Teaching Course 10

Clinical science in muscle disorders (Level 2)

Differential diagnosis of “scapular winging”

Antonio Toscano
Messina, Italy

Email: atoscano@unime.it
Differential diagnosis of “Scapular Winging”

A. Toscano
Head of European Reference Center (ERN EUROMUSCULAR) for Neuromuscular Disorders,
UOC Neurologia e Malattie Neuromuscolari
University of Messina, Italy

DISCLOSURES

Prof. A. Toscano has received reimbursement for educational motivations and having served as a member of scientific boards for Sanofi Genzyme, Amicus, Spark and CSL Behring
Scapular dyskinesis

Collective term that refers to movements of a “dysfunctional scapula”

Scapular dyskinesis has been defined as:

1) abnormal static scapular position and/or dynamic scapular motion, characterized by medial/lateral border prominence; 2) Inferior angle prominence and/or early scapular elevation; 3) rapid downward rotation during arm lowering.

Scapular dyskinesis can also be a painful condition

There are multiple causative factors, both proximally (muscle weakness, nerve injury) and distally (acromioclavicular joint injury, superior labral tears, rotator cuff injury).

Dyskinesis can alter the roles of the scapula in the “scapulo–humeral rhythm”: dynamic interaction between the scapula and the humerus.

This can be due to alterations in the bony stabilizers, alterations in muscle activation patterns or strength in the dynamic muscle stabilizers.

Scapular Winging:
a dysfunction involving the stabilizing muscles of the scapula resulting in imbalance and abnormal motion of the scapula
Why the patients refer to a physician because of a Scapular Winging?

- Muscle weakness
- Pain
- Aesthetic change
**Main causes of Scapular Winging**

**Traumatic**
- Nerves injuries
- Muscles trauma
- Attachments alterations

**Non Traumatic**
- Structural anomalies of the scapula
- Osteochondroma
- Fractures
- Neurogenic causes
- Muscle disorders
Scapular movements abnormalities

Lateral Winging

Medial Winging
The Long Thoracic Nerve originates from branches of the C5 and C6 nerve roots. These branches join beneath the middle scalene muscle and with some variability, either pierce the middle scalene or emerge between the middle and anterior scalene before uniting with a branch of the C7 (and sometimes C8) nerve root. The long thoracic nerve travels through the axilla to innervate the serratus anterior muscle- a shoulder protractor and scapular stabilizer. Injury to the long thoracic nerve denervates the serratus anterior muscle, resulting in scapular winging and shoulder instability.
Neurological examination at admission

- Wasting of supraspinatus, deltoide, dentate, brachial biceps, triceps, flexors and extensors antibrachiali on the left
- Frequent fasciculations of the affected muscles
- Intense myalgia at rest and/or after abduction of left upper limb
- OT reflexes: normal

<table>
<thead>
<tr>
<th>Gruppo muscolare</th>
<th>Dx</th>
<th>Sn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flessori del collo</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Estensori del collo</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Abduttori della spalla</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Rotatori della spalla (laterali esterni)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adduttori orizzontali della spalla</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Flessori del gomito</td>
<td>5</td>
<td>4-</td>
</tr>
<tr>
<td>Estensori del gomito</td>
<td>5</td>
<td>4-</td>
</tr>
<tr>
<td>Estensori del polso</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Flessori del polso</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Estensore comune delle dita</td>
<td>5</td>
<td>4+</td>
</tr>
<tr>
<td>Flessori delle dita</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Estensori dell’anca</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Adduttori dell’anca</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Abduttori dell’anca</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori dell’anca</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Estensori del ginocchio</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori del ginocchio</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori dorsali del piec</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Eversori del piec</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Inversori del piec</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori plantari del piec</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessore dorsale I dito</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori dorsali dita</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Flessori plantari dita</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Orbicolari palpebre</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Peribuccali</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>
Laboratory examination

Blood routine analyses: normal apart from HbA1C (8.5%)

Brain and cervical spine MRI: normal

EMG/ENG: neurogenic pattern with denervation and collateral reinnervation on left supraspinatus, deltoid, triceps and brachial biceps muscles.

