Deceptive Antiphospholipid Syndrome
- Ricard Cervera

The antiphospholipid syndrome (APS) is defined by the occurrence of venous and arterial thromboses, often multiple, and recurrent fetal losses, frequently accompanied by a moderate thrombocytopenia, in the presence of antiphospholipid antibodies (aPL), namely lupus anticoagulant (LA), anticardiolipin antibodies (aCL), or both. Chronic biological false-positive serological tests for syphilis (BFP-STS) may be present in some of these patients, because these tests also detect the presence of aPL. Other autoantibodies have also been detected in many patients with an APS, such as anti-2 glycoprotein I (GPI), antimitochondrial (M5 type), antiendothelial cell, antiplatelet, antiythrocyte, and antinuclear antibodies.

The APS can be found in patients having neither clinical nor laboratory evidence of another definable condition (primary APS) or it may be associated with other diseases. Systemic lupus erythematosus (SLE) is the disorder in which an APS is most commonly associated. Less frequently, aPL and, rarely, an APS may also be encountered in other groups of patients.

“Simple” or “classic” syndrome

The clinical picture of the “simple” or “classic” APS is characterized by venous and arterial thromboses, fetal losses and thrombocytopenia. Deep vein thrombosis (occasionally superficial thrombophlebitis) particularly affecting the veins of the lower limbs are the commonest venous occlusions seen. Strokes, often preceded by transient ischemic attacks, are the most frequent arterial events encountered in these patients. However, not only may a large variety of both veins and arteries be affected but small vessels might also be involved. Therefore, many diverse clinical manifestations due to vascular occlusions in the central nervous system, heart, lungs, liver, adrenal glands, kidneys, skin, eyes, etc, may now be associated with the presence of aPL. Single vessel involvement or multiple vascular occlusions may give rise to a wide variety of presentations (Table). Any combination of vascular occlusive events may occur in the same individual and the time interval between them also varies considerably from weeks to months or even years.

Recurrent fetal losses can occur in any trimester of pregnancy, although they are commonly in the second and third trimester. There are a number of mechanisms that have been proposed in order to explain how these fetal losses occur. The most accepted implies that fetal losses are associated with thrombosis of the placental vessels and subsequent infarction resulting in placental insufficiency, fetal growth retardation, and ultimately fetal loss. Not all placentas examined, however, have shown areas of thrombosis or infarction and other mechanisms may be operative in these patients.

(continued on Page 4)
What an Introduction to British Rheumatology!

First and lasting impressions

Life and career is no fun without twists and turns, without surprises and deviations, either to the left or to the right, sharp left and right turn at corners, hairpin bends, two of them making a loop, a ‘U’ turn becoming an ‘O’ turn. When I joined medical college, I never dreamt that I would end up as a Rheumatologist, but I did... that’s another story. But to get the best of Rheumatology (Arthritis+Rheumatism to simplify) I went for a post-doctoral course at the Mecca of Rheumatology, The Royal National Hospital for Rheumatic Diseases at Bath, England. Around 16th Century or so (I was not around to be so precise), there were hot spring baths where the rich and the famous from near and far came for the treatment of their aches and pains, Arthritis and Rheumatism. A tiny clinic was set up right next to it. It grew into a Hospital to treat rheumatic patients. For its name and fame I opted to be there to imbibe the best of skills, to be amongst the best of Rheumatologists.

Bath’s Spa is 110 miles west of London. An hour and ten minutes of a delightful train ride (Intercity 125) put me at this probably the most enchanting town in the whole of U.K. Most buildings in the country are largely of red bricks; Bath is almost entirely constructed out of white stones... clear Roman influence. Elegant houses, gardens with crescents, artistic bridges over a river and rivulets dotted with seasonal flowers, and of course the inevitable pubs a plenty.

