

The 5th Israel–Italy Meeting: Advances in Rheumatology and Autoimmunity

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The scientific tradition of Israel–Italy meetings on advances in rheumatology and autoimmunity is well maintained. The 5th meeting took place on December 15, 2016, at the Technion–Israel Institute of Technology’s, Rappaport Faculty of Medicine in Haifa, Israel. Updated lectures were presented by leading scientists and physicians from both countries. The topics covered many new developments in the fields of rheumatology as well as autoinflammatory and autoimmune diseases. Discussions included research aspects in the pathogenesis, diagnosis and new therapeutic strategies of these diseases.

ADVANCED ASPECTS IN RHEUMATIC DISEASES

Biomarkers are useful in predicting prognostic features of rheumatoid arthritis (RA), as well as in guiding therapeutic management of different phases of RA. In his talk, Prof. Piercarlo Sarzi-Puttini evaluated the importance of using the rheumatoid factor (RF) and anti-citrullinated protein antibodies to identify pre-clinical signs in RA subjects and start therapy as soon as possible. He also discussed the use of biomarkers such as erythrocyte sedimentation rate and C-reactive protein levels to monitor disease activity.

With this in mind, Prof. Roberto Perricone evaluated a range of predictive factors that could be used to assess clinical beneficial responses in RA patients treated with first line tumor necrosis factor-inhibitors (TNF-i). He showed that positive predictors of remission and low disease activity included male gender and the age at the time that anti-TNF treatment was initiated. The correlation between adjuvants (i.e., aluminum) and the induction of autoimmunity was discussed by Prof. Yehuda Shoenfeld [1]. In his talk he mentioned that aluminum, which is found in many vaccines, has been reported to induce autoimmune disorders, mainly in people with a genetic predisposition for autoimmunity. In addition, Shoenfeld [2] discussed the association between environmental and occupational determinants to autoimmune diseases, such as systemic sclerosis. In that case, silica dust was widely described as an occupational risk factor for diffuse cutaneous systemic sclerosis.

ASPECTS OF FOCAL AND SYSTEMIC VASCULITIS

The issue of primary central nervous system vasculitis (PCNSV) was discussed by Prof. Carlo Salvarani [3]. He explained the

importance of early diagnosis. Updates on systemic vasculitis were presented by Dr. Abdulla Watad [4] who explained the diagnostic importance of anti-glomerular basement membrane antibodies (anti-GBM) for the diagnosis of Goodpasture’s disease. By analyzing the results of 1914 anti-GBM test results, the authors pointed to the lack of sensitivity of serological testing of anti-GBM titers. Thus, renal biopsy is still pivotal for Goodpasture’s disease diagnosis. The association between giant cell arteritis (GCA) and the risk for increased cardiovascular morbidity was evaluated. Information from a database of the leading healthcare provider in Israel, which included 5659 GCA patients and 28,261 age and gender matched controls, were assessed in this analysis. The proportion of those with ischemic heart disease was higher in the GCA group than among healthy individuals. The authors concluded that attention should be paid to avoid missing cardiovascular morbidity in GCA patients [5]. Aspects of autoinflammatory diseases were also discussed by Prof. Yackov Berkun [6]. In this respect, deficiency of adenosine-deaminase 2 (ADA2), a new autoinflammatory disorder, was presented. He discussed how familial polyarteritis nodosa (PAN) vasculitis was associated with autosomal recessive loss-of-function mutation of ADA2.

AUTOIMMUNE RELATED ISSUES

A lecture on the importance of personalized medicine in autoimmunity was given by Prof. Ori Elkayam. She focused on personalized biological therapies for treatment of rheumatic diseases [7]. Prof. Catarina De Carolis explained the interplay between thyroid dysfunction and Hashimoto’s thyroiditis, which is a common feature of systemic sclerosis (SSc) and poor pregnancy outcomes. She summarized her experience in the development of pre-term delivery and intrauterine growth treatments for Italian women suffering from SSc and thyroid disorders. In this respect, a comprehensive talk given by Prof. Roberto Giacomelli [8] focused on the role of mesenchymal stem cells at the crossroad between endothelial damage and fibrosis in systemic sclerosis. The issue of immunodeficiency and autoimmunity, being two sides of the same coin, was summarized by Prof. Claudio Lunardi [9]. Giorgia Bizzaro [10] reviewed the association between vitamin D deficiency and autoimmune disorders. In her review, she pointed to the well-known consequences of vitamin D deficiency on the immune system. She addressed the

fact that vitamin D receptors are present in almost all immune cells, and that some of the polymorphism that is found is associated with increased autoimmune disease incidence. Rare aspects of familial Mediterranean fever were reported. These symptoms included the development of pseudoseptic arthritis with low levels of synovial fluid glucose [11]. The impairment of health-related quality of life (QoL) in patients suffering from non-infectious uveitis (NIU) was also reported.