MEPs: normal

Cerebrospinal fluid examination: 1 cell (n.v 0-5), 80 mg/dl proteins (n.v 0-45)

DIAGNOSIS: Disimmune plexopathy (Parsonage - Turner syndrome)

THERAPY: IVIG (0.4 g/Kg/die for 5 days)
Parsonage-Turner syndrome

Parsonage-Turner syndrome (PTS) is characterized by a rapid onset of severe pain in the shoulder and arm. The acute period may last for few hours till few weeks.

Usually, patients may experience wasting and weakness (Neuralgic Amyotrophy) of the affected muscles.

PTS involves mainly the brachial plexus.

The involved nerves control movements and sensations in the shoulders, arms, elbows, hands, and wrists.

Exact causes of PTS are unknown, but it could be related to alterations of the immune system (immune-mediated disorder).

Affected individuals may recover after specific treatment: strength returns to the affected muscles and pain goes away. Sometimes, a positive evolution occurs without treatment.

However, some affected individuals may experience residual pain and potentially significant disability.
Case report

Male, 47 years of age,

No family history of neuromuscular disorders. Parents not consanguineous.

At the age of 39 years, fatigability in running and in climbing the stairs, muscle cramps, fasciculations, and scapular winging.

In the following years, increased muscle involvement, predominantly affecting upper limbs, pelvic girdle and legs antero-lateral compartment muscles. At 44 years of age, difficulties in swallowing.

At admission, neurological examination showed: waddling gait with bilateral "steppage", not able to raise from the floor and needed support to stand up from a chair and from the bed

**Neurological examination**: Scapular Winging and severe muscle atrophy in the legs (predominantly at the anterior compartment). Marked weakness of the periscapular muscles with severe limitation of the arms abduction bilaterally; weakness (MRC 3) also present at the following muscles: iliopsoas, gluteus, tibialis anterior bilaterally. OT reflexes: brisk at upper limbs, absent at lower limbs.
Laboratory investigations

CK: 204 U/l
EMG: a neurogenic pattern with hallmarks of denervation and collateral re-innervation in all examined muscles
MEPs: normal
Muscle biopsy (vastus lateralis muscle): variability of fiber size, muscle grouping and several angulated fibers


Diagnosis: Lower Motor Neuron disease VCP-related
This mutation has been associated with atypical forms of amyotrophic lateral sclerosis with variable degree of cognitive impairment and in inclusion body myopathy with Paget disease of the bone and frontotemporal dementia (IBMPFD).

Muscle disorders

- Dystrophy
- FSH: Often asymmetric
- LGMD
  - 1F: TNPO3
  - 2A: Calpain 3
  - 2D: α-Sarcoglycan
  - 2E: β-Sarcoglycan
  - 2I: FKRP
  - 2N: POMT2
  - 2S: TRAPPC11
  - 2Z: POGLUT1
- Emery-Dreifuss
- Myopathy + Paget's disease of bone with Dementia (VCP)
  - Type 2
- Desmin myopathy
  - Early onset, Recessive
  - KAESER, Dominant

Scapuloperoneal syndromes

ACTA1: 1q42;
Centronuclear myopathy (Adult-onset): MYF6; 12q21;
Davidenkov's syndrome
Emery-Dreifuss Dystrophies
FSHD with ragged red fibers & cardiomyopathy
Glycogen storage
  - Acid maltase deficiency with scapuloperoneal weakness
  - Phosphorylase deficiency (McArdles)
KAESER: Desmin; 2q35
Myopathy + Paget's disease with Dementia: VCP; 9p13
Retardation & Cardiomyopathy: LAMP-2; Xq24
Scapuloperoneal MD (SPMD) with Hyaline bodies
  - Type 1: FHL1; Xq26; Type 2: MYH7; 14q12; Type 3: MYH7; 14q12;
  - Myosin storage myopathy: MYH7; 14q12
Scapuloperoneal neuronopathy: TRPV4; 12q24

Others neuromuscular forms
FSHD

- Third most common muscular dystrophy
  - prevalence of ~1:15,000-20,000
- Age of onset is variable from presentations at birth to late life
- Penetrance is high with 95% of patients manifesting weakness by age 20
- Classically, the disease presents with facial, proximal arm weakness with winged scapula followed by weakness of foot dorsiflexion and hip girdle muscles
- Asymmetric involvement is frequent
- Bulbar, extraocular, and respiratory muscles tend to be spared
- 20% of the patients wheelchair bound and 1% with respiratory weakness
- Typical symptoms (facial or scapulo-humeral weakness) on presentation in ~70-85%
- No facial involvement in 6-18%
- Case reports of:
  - Facial-sparing scapular myopathy
  - Limb-girdle weakness
  - Late-onset distal myopathy after age 50
  - Asymmetric brachial weakness
  - Isolated axial weakness
  - Monomelic lower limb atrophy

