

Development of a Disease Model for Sporadic Inclusion Body Myositis

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BACKGROUND

Sporadic Inclusion Body Myositis (sIBM)

- sIBM is a progressive, idiopathic inflammatory myopathy characterized by atrophy and weakness of proximal and distal muscle groups.
 - Atrophy of the quadriceps, wrist, and finger flexor muscles, as well as dysphagia are primary characteristics of the disease and result in significant functional disabilities with progression.
 - sIBM primarily affects individuals aged 50 years and older and is more common in men than in women.
 - Symptoms worsen over time, causing most patients to eventually lose ambulatory status and the ability to perform many routine activities of daily living.
 - Progressive weakness results in a loss of independence and the need for assistive devices and supportive care.
 - The diagnosis of sIBM is often delayed by 5 to 6 years due to slow disease progression.¹
- Currently, there are no marketed therapies for the treatment of sIBM but clinical trials are underway.
 - Supportive and symptomatic care is the basis of disease management.²
 - To understand impact on patients, a qualitative study was conducted to support the development of a disease model depicting relationships among patient concepts relevant to disease progression that may be impacted by the treatment of sIBM.
 - No such disease model is currently available.

OBJECTIVE

- To develop a disease model depicting the relationships among concepts relevant to the treatment of sIBM.

METHODS

Literature Review

- A search of published literature indexed on PubMed was conducted to identify concepts relevant for measurement in sIBM studies.
 - Articles published between January 2002 and March 2012 were identified for potential inclusion based on a predefined set of search criteria for studies:
 - Conducted with adults in clinical trials, observational studies, longitudinal studies, naturalistic studies, cross-sectional studies, retrospective or prospective cohort analyses, systematic literature reviews, surveys, or instrument validation studies
 - Published in English and since 2002 or earlier if identified as seminal by the authors

Patient Input

- A single-visit, observational study involving in-depth concept elicitation interviews was conducted in Philadelphia, Pennsylvania, and Columbus, Ohio.
 - Twenty patients across a range of functional limitation were included.
 - Participants met the following criteria:
 - Confirmed clinical diagnosis of sIBM (per Hilton-Jones or European Neuromuscular Centre criteria)
 - Aged 35-80 years
 - Able to read and understand English
 - Willing to participate in a 1-hour interview to discuss experiences related to sIBM

Analytical Methods

- The same two experienced interviewers conducted all participant interviews, following a semistructured discussion guide, and performed all data analysis and coding.
- Standard qualitative data collection and analytical methods followed two main guiding principles: researcher neutrality and systematic processing.
 - Using both interview transcripts and field notes, interviewers identified dominant trends in each interview and compared them with the results of other interviews to generate themes or patterns in the way participants described their disease experiences.
 - Constant comparative analysis³ allows the researcher to confirm an accurate reflection of each participant's views has been captured.
 - No formal statistical analyses were conducted.

RESULTS

Literature Review

- A summary of symptoms, impacts related to physical functioning, and psychosocial impacts were identified.
- Symptoms relating to progressive weakness and atrophy of the quadriceps, wrist, and finger flexor muscles were identified as the clinical hallmarks of sIBM, as were the following findings^{1,4-6}:
 - Progressive weakness over the course of disease
 - Frequent falls
 - Grip strength and fine motor skill impairment
 - Generalized sensory peripheral neuropathy in some patients
 - Foot drop
 - Difficulty standing from a sitting position
 - Dysphagia: swallowing difficulties, choking, interference with nutritional intake
 - Psychosocial impacts
- Age and sex differences were noted.

Patient Input

- Twenty individual concept elicitation interviews (Table 1 and Table 2) were conducted with patients with sIBM from June through September 2012.
- Four high-level concepts were explored:
 - Symptoms
 - Physical functioning
 - Psychosocial impact
 - Treatment expectations

- Tables 1 and 2 provide a summary of patient demographics and physical limitations.
 - Results from the concept elicitation interviews were grouped into the prevailing themes of symptoms, physical function and psychosocial impacts, and treatment expectations.

Table 1. Characteristics of Concept Elicitation Interview Participants

Characteristic	N = 20
Age at diagnosis, mean (range)	58.5 years (41-79 years)
Age at interview, mean (range)	66.9 years (46-81 years)
Sex, n (%)	
Male	18 (90.0%)
Female	2 (10.0%)
Education, n (%) ^a	
High school or equivalent (e.g., GED)	4 (21.1%)
Some college	4 (21.1%)
College degree	4 (21.1%)
Professional or advanced degree	7 (36.8%)
Race/ethnicity, n (%)	
White	18 (90.0%)
Asian	1 (5.0%)
Black	1 (5.0%)

GED = general education diploma.

