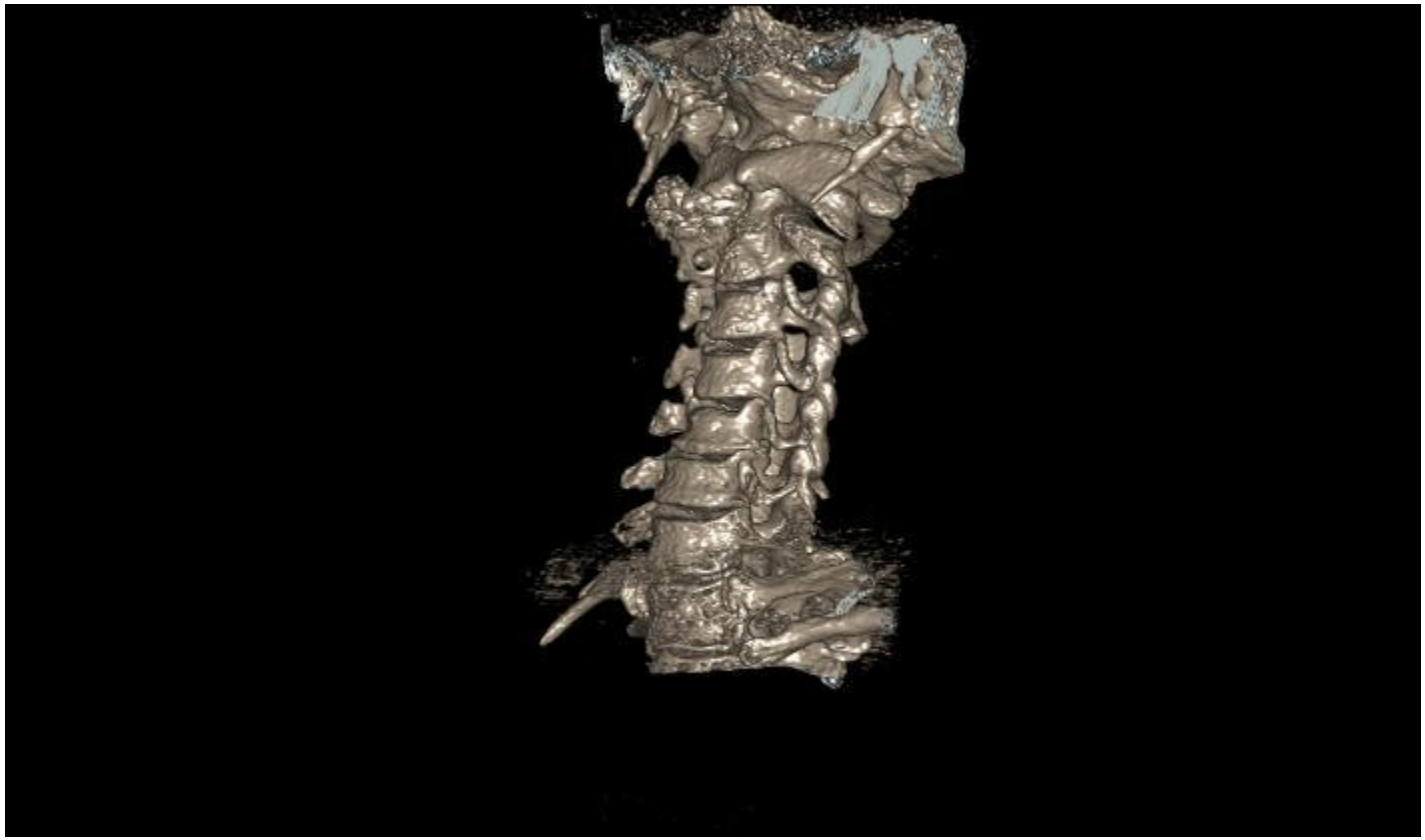
EDS yläniska, dex. C1/2 proliferatiivinen atroosi