At this world famous historic Hospital, Professor Alan Dixon, was waiting at the steps to receive me. “Young man from India, Namaste, and welcome. Ah, let me show you around”. He gave me a quick tour on a Monday morning 9 am precisely, from the cellar to the dome. The top floor was surely intriguing and fascinating for what did I see? A hot water swimming pool wherein crippled arthritic patients were undergoing hydrotherapy by pretty bikini clad Physiotherapists! My expression of surprise was an understatement. I was bewildered at what Her Majesty’s Government could do for her subjects. A mischievous thought must have entered my mind even if so benign and naïve that I was, would I have to be a crippled arthritic so as to enjoy the healing touch of such charming British physiotherapists? And that too free of charge? Of course a better sense of discretion prevailed and my wagging tongue was kept well in control under my cheeks. Could there be better introduction to Rheumatology in Britain? Unforgettable!

On a sunny day I was at the hospital garden where young men were standing in a circle and passing a football with their hands from left to the right, also right to the left. I asked my Professor what was going on. He said “These are ankylosing spondylitis backache patients. That’s our way to encourage them to practice rotator exercises at the spine... not bad, not bad at all, I thought.

I was blessed by such inspiring teachers such as Professor Alan Dixon, Professor Paul Bacon and later in my second sabbatical Professor Andrei Calin whose talks on Ankylosing Spondylitis were simply awesome.
Deceptive APS: Anticoagulation non-stop forever??

“To be or not to be?”
...Taming of the Shrew
by William Shakespeare

Two factual Clinical Episodes:

- Ms. V.N. a 28-year old bright MBA from Mumbai presented with recurrent severe migrainous headache, transient blackouts, frequent attacks of fainting, with momentary seizures, two episodes of swelling in the feet, but no joint pain, rash, fever or alopecia. Her ANA was 1:640 positive, ANCA negative, ACLA negative, Beta-2 glycoprotein negative, LAC negative. CT brain was essentially normal.

When on Aspirin 75 mg o.d. and traditional oral anticoagulant she would respond. INR maintained between 3 and 3.2. When she would skip anticoagulants, her symptoms would recur with blurring of vision and severe headache. Tired of daily anticoagulants she would often skip, especially during bleeding menstruation and approach different specialists with no salvation. Her case was presented to top visiting Rheumatologists - Immunologists in Mumbai who had no specific positive suggestions.

What is her prognosis? Must she continue daily anticoagulants forever? What if she forgets? Will she be able to have family life? What does the future hold for her? I have no clue. Do you?

- A 45-year old Mr. SQ, of Indian origin Singaporean was on a posting in Mumbai, presented a confirmed diagnosis of APS, perfectly well stabilized on oral anticoagulants. After two years of non-stop treatment without any symptom, to his question “Can I take a break from daily anticoagulants?”, I suggested he may give it a try. He did. When he was visiting Chennai he phoned to say he developed a seizure with transient blindness, stroke like weakness of limbs. On returning to Mumbai I put him back on anticoagulants, he recovered. He then asked in frustration. “Can I not live for a single day of my life without these wretched anticoagulants?”.

To date I have no precise answer. Do you?

These two factual clinical anecdotes raise several disturbing questions:

- Can anticoagulants be given at least a short “holiday”?
- Are newer anticoagulants any better never mind their high cost?
- Would any parameter other than INR alone help?
- Would a low cost INR monitoring device in patients’ hands like a glucometer help resolve the issue?
- Any ongoing line of research to address and resolve such practical issues of our long suffering APS patients?

Prakash Pispati, M.D., F.R.S.M.(Lon), M.Sc(Med.)
Editor-in-Chief, VOA
Past President, IRA, APLAR. Master, Hon. Member
Director of Rheumatology, Jaslok, Saifee Hospitals, Mumbai, India.
Several authors have demonstrated a strong association between thrombocytopenia and the presence of aPL, mainly IgG aCL, in patients with SLE. It is usually mild (70,000 to 120,000 platelets/mm3), benign, and does not require any active intervention. In addition, aPL have also been detected in patients with idiopathic thrombocytopenic purpura (ITP). These may represent a separate and distinct subset of ITP patients prone to develop full-blown APS with thrombotic events or SLE in the future.