^aEducation not available for one participant.

Table 2. Category Best Describing Current Level of Limitation

Current Level of Limitation ^a	n (%)
Increased muscular weakness, particularly of the thigh muscles and forearms	3 (15.8%)
Decreased ability to perform certain activities including writing, opening jars, standing from a seated position	2 (10.5%)
Impaired walking (tripping or falling)	2 (10.5%)
Use of cane when walking	3 (15.8%)
Use of a walker	3 (15.8%)
Use of a wheelchair	6 (31.6%)

^aCurrent level of limitation not available for one participant.

Symptoms

- Patients described an awareness of multiple physical symptoms often experienced for a number of years prior to receipt of a clinical diagnosis.
 - Participants noted weakness in lower and upper progressive extremities and corresponding physical limitations in activities.
 - Participants also noted unexplained tripping or falling.
 - Dysphagia was reported by just over half of study participants.
 - Subjects were worried and frightened over progression of symptoms.
 - Slow symptom progression was experienced by all participants and slightly less than half of participants (n = 9) also described visible muscle atrophy in forearms and legs.
 - Disease progression led to the use of assistive devices.
 - Ambulation: cane, walker, or wheelchair
 - Self-care: lift seats on toilets; devices for reaching, gripping, dressing
 - Complete loss of ambulation led to full dependence on a wheelchair and caregiver support for the majority of activities of daily living.
 - About half of participants (n = 9) expressed feelings of fatigue and tiredness.
 - Identification of the most concerning symptoms for participants was dependent upon the stage of disease progression.
 - For more severely impacted patients, the fear of falling (due to fear of injury and an inability to get up from the floor), fear of choking (due to dysphagia), and fear of loss of independence due to self-care issues were most concerning

Physical Functioning

- Functional impacts mirrored the physical symptoms described by participants
 - Ability to perform functions to complete activities of daily living such as the following:
 - Get up from chairs without arms
 - Get up from the floor
 - Ascend or descend stairs
 - Ascend or descend sidewalk curbs
 - Walking (including on different surfaces, inclines, distances)
 - Opening jars
 - Participants also noted a loss of independence and a severe reduction or complete inability to perform everyday household chores such as the following:
 - Cooking
 - Cleaning
 - Yard work
 - Half of participants noted that they had difficulty performing certain tasks required for work for pay or that they either had to retire or had to change professional positions because of their sIBM.
 - Fear of falls and actual falls modified behaviors and attempts at different physical functions.
 - Ability to participate in an active lifestyle including sports, recreational activities, or hobbies was severely impacted due to sIBM.
 - Participants discussed employing a variety of assistive devices such as the following:
 - "Pincher" bars to reach and grab items
 - Canes
 - Walkers
 - Wheelchairs
 - Full leg braces
 - Standing bars

Psychosocial Impact

- Participants reported social and familial impacts including:
 - Inability to go to social events because they can no longer navigate uneven surfaces or stairs at other people's homes or at sporting events
 - Navigating airports/airplanes
 - Eating in restaurants that have only booths or chairs without arms

- Most social interactions become "dramatically and drastically reduced" due to lack of independence and the need for friends to provide assistance with self-care activities.
 - Participants talked about the frustration they felt due to their increasing dependence on others.
 - Worry about becoming a burden
 - Concerns limiting the lifestyle of their significant
 - Disappointing others
 - Participants discussed impacts on sexual intimacy.
 - Half of participants expressed feelings of depression, and some described use of antidepressant medications.
 - Depression attributed to the inability participate or simply the nature of coping with a chronic disease
 - Participants also expressed feelings of anger, boredom, loneliness, fear, and denial.
 - Many participants also talked extensively about the social and emotional support received from spouses, children, other family members, friends, and neighbors.
 - Support groups such as the Myositis Association and a user's group called Keep In Touch and spiritual or religious affiliations were described as key reassurances and inspiration.

Treatment Expectations

- Currently, products are marketed for sIBM treatment.
- However, when queried, over half of participants indicated that halting or slowing the progression of their disease would be a satisfactory outcome.
- Participants also indicated that an increase in muscle mass and strength would be desirable.