Therapeutic Issues in Rheumatic Diseases

The management of systemic lupus erythematosus (SLE) patients in remission was discussed by Prof. Andrea Doria [12]. In SLE, the concept of remission has been widely discussed. However, the disease and treatment variables that should be evaluated need to be taken into account. The activity scores to use to define a patient as in remission have not yet been established. In the past 10 years, facilitated subcutaneous immunoglobulin (fSCIg) has been widely used and has proved to be both efficient and save. In her talk, Prof. Maria Giovanna Danieli summarized her experience in the usage of fSCIg in autoimmune cytopenias associated with common variable immunodeficiency (CVID). Her data documented the efficacy and safety of fSCIg in the treatment of CVID with a good tolerability and being of steroid sparing effect [13]. The usage of a dexamethasone implant in the treatment of Behçet's disease-related uveitis was presented. This mode of therapy was shown to be safe and effective as an additional treatment combined with systemic immune-modulatory drugs [14]. In a short communication, hyperbaric oxygen therapy (HBOT) was shown to have anti-inflammatory and oxygenatory effects in patients with primary and secondary vasculitis. HBOT was also shown to be beneficial for orthopedic and fibromyalgia patients [15].

In another presentation, the possibility of using vitamin D or anti-interleukin-1 as treatment for patients with periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome was shown to be a promising approach [16].

Conclusions

The 5th Israel-Italy meeting to discuss advances in rheumatology and autoimmunity was successfully closed by inviting all

participants to attend the 6th Israel-Italy meeting in Verona, Italy in October 2017.

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References

1. Bragazzi NL, Watad A, Adawi M, Aljaded G, Amital H, Shoenfeld Y. Adjuvants and autoimmunity: why do we develop autoantibodies, autoimmune diseases and lymphoma. *IMAJ* 2017; 7: 403-5.
2. Gomes JP, Shoenfeld Y. Morphea sculpted in silica: a case report of limited cutaneous systemic sclerosis in a woman with long-time exposure to silica dust. *IMAJ* 2017; 7: 459-60.
3. Salvarani C, Brown Jr RD, Hunder GG. Adult primary central nervous system vasculitis. *IMAJ* 2017; 7: 448-53.
4. Watad A, Bragazzi NL, Sharif K, et al. Anti-glomerular basement membrane antibody diagnostics in a large cohort tertiary center: should we trust serological findings? *IMAJ* 2017; 7: 424-8.
5. Dagan A, Mahroum N, Segal G, et al. The association between giant cell arteritis and ischemic heart disease: a population-based cross-sectional study. *IMAJ* 2017; 7: 411-14.
6. Berkun Y, Segal R, Navon-Elkan P. Adenosine deaminase 2 deficiency: more than monogenic vasculitis. *IMAJ* 2017; 7: 435-7.
7. Anaya JM, Duarte-Rey C, Sarmiento-Monroy JC, Bardey D, Castiblanco J, Rojas-Villarraga A. Personalized medicine. Closing the gap between knowledge and clinical practice. *Autoimmun Rev* 2016; 15: 833-42.
8. Cipriani P, Di Benedetto P, Ruscitti P, et al. Impaired endothelium-mesenchymal stem cells cross-talk in systemic sclerosis: a link between vascular and fibrotic features. *Arthritis Res Ther* 2014; 16: 442.
9. Patuzzo G, Barbieri A, Tinazzi E, et al. Autoimmunity and infection in common variable immunodeficiency. *Autoimmun Rev* 2016; 15: 877-82.
10. Bizzaro G, Antico A, Fortunato A, Bizzaro N. Vitamin D and autoimmune diseases: is vitamin D receptor (VDR) polymorphism the culprit? *IMAJ* 2017; 7: 438-43.
11. Awisat A, Slobodin G, Jiries N, et al. Pseudoseptic arthritis with low synovial fluid glucose in familial Mediterranean fever. *IMAJ* 2017; 7: 461-2.
12. Zen M, Gatto M, Nalotto L, Larosa M, Iaccarino L, Doria A. The management of systemic lupus erythematosus (SLE) patients in remission. *IMAJ* 2017; 7: 454-8.
13. Pedini V, Savore I, Danieli MG. Facilitated subcutaneous immunoglobulin (fSCIg) in autoimmune cytopenias associated with common variable immunodeficiency. *IMAJ* 2017; 7: 420-3.
14. Fabiani C, Emmi G, Lopalco G, et al. Intravitreal dexamethasone implant as an adjunct weapon for severe and refractory uveitis in Behçet's disease. *IMAJ* 2017; 7: 415-19.
15. Barilaro G, Masala IF, Parracchini R, et al. The role of hyperbaric oxygen therapy in orthopedics and rheumatological diseases. *IMAJ* 2017; 7: 429-34.
16. Rigante D, Gentileschi S, Vitale A, Tarantino G, Cantarini L. Evolving frontiers in the treatment of periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome. *IMAJ* 2017; 7: 444-7.

“I have not failed. I've just found 10,000 ways that won't work”

Thomas Edison (1847–1931), American inventor and businessman. He developed many devices that influenced life around the world, including the phonograph, the motion picture camera, and the long-lasting, practical electric light bulb

“When you re-read a classic, you do not see more in the book than you did before; you see more in yourself than there was before”

Clifton Fadiman (1904–1999), American intellectual, author, editor, radio and television personality