“Catastrophic” Syndrome (CAPS)

Here the predominant disturbance is on small vessels as opposed to large veins and arteries, which are predominantly involved in patients with “simple” APS. This term is used to define an accelerated form of the APS with consequent multi-organ failure. Precipitating factors, as in patients with the "simple" APS, included surgical procedures (both major and minor), infections, oral contraceptive therapy and anticoagulation withdrawal. Multi-organ presentation and failure was the rule and most patients with catastrophic APS end up in intensive care units with physicians belonging to a wide variety of specialities in attendance. Renal and pulmonary involvement predominate, the majority of patients showing severe renal impairment. Approximately one third developed ARDS. 50% demonstrate cerebral symptomatology and drowsiness and confusion may end in coma. Gastrointestinal, cardiac, hepatic, adrenal and pancreatic disturbances might occur. Unusual organ involvement, such as testes and prostate, has been documented. Skin manifestations are also frequent. Hemolytic anemia (26%) and evidence of DIC (30%) may be evident. Death occurred in 50%. At post-mortem, overwhelming evidence of microthrombotic occlusive disease of small vessels was evident (“thrombotic microangiopathy”). Many organs, including particularly the kidneys, brain and heart, were affected by this process. A minority only of patients demonstrated large vessel occlusions (veins and arteries) in contrast to patients with a “simple” APS and one can speculate as to whether the same etiopathogenic process is operating in this group of patients and whether the patients with catastrophic APS represent a rather different “subset” of patients with the APS in whom the accent of the disease is on the microvasculature particularly.

Deceptive APS

The many manifestations summarized in this article may not be statistically significantly related to the presence of the aPL or indeed be considered as “definite” manifestations of the APS according to the classification criteria. Moreover, the recent literature includes many anecdotal reports of other manifestations possibly associated with aPL (i.e. reactive hemophagocytic syndrome and Sheehan’s syndrome). However, as more cases as reported, the statistical evidence for these associations may become more definite. Many of these conditions are themselves uncommon and the demonstration of aPL has enabled us to more easily understand their pathogenesis, up till now unexplained and complex. One of these conditions (viz adrenal failure) has been linked to the presence of these antibodies even more frequently than tuberculosis. As this latter condition has declined, adrenal hypofunction related to hemorrhagic infarction consequent on the aPL-related coagulopathy is now one of its most important causes. It has taken almost 20 years since the original linkage of AVN to aPL was presented at an International Meeting. It is only recently that it has become evident that asymptomatic AVN is indeed not uncommon in patient with “primary” APS. And so, the list grows and involves all medical specialities and subspecialities.

TABLE: Clinical manifestations of the APS.

<table>
<thead>
<tr>
<th>Large Vessel</th>
<th>Neurologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
<td>Trombotic infarctions</td>
</tr>
<tr>
<td>Large peripheral arterial occlusions</td>
<td>Sneddon’s syndrome</td>
</tr>
<tr>
<td>Aortic occlusions</td>
<td>Transient ischemic attacks</td>
</tr>
<tr>
<td></td>
<td>Multiinfarct dementia</td>
</tr>
<tr>
<td></td>
<td>Acute ischemic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>Embolic stroke</td>
</tr>
<tr>
<td></td>
<td>Cerebral venous and dural sinus thrombosis</td>
</tr>
<tr>
<td></td>
<td>Psychosis</td>
</tr>
<tr>
<td></td>
<td>Cognitive defects</td>
</tr>
<tr>
<td></td>
<td>Transient global amnesia</td>
</tr>
<tr>
<td></td>
<td>Pseudomultiple sclerosis</td>
</tr>
<tr>
<td></td>
<td>Migraine and migranous stroke</td>
</tr>
<tr>
<td></td>
<td>Epilepsy</td>
</tr>
</tbody>
</table>