Beevor's sign

Poly-Hill Sign
A novel clinical tool to classify facioscapulohumeral muscular dystrophy phenotypes

Giulia Rizzo1,2, Lucia Ruggiero1, Liliana Verrelli1, Francesco Scena1, Ana Nikola1, Monica Govi1, Fabiano Mele1, Jessica Dondi1, Corrado Angelini1, Giovanni Antoniazzi1, Angela Berardini1, Elisabetta Busc1, Michelangelo Cavo1, Maria Chiara D'Amico1, Grazia D'Angelo1, Antonio Di Muzio1, Massimiliano Flosio1,2, Lorenzo Maggi1, Maurizio Moggi1, Tatiana Mongini1, Lucia Morandi1, Elena Pegoraro1, Carmelo Rodolico1,2, Luca Santoro1,2, Gabriele Siciliano1, Giuliano Tomelleri1,2, Luisa Villa1,2, Rossella Tupiz1,2

Received: 9 January 2016 / Revised: 6 April 2016 / Accepted: 7 April 2016 / Published online: 28 April 2016
© The Author(s) 2016. This article is published with open access at SpringerLink.com

Abstract Based on the 7-year experience of the Italian Clinical Network for FSHD, we revised the FSHD clinical form to describe, in a harmonized manner, the phenotypic spectrum observed in FSHD. The new Comprehensive Clinical Evaluation Form (CCEF) defines various clinical categories by the combination of different features. The inter-examiner reproducibility of the CCEF was assessed between two examiners using kappa statistics by evaluating 56 subjects carrying the molecular marker used for FSHD diagnosis. The CCEF classifies: (1) subjects presenting facial and scapular girdle muscle weakness typical of FSHD (category A, subcategories A1–A3), (2) subjects with muscle weakness limited to scapular girdle or facial muscles (category B, subcategories B1, B2), (3) asymptomatic/healthy subjects (category C, subcategories C1, C2), (4) subjects with myopathic phenotype presenting clinical features not consistent with FSHD canonical phenotype (category D, subcategories D1, D2). The inter-examiner reliability study showed an excellent concordance of the final four CCEF categories with a κ equal to 0.90, 95% CI (0.71; 0.97). Absolute agreement was observed for cate-

---

G.A., 40 year-old, male

- Parents not consanguineous; no family history of neuromuscular disorders
- Since 20 years of age, unilateral (dx) scapular winging and weakness at upper right limb
- Since 32 years of age, bilateral upper limb weakness
- At 36 years of age, mild distal weakness lower limbs
- CK 504 U/l
- EMG: small MUPs.
- EKG: normal
Laboratory examination

Normal IHC for dystrophin, sarcoglycans, dysferlin, caveolin, desmin

WB for calpain and dysferlin normal

Large presence of vacuoles

GAA, glycolytic and glycogenolytic enzyme activities: normal

Genetic analysis: PFGE analysis of DNA fragments digested with EcoRI and EcoRI/Bln1 and hybridated with p13E-11 showed a 35Kb allele of 4qcr compatible with FSHD diagnosis

Diagnosis

Facio-Scapulo-Humeral Muscular Dystrophy with atypical morphological aspects
Facioscapulohumeral muscular dystrophy presenting with unusual phenotypes and atypical morphological features of vacuolar myopathy

Peter Reilich · Nicolai Schramm · Benedikt Schoser · Peter Schneiderat · Nicola Strigl-Pill · Josef Müller-Höcker · Wolfram Kress · Andreas Ferbert · Sabine Rudnik-Schöneborn · Johannes Noth · Hanns Lochmüller · Joachim Weis · Maggie C. Walter

Received: 23 September 2009 / Revised: 15 January 2010 / Accepted: 15 January 2010 / Published online: 10 February 2010
© Springer-Verlag 2010

LGMD2A
CAPN3 gene mutation: Homozygous 1981delA

Heart: normal function
FVC: 2.28 litres, 92%
**Limb-Girdle Muscular Dystrophy due to Calpain deficiency (LGMD2A)**

Prevalence: 1-9/100000

Autosomal recessive limb-girdle muscular dystrophy
Variable age of onset

Progressive, typically symmetrical and selective weakness and atrophy of proximal shoulder- and pelvic-girdle muscles (gluteus maximus, thigh adductors, and muscles of the posterior compartment of the limbs mainly affected)
Usually no cardiac or facial involvement.
Main clinical manifestations are exercise intolerance, waddling gait, scapular winging and calf pseudo-hypertrophy.

