Preventive Medicine Through Identifying and Addressing Comorbidities of Spondyloarthritides (SpA) to Improve Patient Outcomes Through Patient Organization Partnerships and Allied Healthcare Outreach

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Background: Many patients are not aware of the common comorbidities they may experience. We need to understand if by educating patients and managing or preventing comorbidities, will patient outcomes be improved and the impact on healthcare system.

Objectives: To determine what type and number of comorbidities patients commonly experience in addition to their diagnosed SpA condition. This will help identify how collaboration with other patient organizations and allied healthcare professionals can better raise awareness, educate and support the community. It will convey the conditions, symptoms and importance of early diagnosis and treatment. This will reduce the impact on the Canadian healthcare system and improve patient outcomes.

Methods: Canadian patients were surveyed from February through June 2018. Respondents were asked a variety of questions to gain insights on the comorbidities and how many they experience and live with in addition to their SpA diagnosis.

Results: The most common comorbidities respondents reported included: chronic pain (55%), mental health (depressions & anxiety) (54%), gut (Crohn’s and ulcerative colitis) (35%), eye inflammation (uveitis/iritis) (33%), sleep issues (30%) and chronic fatigue (26%). Interestingly, these results are different from other studies where osteoporosis and cardiovascular disease were most commonly experienced. In addition to the more prevalent comorbidities, a significant number of people experienced skin (psoriasis), fibromyalgia, hypertension and lung disease.

Conclusions: A significant number of patients diagnosed with a SpA condition experience comorbidities and often have more than one condition. On average, people live with 4 different comorbidities. The survey results have confirmed the significance depression and anxiety impacts patients with SpA. Through partnerships with trusted patient organizations, we can provide resources to educate and support our SpA community on the comorbidities commonly experienced. This will empower patients to manage symptoms sooner, thus contributing to a quicker recovery, reduced damage or prevent the complication from occurring all together.

Expanding outreach and collaborating with allied healthcare professionals through Canadian professional associations including family physicians, physiotherapists, chiropractors, ophthalmologists and massage therapists can further educate practicing healthcare professionals on SpA conditions and symptoms to recognize with patients contributing to prevention or earlier diagnosis and treatment intervention.

The CSA will form collaborative agreements by leveraging existing partnerships and creating new partnerships with Canadian organizations and professional associations to support and educate people with credible and valuable resources on the comorbidities identified through this survey with the intended purpose to treat earlier or prevent complications that adds unnecessary financial strain on the Canadian healthcare system.

Together we are stronger.

REFERENCES:
LUPUS EUROPE YOUTH PANEL – WHAT WE LEARNED FROM YOUNG PEOPLE LIVING WITH LUPUS

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Background: Since 2014, Lupus Europe conducts patient panels, where 10 to 12 persons from all over Europe living with lupus discuss the selected topic guided by facilitators living with lupus themselves. This allows to capture qualitative feedback of relevance, without the obstacle of the “white blouse”. In 2018, 10 Young (18-27) European Lupus patients (8 female, 2 male) with diverse Lupus types met to discuss “Lupus and youth”.

Objectives: Understand specificity of being young with lupus to better include young patients in Lupus groups action plans.

Methods: 11 young patients, mostly with little or no involvement in patient groups were recruited through Lupus Europe’s network. They were asked to send ahead of time their top challenges/issues living with lupus as well as their key questions for the panel. This input was used to build the 2 days program itself. Mid May, 10 of the 11 met face-to-face in Brussels, and explored multiple aspects of their input through 7 specifically designed interactive workshops.

Results: While they considered taking pills every day as a key problem, they preferred to focus on the collective issues of being understood by friends and family and having to live with limitations. A big “Wow” was the feeling of guilt expressed by several female patients (guilt of imposing limits to their partners, guilt of not being able to do as much as others, ...), a very important underlying dimension of their social and affective life, which is likely much misunderstood by doctors and patient organizations; young people with lupus remain fundamentally more positive on their life with lupus than the average patients. While they perceive lupus as being “all over their lives”, they refuse to be ruled by it ...