Movement disorders

- Chorea
- Hemiballismus
- Cerebellar ataxia

Spinal syndromes

- Transverse myelopathy
- Guillain-Barré syndrome
- Anterior spinal artery syndrome
- Lupoid sclerosis

Ophthalmic complications

- Retinal vascular occlusions
- Acute retrobulbar optic neuritis
- Ischemic optic atrophy
- Progressive optic atrophy

Cardiac

- Myocardial infarction
- Unstable angina
- Coronary by-pass graft occlusions
- Cardiomyopathy acute, achronic
- Valvethickening and deformity
- Vegetations
- Pseudo-infective endocarditis
- Intracardiac thrombus
- Cyanotic congenital heart disease
- Complications of cardiovascular surgery

...(continued on Page 5)
Pulmonary
- Pulmonary embolism and infarction
- Pulmonary hypertension
- Pulmonary arterial occlusions
  - Major pulmonary arterial thrombosis
  - Pulmonary microthrombosis
- Adult respiratory distress syndrome
- Intraalveolar pulmonary hemorrhage
- Fibrosing alveolitis
- Post-partum syndrome

Renal
- Glomerular capillary thrombosis in lupus nephritis
- Intra-renal vascular lesions ("thrombotic microangiopathy")
- Renal artery occlusions
- Renal vein thrombosis
- End-stage renal failure and hemodialysis
- Renal transplantation
- Pregnancy and post-partum syndromes

Hepatic
- Budd-Chiari syndrome
- Portal hypertension
- Hepatic veno-occlusive disease
- Nodular regenerative hyperplasia
- Hepatic infarction
- Hepatitis
- Alcoholic liver disease
- Cirrhosis

Digestive
- Esophageal necrosis
- Gastric ulceration
- Small and large bowel vascular occlusions
- Mesenteric inflammatory vaso-occlusive disease
- Inflammatory bowel disease
  - Ulcerative colitis
  - Crohn’s disease
- Pancreatitis
- Cholecystitis
- Occlusion of splenic vessels

Obstetric
- Maternal complications
  - Toxemia
  - Pre-eclampsia
  - HELLP syndrome
- Cardio-pulmonary post-partum syndrome
  - Chorea gravidarum
  - Post-partum cerebral infarct
  - Maternal death
- Fetal complications
  - Abortion
  - Fetal death
  - Intrauterine growth retardation

Dermatologic
- Livedo reticularis
- Skin ulcerations
- Small painful leg ulcers of livedoid vasculitis
- Cutaneous necrosis
- Macules and nodules
- Multiple subungual splinter hemorrhages
- Gangrene and digital necrosis
- Anetoderma
- Discoid lupus
- Intravascular coagulation necrosis of the skin
- Pyoderma gangrenosum

CASE HISTORY: DECEPTIVE APS

A 44-year-old Caucasian female with SLE was admitted to the Emergency Department with fever, acute pain in the second finger of her right hand and a heart murmur. Diagnosed with SLE 8 years ago based on arthritis, photosensitivity, serositis, thrombocytopenia, positive ANA and anti-dsDNA antibody, hypocomplementaemia and presence of anticardiolipin IgG (67 GPL) and anti-β2-glycoprotein I IgG (78 IU/ml) antibodies (confirmed in a second assessment). Physical examination revealed a mitral murmur and splinter haemorrhages in the second finger of her right hand (Slide #1). An echocardiogram disclosed a verrucous lesion on the mitral valve (Slide #2). Treatment with empirical antibiotic and enoxaparin (60 mg/day) was initiated. The laboratory tests showed similar results and blood cultures (4) were negative. In the next 36 hours, the patient was afebrile and the general state improved. The final diagnosis was pseudoinfective endocarditis in a patient with APS associated to SLE.
Psoriasis Tamed? : Exciting new innovations
Deeper understanding of Psoriasis has led to new innovations at a furious pace
- Carlo Selmi

