Early Symptoms of Autoimmune Arthritis (AIA)

International Foundation for Autoimmune Arthritis

Investigation into patient-reported symptoms of early disease and onset experiences

Problem / Question

Patients with AIA diseases may present with complex mix of onset symptoms which do not necessarily match traditionally understood symptom models. This broad symptom presentation can lead to misdiagnosis and delay in detection, referrals, diagnosis, & treatment.

Hypothesis

- Patients report a complex mix of onset symptoms in early disease which do not necessarily match traditionally understood symptom models.
- Results will support development of continued Symptom Mapping (SM) & Early Patient Symptom Models (EPSMs), for each individual disease & for the group as a whole, to aid earlier detection, referrals, diagnosis, & treatment.
- We will show the percent of Undifferentiated Connective Tissue Disease (UCTD) and Undifferentiated Spondyloarthropathy (USpA) diagnoses leading to full disease is higher than 15%, thus justifying aggressive treatment in the UCTD/USpA phase.

Project Overview

When asked, patients reported the inability to obtain a diagnosis that is correct & timely as a top frustration. This investigation begins a look into symptom reporting by the patient to determine what they are experiencing in early disease, if those symptoms match what is currently published about the diseases, & if their experiences overlap with other similar diseases, thus lending to delay in detection, referrals, & diagnosis.

Methods

Current Publications Master Lists (CPMLs) was created by logging symptoms reported by the American College of Rheumatology (ACR), National Institutes of Health (NIH), National Library of Health (NLH), & Mayo Clinic (MC), grading the frequency of listed symptoms, & asking Nonprofit Expert Organizations (NEOs) to review for validation of accuracy & to submit any missing symptoms. These were compared to respondent recall of onset in AIA. A survey was developed in FluidSurveys & administered online. Respondents were recruited from a variety of sources, including US rheumatologists & collaborating nonprofit organizations. Data was analyzed in Statwing, associations between symptoms & diseases were expressed in terms of Cramér's V, then ranked using a 5 Star symptoms rating scale.

Procedure

1. Reviewed & compared published symptoms lists to create Current Publications Master Lists (CPMLs) for each disease.
2. Symptoms recorded on CPMLs were based on the frequency in which they appeared (i.e. all, two, and/or one resource). Each CPML was distributed to a Nonprofit Expert Organization (NEO) to review for validation of accuracy & to submit any missing symptoms. The NEO Reviewers were: Spondylitis Association of America (SAA) for Ankylosing Spondylitis (AS) & Psoriatic Arthritis (PsA), Lupus UK (LUK) for Systemic Lupus Erythematosus (SLE), Sjögren's Syndrome Foundation (SSF) for Sjögren's Syndrome (SS), International Still's Disease Foundation (ISDF) for Adult-Onset Still's Disease (AOSD), & IFAA for Rheumatoid Arthritis (RA)
3. From these results IFAA established an updated list for each disease that included the published symptoms & NEO additions. These were used to develop the study survey content & later to cross-reference with patient-reported symptoms that first occurred between onset ≤ 24 months (Early Disease/ED).

Results

Patient-reported symptoms occurring for the first time between onset & ED in ≥ 30 percent of all respondents, regardless of diagnosis

Symptoms ED	Based on 5****Star Symptom Rating (SRS)						
	RA	PsA	SS	AS	SLE/US	SLE/UK	AOSD
Number of Respondents	153	80	103	135	91	151	68
Fatigue							
Myalgia							
Mental cloudiness/'brain fog'							
Numbness and tingling in the extremities							
Stiffness after significant rest							
Swelling							
Raynaud's Phenomenon "Symptoms" (prior to or during ED)							
Redness and warmth around joints							
Anemic (prior to onset or in ED)							

≥ 75 percent response; **50 ≤ 75 percent response**; **30 ≤ 50 percent response**
Responses < 30 percent are considered low incidence

- When patient-reported symptoms were compared to CPMLs, the results showed that patients present with a more robust disease scope than may be understood by the scientific community.
- Symptoms attributed to a particular disease were often recorded in other diseases. These cross-over symptoms suggest the risk of undifferentiated diagnosis is increased.
- Participants commonly reported symptoms that were not listed in the CPML documents. These included fatigue, myalgia, mental cloudiness/"brain fog", flu-like symptoms, & Raynaud's Phenomenon.
- Moreover, one in three respondents, regardless of diagnosis, also reported swelling, fever, rash, anemia, numbness & tingling in the extremities.
- Gastrointestinal issues had low incidence in early disease, but at least one in four of all patients reported these symptoms starting prior to any disease onset.
- While specific cause of tenderness was not investigated (e.g. joint versus enthesitis), similar onset location occurred frequently in early disease, regardless of diagnosis. These areas included the neck and hips (> 50%), low & upper back, shoulders, shoulder blades, knees, chest, hands, & wrists (> 30%).
- Some differentiating factors included sacroiliitis, rib/spine tenderness & low incidence of fevers in AS & PsA, canker sores, lymph node inflammation, sore throat in SS, & fever/rash specific combinations for AOSD.
- The current standard to treat Undifferentiated Connective Tissue Disease (UCTD) & Undifferentiated Spondyloarthropathy (USpA) non-aggressively is based on 15% of patients ever advancing to full disease. Our investigation found that UCTD/USpA occurred in over 50% of respondents. This suggests more emphasis should be placed on treating UCTD/USpA earlier in the disease progression to lessen the chance for permanent, irreversible damage & disability.
- Geographic comparison of SLE responses suggest different healthcare systems do not account for reported early symptom variations.
- All respondents reported >75% of initial symptoms beginning between 0 ≤ 12 months, with a significant drop between 12 ≤ 24 months, suggesting more symptoms are present in ED.

Conclusion

Understanding correlations between cross over & the potential differentiating symptoms could expedite detection, referrals, diagnosis, & treatment. Patient-reported symptoms in ED showed inconsistencies with CPMLs, including potentially missing data, & therefore warrants further Symptom Mapping to establish robust & cohesive disease models. Significant overlap in symptoms that present early in onset, regardless of the final diagnosis, were demonstrated which could indicate a stronger relationship between the group, greater frequency of comorbidities, &/or possible misdiagnosis. UCTD/USpA progression to full diagnosis is more common that currently suggested. Establishing a complete & cohesive model for UCTD/USpA, including an aggressive treatment plan in ED, should be considered. Earlier public & professional education about AIA symptoms is essential to ensure correct diagnosis early in the course of an AIA disease.

Works Cited

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