They view the future of a LUPUS EUROPE youth group as a ‘virtual group’ on social media, with minimal commitments required, but bringing together friends around highly visual messages, short stories and the exchange of ideas that could lead to small group gatherings.

On the medical front, when we probed what would drive them to consider joining a clinical trial, clear first media is their lupus doctor, second are national lupus groups and LUPUS EUROPE. Other medias have a very limited impact.

Conclusion: Young patients needs must be addressed in a more aspirational way and using more virtual tools than average patients (more focused on health issues and geographic proximity).

The feeling of guilt of young women with regards to their affective life must be further explored to give them confidence and reassurance.

REFERENCE:
[1] Lupus Europe Patient panel 3 project report, available on request at secretariat@lupus-europe.org

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SINGLE-CELL TRANSCRIPTOMIC AND FUNCTIONAL ANALYSES REVEAL NOVEL HETEROGENEITY IN PATHOGENIC PATHWAYS MEDIATED BY HUMAN SYNVOIAL TISSUE MACROPHAGES

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Background: We hypothesise that synovial tissue macrophages (STM) are heterogeneous and mediate discrete pathogenic pathways that may underlie partial or absent therapeutic responses in RA patients. Better understanding of STMs will provide novel targets for re-instating synovial homeostasis. We have shown that the human synovium contains at least two major populations of STMs (CD206/MerTk<sup>pos</sup> and CD206/MerTk<sup>neg</sup>) with transcriptomes suggesting different function.

Objectives: To dissect the phenotypic and functional heterogeneity of STMs using single-cell transcriptomics and associated functional assays.

Methods: The relative proportions of the two major populations of STMs were quantified in 64 RA synovial biopsies (including 26 from RA patients in sustained remission), and in 8 healthy synovial tissues by flow cytometry. To uncover STM phenotypes, single-cell RNA sequencing of STMs from healthy donors (n=4), active RA (n=7; DAS28 >5.1) and RA in remission (n=4; DAS28<2.6) was performed with 10X Genomics. 21,000 STMs were sequenced and analysed (Seurat). For functional analysis, CD206/MerTk<sup>pos</sup> and CD206/MerTk<sup>neg</sup> STMs were sorted from biopsies of active RA (n=15) and RA in remission (n=8). These were stimulated in vitro with LPS (to mimic activation by joint damage) or with LPS plus the MerTk agonist GAS6 to activate MerTk<sup>pos</sup> STMs; or co-cultured with FLS.

Results: The synovium of healthy subjects and RA patients in remission contain predominantly CD206/MerTk<sup>pos</sup> STMs, whereas RA patients with any disease activity additionally contain substantial proportions of CD206/MerTk<sup>neg</sup> STMs. In active RA, the CD206/MerTk<sup>neg</sup> STMs produce TNF while CD206/MerTk<sup>pos</sup> STMs produce type I interferon following TLR4 activation. Interestingly, CD206/MerTk<sup>pos</sup> STMs from RA patients in remission showed a limited response to TLR4 stimulation, and their cytokine production was further inhibited by GAS6. This regulatory function of GAS6/MerTk was confirmed in macrophage-fibroblast co-culture assays: inhibition of MerTk in macrophages increased macrophage-induced cytokine production by FLS. STM single-cell transcriptomic analysis uncovered further STM heterogeneity in healthy, active RA and RA in remission (5 distinct subpopulations). These included three subpopulations that were not present in healthy and remission RA. These inflammatory subpopulations differ in their expression of surface receptors, spectrum of activated pathways and in their frequency in the synovium of patients with similar high DAS28. One of the subpopulations, characterised by increase metabolism, pro-inflammatory cytokines (e.g. IL-1, B, BAFF) and chemokines, dominated in 3 out of 7 RA patients with active RA assessed; the second, characterised by high levels of MHC II and GPR receptors in 2 out of 7 patients while the third one characterised by high levels of alarmins (e.g. S100A8, 9 and 12) dominated in the remaining 2 inflamed RA synovia.

Conclusion: Pathogenic diversity of inflammatory synovial tissue macrophage subpopulations may partially account for unpredictable clinical responses in RA. Identifying and targeting the predominant STM subpopulation may facilitate novel therapeutic development and eventually patient stratification.

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