**Heart:** normal function

**FVC:** 2.77 litres, 59%

**LGMD2D**

**SGCA gene mutation:** 371C>T & 739G>A

Courtesy
GL Vita
V. Straub
Limb-girdle muscular dystrophy due to alpha-sarcoglycan deficiency (LGMD2D)

Autosomal recessive limb-girdle muscular dystrophy type 2D (LGMD2D)
Prevalence: unknown

Adolescent or childhood onset

Progressive proximal weakness of the shoulder and pelvic girdle muscles
Main clinical aspects: difficult walking, scapular winging, calf hypertrophy and Achilles tendon contractures, often leading to a tiptoe gait pattern.
Cardiac and respiratory involvement is quite rare
**Limb-Girdle Muscular dystrophy due to FKRP deficiency (LGMD2I)**

An autosomal recessive limb-girdle muscular dystrophy type 2I

Highly variable age of onset
Slowly progressive proximal weakness of the pelvic and shoulder girdle musculature (predominantly affecting the lower limbs)

Main clinical manifestations: waddling gait, scapular winging, calf and tongue hypertrophy, exercise-induced myalgia, myoglobinuria and/or elevated creatine kinase serum levels. Abdominal muscle weakness, cardiomyopathy, respiratory muscle involvement and various brain abnormalities reported.
TRPV4 related scapuloperoneal spinal muscular atrophy: Report of an Italian family and review of the literature
F. Biasini a, S. Portaro a, A. Mazzon c, G. Vita a, G.M. Fabrizi a,d, F. Taioli a,d, A. Toscano a, C. Rodolico a,b,∗
a Institute for Neuroscience, University of Modena, Modena, Italy
b Department of Neurological, Biomedical and Movement Sciences, University of Verona, Verona, Italy
c Department of Neurosciences, University of Padua, Padua, Italy
d Department of Neurosciences, University of Modena, Modena, Italy
Received 13 December 2015; accepted 15 February 2016

Abstract
Scapuloperoneal spinal muscular atrophy (SPSMA) is a rare autosomal dominant disorder caused by heterozygous mutations in the transient receptor potential cation channel (TRPV4) gene, characterized by progressive scapuloperoneal atrophy and weakness. Additional features, such as vocal cord paralysis, rhinorrhea and/or arthrogryposis, are likely to occur. We report the first Italian family with SPSMA, harbouring the c.860G>A mutation in TRPV4 gene (p.R269H). The pattern of expression was variable: the father showed a mild muscular involvement, while the son presented at 16th skeletal dysplasia and a progressive course. We reinforce the concept that the disease can be more severe in the following generations. The disorder should be considered in scapuloperoneal syndromes with autosomal dominant inheritance and a neurogenic pattern. The presence of skeletal deformities strongly supports this suspicion. An early diagnosis of SPSMA may be crucial in order to prevent the more severe congenital form.

© 2016 Elsevier B.V. All rights reserved.
Winged scapula in patients with myotonic dystrophy type 1 1,2

Tadahito Hamamoto 3, Tatsuro Murakami 4,5, Mikko Hirayama 6, Hidenasu Uenaito 5, Isao Hirochi 7, Hiroshi Kogo 8, Fujio Umehara 9, Kyoichi Konakami 5, Masaru Kariyama 6

1 Surgical Department of Internal Medicine, Faculty of Medical Science, University of Hokkaido, Sapporo, Japan
2 Department of Neurology, People's Health University, Toyama, Japan
3 Department of Neurology, Keisai Municipal Hospital, Kanagawa, Japan
4 Third Department of Neurology, Showa University Medical School, Kiyose, Tokyo, Japan
5 Department of Neurology, Jikei University School of Medicine, Minato-ku, Tokyo, Japan
6 Department of Radiology, Sapporo Medical University, Sapporo, Japan

Received 18 October 2001; revised in revised form 21 February 2002; accepted 17 April 2002

Abstract
We report two patients with myotonic dystrophy type 1 (DM1) showing winged scapula in a single family. Genetic analysis revealed a muscle-specific expansion of CTG repeats in the 3'-untranslated region: 1180 in patient 1 and 647 in patient 2. Muscle biopsy findings showed normal muscle architecture and variation in fiber size. One of the patients showed capture of cells in muscles of the upper limbs. To our knowledge, this is the first report of winged scapula in DM1.

