Rheumatology International (2018) 38:1–2
https://doi.org/10.1007/s00296-017-3921-0

Rheumatology
INTERNATIONAL

EDITORIAL

Autoinflammation in rheumatic and musculoskeletal disorders

Durga Prasanna Misra[1]

Received: 20 December 2017 / Accepted: 22 December 2017 / Published online: 27 December 2017

The autoinflammatory syndromes (AIS) refer to a group of disorders characterized by recurrent episodes of endogenous inflammation resulting from uncontrolled activation of the innate immune system [1]. Autoinflammation is a critical pathophysiological process in Behçet disease (BD), systemic onset juvenile idiopathic arthritis, adult-onset Still's disease, psoriatic arthritis, gout, and certain hormonal and cardiac disorders [2].

AIS can manifest at varying ages, ranging from the neonatal period to young adulthood, and rarely at older ages. Each syndrome or related nosological entity is identified by distinct clinical features [1]. A significant proportion of AIS manifest with episodes of fever of varying periodicity. Endogenous (auto)inflammation of varying intensity can also present in classic autoimmune rheumatic and musculoskeletal diseases, sometimes following therapy.

Generally, AIS, and particularly familial Mediterranean fever (FMF), are prevalent among individuals of Mediterranean descent. However, more and more reports on various autoinflammatory features from all over the world point to the fact that physicians of any country may encounter AIS. Classification and diagnostic criteria for most of AIS are not uniformly described and validated. A recent set of clinical criteria was published for the four common periodic fever syndromes (PFS): FMF, mevalonate kinase deficiency (MKD), tumor necrosis factor (TNF) receptor-associated periodic fever syndrome (TRAPS), and cryopyrin-associated periodic fever syndromes (CAPS). These criteria were based on a multicentric registry from European countries (the Eurofever registry) which included more than 500 patients [3].

The recognition of AIS is challenging, unless the physician is adequately trained to recognize them. This is especially a conundrum in low- and middle-income countries, where infectious etiologies of fever are highly prevalent and even in a child with recurrent fever, AIS may be missed unless carefully looked for. Once suspected or diagnosed, it is advisable to analyze the genome of the proband, parents, and other affected siblings.

Management of AIS depends on a particular disease. Inflammasome activation and increased serum interleukin-1 levels characterize the underlying pathophysiology in a significant number of AIS [4]. Blocking inflammasome activation by colchicine is a useful therapeutic strategy in FMF, whereas antagonism of interleukin-1 (anakinra, rilonacept, canakinumab) is useful in colchicine resistance in FMF, MKD, TRAPS and CAPS [1, 4]. Certain newer AIS such as deficiency of adenosine deaminase 2 (DADA2) show a favourable response to therapeutic blockade of TNF-alpha [5]. Hematopoietic stem cell transplantation to reset the defective immune system is another option in treatment-refractory AIS [6]. Many of the monoclonal antibodies and targeted biologic therapies have come into clinical practice in the last 20 years. Therefore, more and more children with AIS are surviving into adolescence, and problems associated with long duration of uncontrolled (often unrecognized) systemic inflammation such as increased risk of premature cardiovascular events are being recognized [7].

In this context, the present theme-based issue of the journal specifically focusing on AIS is relevant. Such issues help bring attention to a particular group of diseases, enriching knowledge of the readers in areas that may not have been adequately emphasized during traditional rheumatology training. This issue includes narrative reviews, cohort studies, and case-based reviews from different parts of the world, highlighting various aspects of diagnosis and therapy of AIS. Included articles also focus on comorbid conditions, and primarily cardiovascular disease, fatigue, and sleep disturbances. Additionally, articles focusing on endogenous inflammation in rheumatic as well as non-rheumatic diseases and their potential modulation by drug therapy serve to enlighten lesser emphasized areas in the practice of medicine. Readers are invited to carefully digest this information

✉ Durga Prasanna Misra
durgapmisra@gmail.com; dpmisra@sgpgi.ac.in

[1] Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

and utilize it in their clinical practice, hopefully to help them identify more such cases amongst their patients.

References

1. Verbsky JW (2017) When to suspect autoinflammatory/recurrent fever syndromes. Pediatr Clin North Am 64:111–125. https://doi.org/10.1016/j.pcl.2016.08.008
2. Dinarello CA (2011) Interleukin-1 in the pathogenesis and treatment of inflammatory diseases. Blood 117:3720–3732. https://doi.org/10.1182/blood-2010-07-273417
3. Federici S, Sormani MP, Ozen S et al (2015) Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers. Ann Rheum Dis 74:799–805. https://doi.org/10.1136/annrheumdis-2014-206580
4. Manthiram K, Zhou Q, Aksentijevich I, Kastner DL (2017) The monogenic autoinflammatory diseases define new pathways in human innate immunity and inflammation. Nat Immunol 18:832–842. https://doi.org/10.1038/ni.3777
5. Navon Elkan P, Pierce SB, Segel R et al (2014) Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. N Engl J Med 370:921–931. https://doi.org/10.1056/NEJMoa1307362
6. Roifman CM, Fischer A, Notarangelo LD, de la Morena MT, Seger RA (2010) Indications for hemopoietic stem cell transplantation. Immunol Allergy Clin North Am 30:261–262. https://doi.org/10.1016/j.iac.2010.03.004
7. Hintenberger R, Falkinger A, Danninger K, Pieringer H (2017) Cardiovascular disease in patients with autoinflammatory syndromes. Rheumatol Int 10.1007/s00296-017-3854-7.(Epub ahead of print)