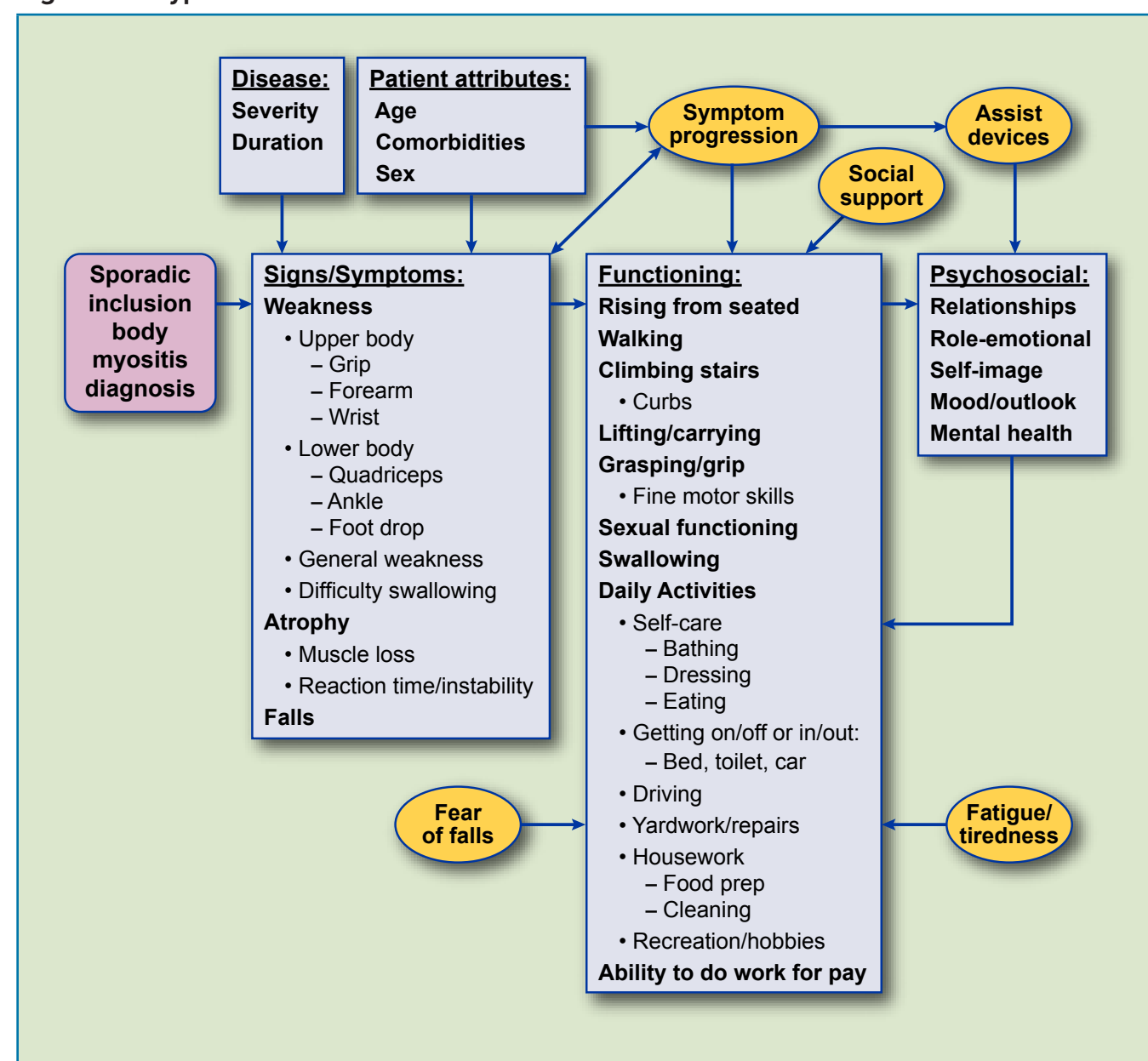
Other

- The majority of participants stated that the lack of awareness about sIBM in society and the general medical community was problematic.
- Participants frequently described extremely long time periods seeking diagnosis, misdiagnosis, and general frustration in finally obtaining a diagnosis and finding expert care.
- Participants expressed that an increase in scientific focus and general knowledge of sIBM would be very meaningful to them as new treatment options emerge.

Disease Model

- A disease model depicting a proposed pathway from a confirmed clinical diagnosis of sIBM, modifying factors, proximal concepts of signs and symptoms of disease, and functioning through more distal psychosocial concepts was generated to graphically portray the relationships of these concepts (Figure 1).

Figure 1. Hypothesized sIBM Disease Model



CONCLUSIONS

- This disease model is the first available for sIBM.
 - Illustrates how sIBM impacts patients
 - May be useful for the selection of clinical trial endpoints as well as increasing disease awareness

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