Psoriatic arthritis (PsA) is an ideal paradigm of a complex disease with clinical manifestations ranging from articular inflammation to metabolic disturbances. The estimated prevalence of PsA in the general population is 0.16%-0.25%, but the rate rises to 20-25% in subjects with skin psoriasis, commonly considered a pre-arthritic condition. Axial involvement in PsA is associated with the HLA-B27 allele, but this remains the only known genetic biomarker used in clinical practice. The role of the environment in PsA is well represented by the largely incomplete concordance of psoriasis and PsA among monozygotic (MZ) and dizygotic (DZ) twins. Different from most rheumatic diseases, sexes are equally affected by PsA and no serum autoantibody is available for an early diagnosis. As a consequence, the research agenda is currently moving toward the identification of predictors of PsA at a preclinical stage in patients with skin manifestations.

Genome-wide association studies have in the past years provided numerous associations, including HLA and IL23RA, but genetic predisposition seems having a minor role compared to other factors, as illustrated by the incomplete concordance among MZ compared to DZ twins. Of note, several genes associated with psoriasis and PsA are shared by other inflammatory diseases (Figure 1). Gene expression and phenotypes has been extensively investigated in healthy MZ twins over time showing the predominant influence of the environment compared to hereditary factors, particularly in autoimmunity, as extensively discussed in a 2010 NIEHS Workshop to which the proponent was part. In recent years, studies reporting the influence of environmental factors such as UV light and the microbiome in the skin-joint-gut axis, and this may trigger an inflammatory response as demonstrated in psoriasis plaques through a T-cell mediated response.

PsA clinical manifestations may vary widely to include different rheumatological domains (Figure 2) and extra-articular sites as in the case of uveitis or inflammatory bowel disease while treatment options range from non-steroidal anti-inflammatory drugs to biologics targeting TNF-alpha or the Th17 pathway. Different from most rheumatic diseases, no serum autoantibody is associated with PsA while other biomarkers have been proposed for the disease early diagnosis or to predict treatment response for a more adequate resource allocation and have been recently the subject of a systematic review of the literature by our group. Cross-sectional studies suggest that specific forms of skin psoriasis involvement may be strongly associated with PsA but longitudinal data are limited to estimate the absolute and relative risks. As a result, our current understanding of the probability of developing PsA in psoriasis or to achieve an early diagnosis could be defined as primitive, with limited agreement on the clinical manifestations to be sought. Despite the presence of an obvious risk factor for PsA in the skin manifestation, the individual clinical judgment remains the main driver of PsA screening, different from rheumatoid arthritis with serum autoantibodies specific for the disease and predating the clinical manifestations. In the case of PsA, the study of biomarkers has been disappointing and we believe this is largely due to the wide variability of the study populations, encompassing the whole spectrum of PsA manifestations (axial involvement, peripheral arthritis, dactylitis, enthesitis, among others).

.... continued from page 7
Indeed, PsA can manifest with many different clinical manifestations, such as peripheral arthritis, axial involvement, enthesitis or dactylitis. Earlier reports suggested that spondyloarthritides were predominant in men, but PsA is currently considered a disease affecting both sexes equally, with some studies reporting a male or a female preponderance. Sex differences in PsA include a more frequent axial involvement in men and a predominant peripheral arthritis with higher disability scores in women. Nonetheless, few studies have assessed the differences in clinical manifestations between sexes, especially in large cohorts of patients. The treatment of PsA is based on nonsteroidal anti-inflammatory drugs (NSAIDs), traditional disease-modifying antirheumatic drugs (DMARDs) and biologic agents, currently blocking TNFalpha, but developing also for interleukin (IL)-12/IL-23, IL-17 and anti-phosphodiesterase-4 (anti-PDE4). Indeed, PsA therapy historically begun with cytotoxic drugs targeting proliferating immune cells, reached new heights with biologic agents directed against single cytokines (mainly TNF-alfa) and now stemmed into small molecules that interfere with pathways leading to inflammatory cytokine productions as phosphodiesterase-4 (PDE-4)-inhibitors in different cell types. Selective PDE4 inhibitors exert their anti-inflammatory effects, being PDE4 mainly expressed within inflammatory cells, thus leading to the approved use of apremilast in PsA.