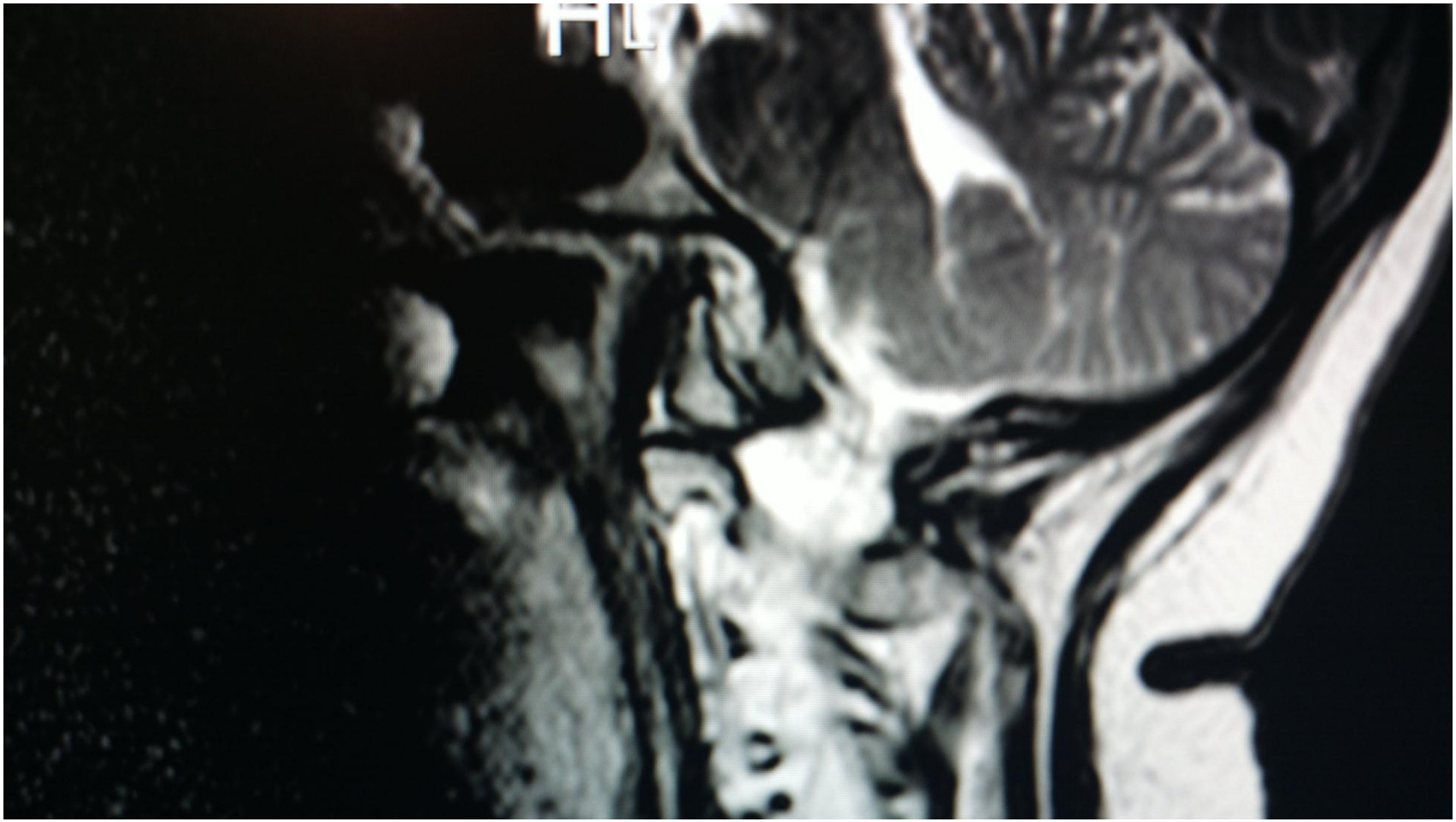
dex. C1/2 artroosi



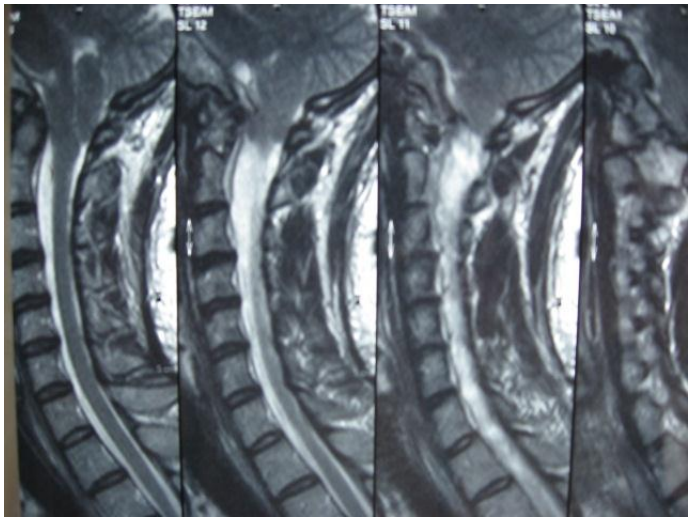
3DCT



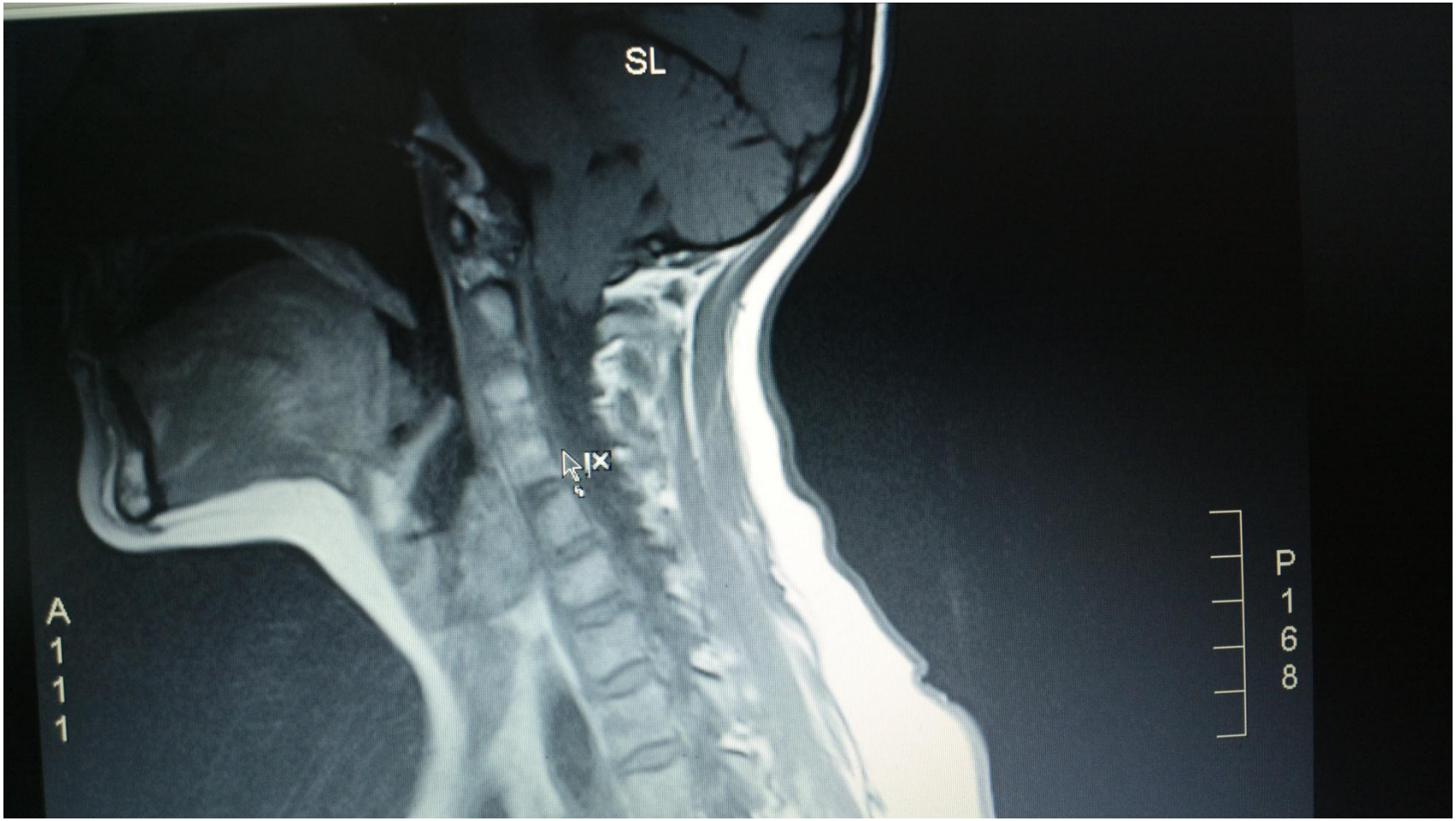
EDS ja c0/c1 anomalia



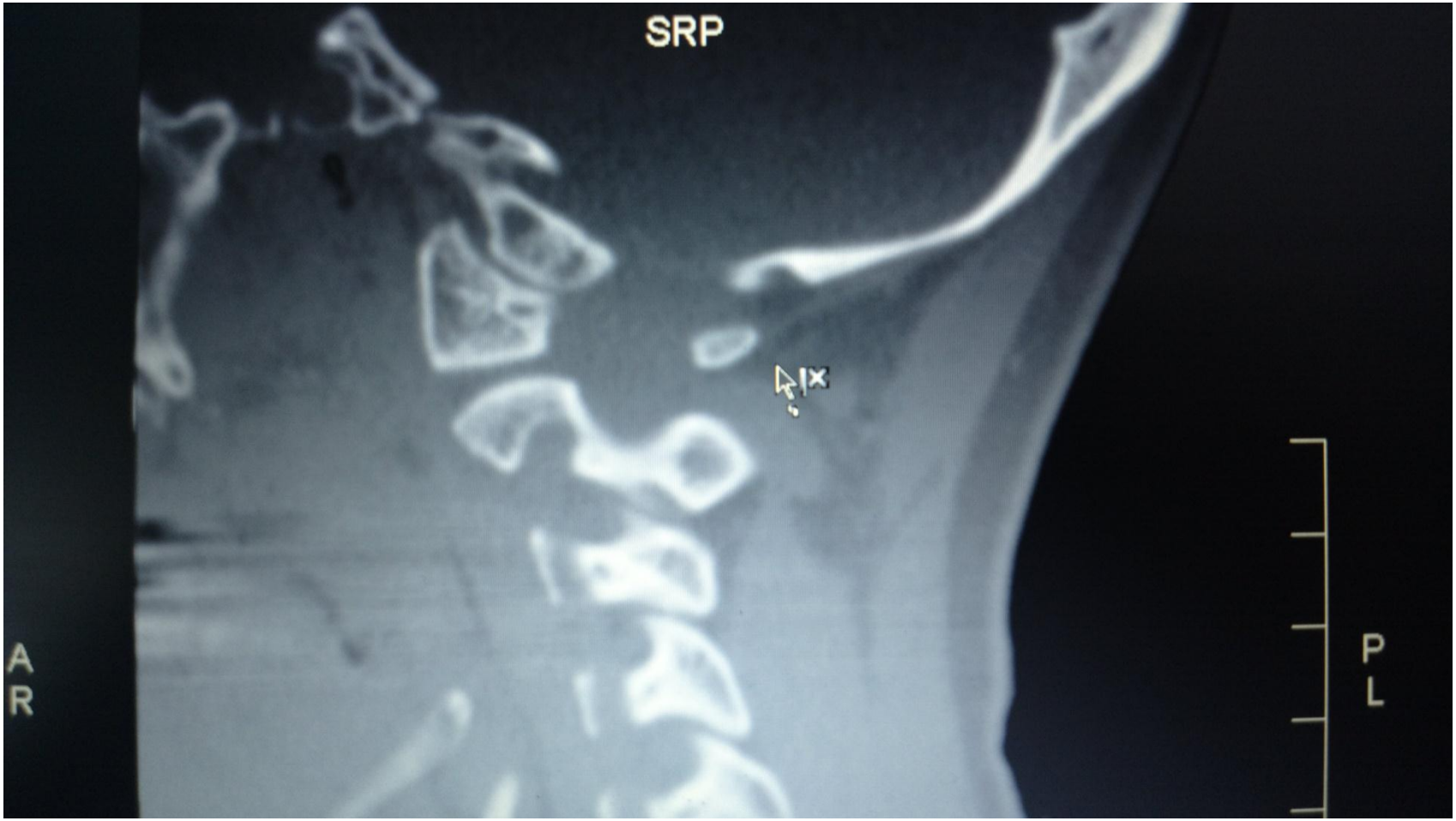
chiari



EDS klassinen ja chiari I



EDS klassinen, CO/CI variantti



tutkimuksia tuki-ja liikuntaelimistöstä

- Kantaiskun heikkous ja nopea väsyminen (FSS) yhteneviä (Celletti 2011)
- EDS potilaiden kävely Down syndr tyyppistä (Rigoldi 2012)
- Polven asentotunto erilainen, vibraatiotunto sama kuin verrokeilla (Rombaut 2010)
- Myopatia CHST14 mutaatiossa (Voermans 2012)
- Dynamometrillä matala lihastensio nilkan alueella (Rombaut 2012)
- Polven isokineettisessä lihastestauksessa matalat arvot kontrolleihin verrattuna (Sahin 2008)
- Scolioosi voi edetä nopeasti, hengitys funktio alentuu (Natarajan 2011)

EDS III ja muut sairaudet (noin 150 potilasta v. 1986-2012)

- EDS ja päänsärky, blepharoclonus, tensio, migreeni, Chiari , niskapäänsärky, vammat (Jacome 1999)
- Lihasheikkous 85%, lihaskivut, myopatia ja neuropatia 60% (Voermans 2009)
- EDS ja nivelkivut lähes kaikki (Grahame 2000) (Sacheti 1997)
- EDS ja väsymys 75% (Voermans 2010)