Fig. 2. Muscle MRI findings of the upper thoracic level. Atrophy of the sternocostal head (A: arrow head) and internal intercostal (B: arrow) muscles was observed in patient 1 (A) and patient 2 (B). Muscle MRI of the thoracic level in a myotonic dystrophy type 1 patient (60-year-old man)

Case report
50 years to diagnosis: Autosomal dominant tubular aggregate myopathy caused by a novel STIMI mutation

Maggie C. Walter 1,2, Martina Rossius 1, Manuela Zitzelsberger 1, Matthias Vogler 1, Wolfgang Müller-Felber 1, Birgit Ertl-Wagner 1, Yaxin Zhang 1, Heinrich Brinkmeier 1, Jan Senderek 4, Benedikt Schoser 1

1 Friedrich-Baur-Institut, Department of Neurology, Ludwig-Maximilians-University of Munich, Munich, Germany
2 Institute of Pathobiology, Ernst Moritz Arndt University Greifswald, Greifswald, Germany
3 Department of Neurophysiology, Dr. von Hauner Children's Hospital, University of Munich, Munich, Germany
4 Departments of Radiology, Ludwig-Maximilians-University of Munich, Munich, Germany

Received 1 October 2004; revised in revised form 6 April 2015; accepted 8 April 2015

Abstract
Tubular aggregates in human muscle biopsies have been reported to occur in a variety of acquired and hereditary neuromuscular conditions since 1964. Recently mutations in the gene encoding the main calcium sensor in the sarcoplasmic reticulum, stromal interaction molecule 1 (STIM1), have been identified as a cause of autosomal dominant tubular aggregate myopathy. We studied a German family with tubular aggregate myopathy and defined cellular consequences of altered STIM1 function. Both patients in our family had early progressive myopathy with proximal and distal weakness, scapular winging, respiratory failure, joint contractures and external ophthalmoplegia. One patient had a well-documented disease course over 50 years. Sequencing of the STIM1 gene revealed a previously unreported nonsense mutation (c.2620G>A; p.Gly81Amp) located in the first calcium binding EF domain. Functional characterization of the new STIM1 mutation by calcium imaging revealed that calcium influx was significantly increased in primary myoblasts of the index patient compared to controls pointing at a severe alteration of intracellular calcium homeostasis. This novel family widens the spectrum of STIM1-associated myopathies to a more severe phenotype.
Conclusions

Scapular Winging is a rare, potentially debilitating disorder with many causative factors.

Diagnosis is largely clinical and relies on a large number of different suspects.

A common pitfall is the failure to undress the patient’s shoulders and back to the waistline, which permits adequate visualization of any obvious deformity.

Early diagnosis, rehabilitation and, in some cases, surgical intervention improve the outcomes of patients.
AIM GROUP

Torino (T. Mongini - L. Vercelli)
Padova (C. Semplicini - E. Pegoraro)
Milano - Policlinico (M. Moggio - GP Comi)
Milano - Besta (L. Maggi)
Verona (P. Tonin)
Pavia (S. Ravaglia - C. Danesino)
Roma Gemelli (S. Servidei - G. Primiano)
Roma Tor Vergata (R. Mas - C. Terracciano)
Roma S. Andrea (G. Antonini - M. Garibaldi)
Chieti (A. Di Muzio - F. Ciccocioppo)
Brescia (M. Filosto - A. Todeschini)
Pisa (G. Siciliano - G. Ricci)
Bologna (R. Liguori)
Cagliari (G. Marrosu - R. Piras)
Napoli (G. Di Jorio)
Venezia (C. Angelini)

UOC Neurologia e Malattie Neuromuscolari
G. Vita
P. Girlanda
C. Rodolico
A. Mazzeo
O. Musumeci
S. Messina

Prof. A. van der Ploeg, The Netherlands
Prof. B. Schoser, Germany
Prof. P. Laforêt, France
Prof. M. Roberts, U.K.
Prof. J. Vissing, Denmark
Dr. Jordi Diaz Manera, Spain