Unforgettable Cases ... PsA

Are clinical anecdotes relevant in today’s rahter overwhelming era of Evidence Based Medicine ... I believe they are after all the triggers to scientific inquiry, experimentation and the very basis of EBM.

A 17 year old handsome lad Abdul was brought in a depressed state of mind by his mother herself an RA patient from poorer strata of society. She was recently maintained on poorman’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Mr J, a 50 year old gentleman was a director of an Indian multinational steel company based in London, a frequent world traveller he presented with Psoriatic Arthritis unmistakable with embarrassing skin lesions on his face. He said that he has had pulmonary tuberculosis in his youth, was willing to take the risk of possible exacerbation but I would treat him with a biological? I did. Now he comes annually for a checkup but insists I give a prophylactic shot of biological.

Of all the 108 types of Arthritis, I find psoriasis most gratifying to treat ... as patients can see the outcome maintained on poor man’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Laugh it off Doc!

By
Harish, Final year student M.B.B.S
Yuva Vishalini Ravindran, Final year student M.B.B.S
Dr. Subramanian Nallasivan
Madurai, India

A P L A R
Asia Pacific League of Associations for Rheumatology
e-Bulletin | Quarterly | Volume 1 | Issue 4 | July 2017

... by Carlo Selmi

Unforgettable Cases ... PsA

Are clinical anecdotes relevant in today’s rahter overwhelming era of Evidence Based Medicine ... I believe they are after all the triggers to scientific inquiry, experimentation and the very basis of EBM.

A 17 year old handsome lad Abdul was brought in a depressed state of mind by his mother herself an RA patient from poorer strata of society. She was recently maintained on poorman’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Mr J, a 50 year old gentleman was a director of an Indian multinational steel company based in London, a frequent world traveller he presented with Psoriatic Arthritis unmistakable with embarrassing skin lesions on his face. He said that he has had pulmonary tuberculosis in his youth, was willing to take the risk of possible exacerbation but I would treat him with a biological? I did. Now he comes annually for a checkup but insists I give a prophylactic shot of biological.

Of all the 108 types of Arthritis, I find psoriasis most gratifying to treat ... as patients can see the outcome maintained on poor man’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Laugh it off Doc!

By
Harish, Final year student M.B.B.S
Yuva Vishalini Ravindran, Final year student M.B.B.S
Dr. Subramanian Nallasivan
Madurai, India

A P L A R
Asia Pacific League of Associations for Rheumatology
e-Bulletin | Quarterly | Volume 1 | Issue 4 | July 2017

... by Carlo Selmi

Unforgettable Cases ... PsA

Are clinical anecdotes relevant in today’s rahter overwhelming era of Evidence Based Medicine ... I believe they are after all the triggers to scientific inquiry, experimentation and the very basis of EBM.

A 17 year old handsome lad Abdul was brought in a depressed state of mind by his mother herself an RA patient from poorer strata of society. She was recently maintained on poorman’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Mr J, a 50 year old gentleman was a director of an Indian multinational steel company based in London, a frequent world traveller he presented with Psoriatic Arthritis unmistakable with embarrassing skin lesions on his face. He said that he has had pulmonary tuberculosis in his youth, was willing to take the risk of possible exacerbation but I would treat him with a biological? I did. Now he comes annually for a checkup but insists I give a prophylactic shot of biological.

Of all the 108 types of Arthritis, I find psoriasis most gratifying to treat ... as patients can see the outcome maintained on poor man’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Laugh it off Doc!

By
Harish, Final year student M.B.B.S
Yuva Vishalini Ravindran, Final year student M.B.B.S
Dr. Subramanian Nallasivan
Madurai, India

A P L A R
Asia Pacific League of Associations for Rheumatology
e-Bulletin | Quarterly | Volume 1 | Issue 4 | July 2017

... by Carlo Selmi

Unforgettable Cases ... PsA

Are clinical anecdotes relevant in today’s rahter overwhelming era of Evidence Based Medicine ... I believe they are after all the triggers to scientific inquiry, experimentation and the very basis of EBM.