- EDS ja SPA tai AS, suolistotulehdus, useita
- EDS, asthma ?, immuunipuutoksia, lihaskato (kortisoni, sytostaatit)
- EDS ja osteopenia,
- EDS ja niveluksaatiot, yöllä/päivällä
- EDS ja discusprolapsit (kaula-, th- ja lanneranka)
- EDS ja vuodot, yksi nivelvuoto+EDS
- EDS ja hidas suoli – huom opiaatit!!

EDS ja muut sairaudet 2.

- EDS ja dysfonia, ylil. kieli (Richmon 2009) 1 potilas
- EDS ja massiivit discusprolapsit , useita
- EDS ja lihasheikkous (kestovoiman puute), kaikki
- EDS ja muut anomaliat, C0-C2, polvet lonkat, useita
- EDS ja mitraali tai aorttavuoto, useita
- EDS ja purenta , malocclusio, TMD (Barrera-Mora 2012), TMJ tähystys (Jerjes 2010), lähes kaikilla . Ienvuodot (Marttala)
- EDS ja MS 2 potilasta
- EDS kuivat silmät, patologinen myopia, syvät corneat ja lasiaisvirheet (Gharbiya 2012)
- EDS ja psyykkiset ongelmat (Lumley 1994), pelkotilat (Garcia-Campayo 2011)
- Keuhkojen hypoplasia ja patellojen agenesia (Pradhan 2009)

EDS-HT ja muut sairaudet

- Vertailu EDS, fibromyalgia, nivelreuma, 206 naispotilasta, EDS-HT 72, FM 69 ja RA 65); FM potilailla menee huonoiten, EDS on siinä välissä ja RA potilaat ovat ilmeisen asiallisessa hoidossa (Rombaut 2011)
- Vertailussa normaaliväestöön ruotsalaiset EDS potilaat kokevat itsensä sairaampina, väsyneinä ja kipeämpinä (Maeland 2011)

EDS IV

- Voi olla uusi mutaatio, prokollageeni III virhe
- Acrogeria, läpinäkyvä iho, laskimot näkyvissä, mustelmia
- Verisuoniston ja eri elinten ruptuuroita
- Myopatiaa ja neuropatiaa (Barboi 2009)
- 35 potilasta EDS IV verimuutoksia 78%: 41 aneyrysmaa, 19 dissectiota, 12 ectasiaa 10 occluusiota ja yksi fisteli. Carotis-sinuscavernosus fistelit, Infarcteja 10; aivot, munuaiset, perna. 10 vuotoa, joista viisi leikkauksessa ja 5 spontaaneja. (Zilocchi 2007)
- Aorttadissekaatio 13 v pka (Morais 2011)
- Onnistuttu aortoatriaalisen fistelin, aorttavuodon, mitraaliprolapsin ja tricusp vuodon operat h. (Jiang 2012)
- Jos nuorella poikkeava dissekaatio tms niin pitää selvittää onko EDS IV – lähete perin. lääket yksikköön ja laajat perustutkimukset suonistoon. Huom ruptuuroita voi olla myös muissa EDS ryhmissä esim. III 15 v tyttö (Im 2010)

RESEARCH ARTICLE

AMERICAN JOURNAL OF medical genetics PART A

Natural History and Manifestations of the Hypermobility Type Ehlers–Danlos Syndrome: A Pilot Study on 21 Patients