A 17 year old handsome lad Abdul was brought in a depressed state of mind by his mother herself an RA patient from poorer strata of society. She was recently maintained on poorman’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Mr J, a 50 year old gentleman was a director of an Indian multinational steel company based in London, a frequent world traveller he presented with Psoriatic Arthritis unmistakable with embarrassing skin lesions on his face. He said that he has had pulmonary tuberculosis in his youth, was willing to take the risk of possible exacerbation but I would treat him with a biological? I did. Now he comes annually for a checkup but insists I give a prophylactic shot of biological.

Of all the 108 types of Arthritis, I find psoriasis most gratifying to treat ... as patients can see the outcome maintained on poor man’s cocktail of MTX+SSZ+HCQ. She said “Doctor, please stop my treatment but treat my son who has horrible psoriasis. He has stopped going to college. Leave aside girls even boys don’t wish to sit next to him. Yesterday as he went for a haircut the barber asked him to leave” Abdul was administered a course of TNF blocking agent. Six months later Abdul showed up at the clinic suited-booted with a gift for me saying he landed a job in Singapore and was willing to finance his mother’s treatment with a biological! ... what a touching story! ... unforgettable!

Laugh it off Doc!

By
Harish, Final year student M.B.B.S
Yuva Vishalini Ravindran, Final year student M.B.B.S
Dr. Subramanian Nallasivan
Madurai, India
Proteomics in Rheumatology

New kid on the block - Shankar Subramanian

The word “proteome” represents the complete protein pool of an organism encoded by the genome. In broader term, Proteomics, is defined as the total protein content of a cell or that of an organism.

Fig 1: The central dogma of Biology

Proteins form the building block of cells and form an integral part of cell structure and function in form of enzymes, receptors, transport protein etc. (Fig 1) Though humans have about 20000 genes, two cellular processes ensure the development of multiple proteins. Firstly, the messenger RNA can undergo a process called alternate splicing and thus give rise to about 30000 proteins. The second key process is that of post translational modifications in the form of phospho-rylation, glycosylation etc that give rise to about 500000 proteins.

Whenever we do an immuno-logical test, it is only possible if we have an ability to detect the antigen of interest using a suitable antibody. The key requirement is awareness of the antigen (Fig 2). Proteomics uses a different approach and identifies all the proteins. One can then identify novel proteins (antigens) associated with a particular condition and use strategies to make use of this information.

The study of proteins forms an interesting field in itself as protein alterations cannot be deduced from DNA alone. RNA expression too does not reflect the protein levels. More importantly, study can proteins can help in biomarker discovery. The study of proteins requires a multidisciplinary approach spanning sophisticated equipments to complex bioinformatics. (Fig 3)

There are two commonly used proteomic platforms that are used. These are Protein chip array that use intact proteins (e.g. protein, peptide tissue and antibody arrays) and the Mass spectrometry based methods that involve total tryptic digestion of proteins and Quantitation by stable isotope labeling (e.g. SILAC, ICAT, iTRAQ). (Fig 4) The MS based proteomic flow is depicted in Fig 5.
b. Comparing differential protein expression: One can compare the variable protein expression between different diseases as it provides valuable insights into biomarker discovery. Our team compared the protein expression between Rheumatoid and Spondyloarthritis and between RA and osteoarthritis. Studies like the ones above can be integrated into databases which provide the nidus for further studies.

C. Biomarker discovery: The next logical step is to analyse the data, identify the promising proteins, develop antibodies and evaluate and validate them in clinical studies. Biomarker discovery can help in early disease detection, identification of therapeutic targets and therapy monitoring.