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Hypermobility type Ehlers–Danlos syndrome (HT-EDS) is a relatively frequent, although commonly misdiagnosed variant of Ehlers–Danlos syndrome, mainly characterized by marked joint instability and mild cutaneous involvement. Chronic pain, asthenia, and gastrointestinal and pelvic dysfunction are characteristic additional manifestations. We report on 21 HT-EDS patients selected from a group of 40 subjects with suspected mild hereditary connective tissue disorder. General, mucocutaneous, musculoskeletal, cardiovascular, neurologic, gastrointestinal, urogynecological, and ear–nose–throat abnormalities are investigated systematically and tabulated. Six distinct clinical presentations of HT-EDS are outlined, whose tabulation is a mnemonic for the practicing clinical geneticist in an attempt to diagnose this condition accurately. With detailed clinical records and phenotype comparison among patients of different ages, the natural history of the disorder is defined. Three phases (namely, hypermobility, pain, and stiffness) are delineated based on distinguishing manifestations. A constellation of additional, apparently uncommon abnormalities is also identified, including dolichocolon, dysphonia, and Arnold–Chiari type I malformation. Their further investigation may contribute to an understanding of the pathogenesis of the protean manifestations of HT-EDS, and a more effective approach to the evaluation and management of affected individuals.

Key words: evolution; extra-articular; joint hypermobility; pain; presentation

How to Cite this Article:
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INTRODUCTION

Ehlers–Danlos syndrome (EDS) comprises a clinically variable and genetically heterogeneous group of inherited connective tissue disorders mainly characterized by skin hyperextensibility, joint hypermobility, and vascular and internal organ fragility [Callewaert et al., 2008]. The overall incidence of this condition has been estimated at approximately 1:5000 [Steinmann et al., 2002]. According to the most recent classification, six major forms exist, while other variants are considered rare [Beighton et al., 1998]. The clinical variability of each EDS subtype is extremely wide and the diagnosis is not always straightforward even for the experienced clinician. Misdiagnosis or lack of diagnosis represents a major burden for patients with EDS. In fact, a recent survey by the European Organization for Rare Diseases (EURORDIS) has demonstrated that among patients belonging to 16 major rare diseases, those affected with EDS have the longest delay in diagnosis and request consultation of up to 20 specialists before obtaining the correct diagnosis [Kole and Faurisson, 2009]. This has severe consequences on the quality of life of the patients [Castori et al., 2009], usually in term of excessive financial and time expense, superfluous investigations, wrong therapies, delay of appropriate treatments, and preventable worsening of the disease state.

Among the different forms of EDS, the hypermobility type (HT-EDS) is the most difficult to diagnose. This condition is an autosomal dominant trait and is more common in females. The HT-EDS represents a clinical continuum with the so-called (benign) joint hypermobility syndrome (JHS) [Grahame, 1999; Tinkle et al.,

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TABLE II. General, Neurological, Cardiovascular, Gastrointestinal, Urogynecological and Ear–Nose–Throat Findings

Characteristic	Patients																					Total (%)
Patient no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Sex	F	F	F	F	F	F	M	M	F	F	F	F	M	F	F	F	F	F	F	F	F	18F/3M
Age at diagnosis	49	39	58	57	25	41	53	15	25	36	8	45	26	41	13	38	36	32	34	14	45	n.a.
Neurological																						
Monolateral eyelid ptosis	+	−	+	−	+	+	−	+	−	−	−	+	−	−	−	−	−	+	+	−	−	8/21 (38.1)
Chronic asthenia/fatigue	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+	+	−	+	18/21 (85.7)
Recurrent headaches	+	+	+	+	−	+	+	+	+	−	+	+	+	−	−	−	+	+	+	−	+	15/21 (71.4)
Memory disturbances	+	+	+	+	−	n.a.	+	+	−	−	−	+	+	+	−	+	−	−	+	−	+	12/20 (60.0)
Anxiety/depression	+	+	+	+	−	+	+	+	+	+	−	+	−	+	−	−	+	−	−	−	+	13/21 (61.9)
Cardiovascular																						
Cardiac valve disease[a]	+	+	+	+	+	+	−	−	+	+	n.a.	n.a.	+	+	+	+	+	+	−	+	+	16/19 (84.2)
Respiratory insufficiency	+	+	+	n.a.	−	+	n.a.	n.a.	+	−	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	+	n.a	n.a.	n.a.	+	7/9 (77.8)
Varicous veins/hemorrhoids	−	−	+	−	−	+	+	−	−	−	−	−	−	−	−	−	−	−	+	−	+	5/21 (23.8)
Gastrointestinal																						
Dyspepsia/chronic gastritis	+	+	+	−	+	+	−	+	−	+	−	+	+	−	−	+	+	+	−	+	+	14/21 (66.7)
Gastroesophageal reflux	−	+	−	−	+	+	−	+	−	+	+	−	−	+	−	+	+	+	+	−	+	12/21 (57.1)
Recurrent abdominal pain	−	+	+	−	+	+	−	+	−	+	+	+	−	−	−	+	+	+	−	+	+	13/21 (61.9)
Constipation/diarrhea	+	+	+	+	+	+	−	+	−	+	+	+	−	−	−	−	+	+	+	−	+	7/21 (33.3)
Umbilical hernia	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	1/21 (4.8)
Urogynecological																						
Prolapses	−	+	−	−	−	−	−	−	−	+	−	+	−	−	−	−	−	−	−	−	+	4/21 (19.0)
Stress incontinence	+	+	−	+	+	+	−	−	−	+	−	+	−	−	−	−	−	−	−	−	+	8/21 (38.1)
Dyspareunia	n.a.	n.a.	+	+	n.a.	n.a.	n.a.	n.a.	−	−	n.a.	n.a.	n.a.	−	n.a.	+	−	−	−	n.a.	−	3/10 (30)
Ear-throat-nose																						
Dysphonia	+	+	+	+	−	−	−	−	−	+	+	−	−	+	−	−	−	+	−	−	−	8/21 (38.1)
Conductive hearing loss	+	−	+	−	−	+	−	−	−	−	−	−	−	+	−	−	−	+	−	−	−	5/21 (23.8)

TABLE I. Mucocutaneous and Muscoloskeletal Manifestations

Manifestations	Patients																					Total (%)
Patient no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Sex	F	F	F	F	F	F	M	M	F	F	F	F	M	F	F	F	F	F	F	F	F	18F/3M
Age at diagnosis	49	39	58	57	25	41	53	15	25	36	8	45	26	41	13	38	36	32	34	14	45	n.a.
General																						
Precipitous/Preterm delivery	−	−	+	−	−	−	−	−	−	+	−	−	−	−	−	+	+	+	+	−	−	6/21 (28.6)
Congenital dislocations	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	1/21 (4.8)
Failure to thrive	+	+	−	−	+	+	−	−	+	−	−	−	−	−	−	+	−	−	−	−	−	6/21 (28.6)
Delayed motor development	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	1/21 (4.8)
Mucocutaneous																						
Velvety/smooth skin	+	+	+	+	−	+	+	+	+	−	+	+	+	+	−	+	+	+	−	+	+	17/21 (80.9)
Hyperextensible skin	+	−	+	−	−	−	+	+	−	−	+	−	+	−	+	−	−	−	−	−	−	7/21 (33.3)
Skin fragility	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	+	−	−	−	−	2/21 (9.5)
Easy bruising	+	+	−	−	−	−	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	15/21 (71.4)
Piezogenic papules	+	+	−	+	−	+	+	+	−	n.a.	−	n.a.	−	+	−	+	+	+	−	+	+	12/19 (63.2)
Keratosis pilaris	−	−	−	−	−	−	+	+	−	−	−	−	+	+	−	−	+	−	+	−	−	6/21 (28.6)
Raynaud/Acrocyanosis	−	+	−	−	+	−	+	+	−	−	−	+	+	−	−	−	−	+	−	+	−	8/21 (38.1)
Gingival fragility	+	−	+	−	−	+	−	−	−	+	+	+	+	+	−	−	−	+	−	+	+	11/21 (52.4)
Recurrent caries	+	−	−	+	−	+	+	−	−	−	+	+	+	+	−	+	−	+	+	−	+	12/21 (57.1)
Muscoloskeletal																						
Infancy/childhood joint hypermobility	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	21/21 (100)
Residual joint hypermobility	+	+	+	−	+	+	−	+	+	+	n.a.	−	−	−	+	−	+	−	−	+	+	13/20 (65)
Articular dislocations	+	+	+	+	+	+	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	18/21 (85.7)
Ankle	+	+	+	+	+	+	−	−	−	−	+	+	−	+	−	+	+	+	+	−	+	14/21 (66.7)
Knee/patella	+	−	+	−	−	+	−	−	−	−	−	−	−	+	+	−	−	−	−	−	+	6/21 (28.6)
Hip	−	−	−	−	−	+	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	2/21 (9.5)
Fingers	−	−	+	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	3/21 (14.3)
Wrist	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	1/21 (4.8)
Elbow	+	−	+	−	−	−	−	−	−	−	+	+	−	−	−	+	−	−	−	−	−	5/21 (23.8)
Shoulder	−	−	+	−	−	+	−	−	−	−	−	+	−	−	−	+	−	+	−	−	−	5/21 (23.8)
Rib	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	1/21 (4.8)
Temporomandibular	+	+	+	−	+	+	−	−	+	−	−	+	−	+	−	−	−	+	+	+	+	12/21 (57.1)
Ligament ruptures	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	+	3/21 (14.3)
Joint effusions	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	2/21 (9.5)
Rec/chronic back pain	+	+	+	+	+	+	−	+	−	+	−	+	+	+	−	+	+	+	+	+	+	17/21 (80.9)
Rec/chronic myalgias	+	+	+	+	+	−	−	−	+	−	+	+	+	+	+	+	+	+	−	+	+	16/21 (76.2)
Rec/chronic arthralgias	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	20/21 (95.2)

Stanitski D ym Orthopaedic Manifestations of Ehlers-Danlos Syndrome. Clin. Orhthopaedisc and Related Research 2000; vol 376 July:213-221

	EDS I	EDS II	EDS III	EDS IV
skolioosi	54%	11%	39%	33%
Selkä- ja niskakipu	77%	89%	83%	83%
nivelkipu	69%	89%	100%	67%
nivelturv.	31%	67%	60%	50%
dislok.	54%	78%	83%	50%

Stanitski jatkoa – huom EDS potilaiden kokonaistilanne ei ole ole parantunut vuosien aikana

	EDS I	EDS II	EDS III	EDS IV
kävelyvaik.	33 %	44%	85%	33%
portaiden nousuongelmia	45%	33%	63%	33%
grip-heikkous	38%	50%	83%	40%
ylär. ongelmat	56%	50%	92%	33%
apuvät. tarve	46%	78%	77%	67%

EDS ja raskaus

- Yhdyntäkipuja , hauras iho, mustelmia
- Lantio löystyy huomattavasti, vaikeuksia pukea, liikkua, - tukiliivi
- Kuuluu riskiraskauksiin, erityisesti EDS IV !!
- Synnytys yleensä hyvin nopea (taksi, koti…)
- Hankalia vuotoja harvoin (2 kpl)
- Synn. lonkat menneet sijoiltaan ponnistusvaiheessa
- Suositetaan sectiota(Dutta 2011) (Sakala 1991)
- Lapsen käsittelyssä ongelmia (kantaminen, pukeminen)

EDS ja lapsuus

- ”veltto lapsi”, löysät lonkat, hidas motorinen kehitys, kipuja, niskaongelmia ?
- Koulussa liikuntanumero luokkaa 6 (4-10), ei voi tehdä rekkiliikkeitä, ei nojapuita, ei pallopelejä
- Kirjoittaminen käsin ja koneella hankalaa, huono käsiala
- ”ei tee ryhdikästä vaikutelmaa” velton ja laiskan leima herkästi

EDS ja kipu

- EDS- potilailla kipua on jatkuvasti, kivun ”syy” on auki??
- puudutteet eivät toimi (III-ryhmä), iho ei kestä laastareita
- ”et voi olla kipeä koska olet niin notkea” Suomen hoitojärjestelmä on kehitetty jäykille.
- panadoli ja kodeiini linjaus, ei mielellään tulehduskipul. (vuotoriski), opiaatit - suolistolama vaarana, lihasrelaksantit eivät ole järkeviä? baclofeeni?
- fys. hoidot, manipulaatiot, ortoosit
- kipuihin ei ole oikein löytynyt toimivaa ratkaisua.
- kyseessä ei ole ”kivun kroonistuminen” vaan kipu ollut aina enempi läsnä syntymästä lähtien.

Medication, Surgery, and Physiotherapy Among Patients With the Hypermobility Type of Ehlers-Danlos Syndrome

Lies Rombaut, PT, MSc, Fransiska Malfait, MD, PhD, Inge De Wandele, PT, MSc, Ann Cools, PT, PhD, Youri Thijs, PT, PhD, Anne De Paepe, MD, PhD, Patrick Calders, MSc, PhD

ABSTRACT. Rombaut L, Malfait F, De Wandele I, Cools A, Thijs Y, De Paepe A, Calders P. Medication, surgery, and physiotherapy among patients with the hypermobility type of Ehlers-Danlos syndrome. Arch Phys Med Rehabil 2011;92:1106-12.

Objectives: To describe medication use, surgery, and physiotherapy, and to examine the effect of these treatment modalities on functional impairment and amount of complaints among patients with the hypermobility type of Ehlers-Danlos syndrome (EDS-HT).

Design: Cross-sectional study.

Setting: Physical and rehabilitation medicine department and center for medical genetics.

Participants: Patients with EDS-HT (N=79; 8 men, 71 women) were recruited for this study.

Interventions: Not applicable.

Main Outcome Measures: Patients filled out questionnaires regarding type of complaints, medication use, surgery, physiotherapy, and outcome of treatment. Functional impairment in daily life was measured by the Sickness Impact Profile. Pain severity was assessed with visual analog scales.

Results: Patients reported a large number of complaints, a considerable presence of severe pain, and a clinically significant impact of disease on daily functioning. Most patients (92.4%) used medications, among which analgesics were the most prevalent. Fifty-six patients (70.9%) underwent surgery, including mainly interventions of the extremities and abdomen. Forty-one patients (51.9%) are currently enrolled in a physical therapy program, mainly comprising neuromuscular exercises, massage, and electrotherapy. Patients with a high consumption of analgesics, who visited the physiotherapist, or who underwent surgery had a higher dysfunction in daily life. Only 33.9% of the patients who underwent surgery and 63.4% of patients in physical therapy reported a positive outcome.

Conclusions: Patients with EDS-HT have numerous complaints and an impaired functional status that strongly determine their high rate of treatment consumption. The outcome of surgical and physiotherapy treatment is disappointing in a large percentage, which illustrates a strong need for evidence-based therapy.

Key Words: Ehlers-Danlos syndrome; Drug therapy; General surgery; Physiotherapy; Rehabilitation.

EHLERS-DANLOS SYNDROME (EDS) is a group of heritable connective tissue disorders characterized by defects in the biosynthesis of fibrillar collagens, the secretion of fibrillar collagens, or both.[1-3] Among all connective tissue disorders, EDS is thought to be the most prevalent (1:5000–1:10,000).[1,3] The 3 prominent features of this disorder are skin laxity, joint hypermobility, and tissue fragility.[4,5] According to the Villefranche criteria, 6 major types are recognized on clinical, genetic, and biochemical grounds.[5,6] However, most patients with EDS have the hypermobility type (EDS-HT), in which generalized severe joint hypermobility, joint dislocations, and chronic pain are important manifestations.[6] Furthermore, fatigue, muscle weakness, and muscle cramps are common associated features.[7-12] Overall, EDS-HT is considered to be a severe, chronic musculoskeletal disorder.

Chronic musculoskeletal disorders require more attention from society and health care systems because they are the most common causes of impairment leading to deterioration in health-related quality of life.[13] Moreover, these conditions inflict an enormous direct (health care utilization) and indirect (loss of productivity) cost on health care systems.[14]

Regarding EDS-HT, many patients are subject to the burden of delayed diagnosis and misdiagnosis, incredibility when seeking health care, and inappropriate treatment.[15-17] Because EDS is a complex disorder that is often not visible externally at first glance, and because knowledge concerning EDS is very limited among health care professionals, this challenging disorder generally receives little attention in clinical practice and research. Consequently, treatment of EDS-HT is currently poorly defined and described.

Levy[18] mentions different types of treatment for EDS, such as physiotherapy (electrotherapy, hydrotherapy, massage, low-resistance muscle-toning exercise, core stability training), medication (mainly pain management, supplementation with magnesium, glucosamine, and chondroitin), surgery (orthopedic, gastrointestinal, and cardiovascular procedures), and psychological treatment (consumer support groups, cognitive-behavioral therapy). However, the description of these treatment modalities is based on theoretic concepts and practical knowledge of other disease states with local or general problems comparable to those of EDS-HT. Currently, objective data on the different types of treatments consumed by patients with EDS-HT and the effect of these treatments are lacking. Therefore, the purpose of this study was to describe medication use,

List of Abbreviations

EDS	Ehlers-Danlos syndrome
EDS-HT	hypermobility type of EDS
NSAIDs	nonsteroidal anti-inflammatory drugs
SIP	Sickness Impact Profile
TENS	transcutaneous electrical nerve stimulation
VAS	visual analog scale
WHO	World Health Organization

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EDS ja fysioterapia

- EDS perinnöllinen sairaus jossa perusvika on kudosten tukirakenteissa eli kollageeneissa.
- EDS ei ole sisutauti. ts kovakaan harjoittelu ei paranna pikemmin päinvastoin.
- Fysioterapia on lähempänä neurologista kuntoutusta, ohjataan liikeratoja, koordinaatiota, proprioseptiikkaa, apuna eri ortoosit, kinesioteippaus, peilit, musiikki.
- Ei venytyksiä, ei max. voimaharjoitteita (dyn. tai staattinen)
- Kuorma luokkaa 20 % maksimista, liikeradan pitää säilyä ehjänä. Toistoja normaalia vähemmän
- Rombautin (2011) tutk. 63.4 % hyötyi fys. terap. eri muodoista.
- Miten saadaan harjoitusvaikutus?

Työ- jatoimintakyky

I. notkea ei haittaa: beighton 5-9/9, kestovoima hyvä, koordinaatio hyvä, ei kovia kipuja. Ei ehkä hammaslääkäri, ei fysioterapeutti.

II. Lievä haitta: ajoittain kipuja, vaikeuksia olla pitkän aikaa samassa asennossa, kestovoimaa ei ole, pinsettiote on pitävä, sormet eivät subluksoidu, pystyy kantamaan käsillä (olat eivät luksoidu). Ammatinvaidoksia.

III. Keskivaikea haitta: kestovoimaa ei ole, sormet ja olat luksoituvat, vaikea kävellä, nilkat nyrjähtelevät, hankalat kivut, huono käsiala, vaikea pukea, pinsettiote löysä, purkkeja ei saa auki, kovaa ruokaa ei voi purra. Norm. lyhyempi työura. Työura katkonainen. Ammatinvaihdoksia.

IV. Vaikea haitta: ADL ongelmia jatkuvasti, leukalukkoja, niveliä sijoiltaan esim yöllä itsestään, jatkuvat hoitoresistentit kivut, mustelmat, suolisto-ongelmat, kävelyongelmat (vrt MS), niskapäänsärky. Näillä on henk. Koht. avustaja, pyörätuoli. Eivät ole työelämässä. Vaikeavammaisia.

1. Usein muut sairaudet esim. chiari määrittävät työkykyä merkittävästi
2. Kaikissa maissa EDS potilaiden tilanne on samansuuntainen: keskeinen osa työttömiä osa työkyvyttömiä, piilotyöttömyys ongelmana, osa kotiäitejä, osa jatkaa opiskeluja

45 v nainen, EDS klassinen

- Lapsuudessa kipsimuotit ja jalkatuet, ortopediset jalkineet
- Koulussa lihasrepeämiä, liikuntatunnit vaikeita
- Vaikea käyttää busseja - olat menevät sijoiltaan, bussiin nousu hankalaa
- L5 listeesi ja lyysi
- Von Willebrandtin tauti
- Lasiaisen irtoama
- Osteoporoosi
- Aorttaläpän vuoto Mri:llä 49-55%
- Anestesioista ollut vaikea herätä…Chiari!
- Lähisukul. kuollut massiiviseen vuotoon leikkauksessa

Yhteistyö on keskeistä, team

- Perinnöllisyyslääkäri, alaryhmät, diagnoosi, harvinaisten osalta – erityisesti IV
- Fysiatri ehkä päävastuussa: ADL, kuntoutus, työkyky.
- Sisätautilääkäri; reumatologi, gastroenterologi, gastrokir.
- Infektiolääkäri, keuhkolääkäri, ihot lääkäri
- Verisuonikirurgi huom ryhmä IV. CT herkästi!!!
- Ortopedi, neurokirurgi, hammaslääkäri, suukirurgi
- Fysioterapeutti, Toimintaterapeutti, Psykologi
- European Organisation for Rare Diseases (EURORDIS), potilaskortti
- Yhdistykset eri maissa: esim. Suomi, Englanti
- www.ehlers-danlos.org (UK-support group)
- Orphanet, OMIM 13000, *10, *20 ja *50
- Suomen Ehlers-Danlos Yhdistys SEDY-ry

kiitos