**Future applications**

The study of proteomics is promising and seems set to revolutionize the field of rheumatology. One can expect the following changes in the next decade.

a. Clinical Diagnosis: Most current rheumatologic tests rely on ELISA-based methodology in which individual tests (e.g., for autoantibodies against dsDNA, Sm, Ro, or RNP) are performed on multiple different serum samples within individual wells in the same microtiter plate. Antigen microarrays will enable multiplex parallel testing that will most likely replace currently utilized autoantibody testing methods.

b. Identification of novel biomarker predictors: For eg one could study cohorts of lupus patients with serial serum collection over time. Flares would occur and the differential proteomic analysis would likely identify novel proteins that represent the perturbation in serum and can be further characterized to predict flares in future.

c. Understanding pathogenesis of autoimmunity: Several reports have described transcriptional profiles of tissue from patients with autoimmune diseases, including rheumatoid synovium. One can correlate these findings with the results of proteomic analysis from the same tissues. Such studies could identify and further define critical signaling pathways involved in disease pathogenesis, cell surface receptors that may serve as novel targets of drug discovery, and proteomic characteristics of lymphocytes that are anergic, autoreactive, or regulatory.

**Conclusion**

Proteomics based approach is the new kid on the block in the field of rheumatology and holds the promise of changing the way we would diagnose and manage rheumatological illnesses in future.

References


Gp Capt Shankar Subramanian
Professor of Medicine & Rheumatology,
Command Hospital,
(Air Force), Bangalore, India.
Associate Editor, VOA
Hi. I am Yuva Ravindran, 4th year M.B.B.S student from Velammal Medical College and Research Institute, Tamil Nadu. I had one of the rarest opportunities, along with my friends Dhivya, Jane and Harish, of being a part of the 4th Annual South Zone Indian Rheumatology Association Conference 2017 and being able to lend my ears to the talks of erudite professors from across the globe.

This very well attended conference was organized by the Chairman, Professor G. Narsimulu a doyen of Rheumatology who nurtured the discipline and many students. In fact Professor Narsimulu initiated Rheumatology OPD at National Institute of Medical Sciences (NIMS), Hyderabad; organized IRACON 1998, CMEs: 1999, 2000, 2002, 2004. He set up a full-fledged Department in 2001, offering DM Rheumatology and later for the first time DNB Rheumatology in 2004 heading the Department. Working tirelessly to promote Rheumatology is now the Dean-elect of Indian College of Physicians. The Organising Secretary, Dr Rajkiran Dudam was on his toes ensuring everything polished to perfection. At a glittering Inaugural Ceremony the Hon’ble Health Minister and Medical Minister, Dr C. Laxma Reddy Guru, Telengana State delivered an informative, inspiring talk. Also speaking from the dais was Dr Ameeta Agarwal, President of Indian Rheumatology Association and Dr Prakash Pispati, Past President - Asia Pacific League of Associations for Rheumatology and Indian Rheumatology Association.

SZIRACon 17 was a three day event. The banquet hall of Taj Krishna, the venue for the curtain raising event - the preconference CME, served knowledge to those gathered on the various rheumatological conditions and their management trends at present. The latest updates were well received by the audience.

The post lunch symposium started with the captivating talk by Prof. Shoenfeld Yehuda about 'Microbiome and autoimmunity' which lured the concentration of the audience, following which we had an intriguing lecture about 'Why women are more prone to develop autoimmune diseases?' by Prof. Carlo Selmi, after which the hall broke into a brainstorming discussion about 'why women' and both the post-presentation questions and answers led to an enigma about the biology of women and left us in a quandary. At this point Dr Pispati recited a famous line by George Bernard Shaw in his play Pygmalion, later screened My Fair Lady, "Why can't a woman be more like a man!" The scientific session ended with Prof. Justin C.Mason's presentation about 'Vascular cytoprotection and premature atherosclerosis'. It'd be inequitable if I don't mention that the post-lunch symposium never did fail to kindle our love for research and encouraged us to explore the yet-to-be-revealed areas of rheumatology. Added to this, the cultural activities and the inaugural dinner were a feast to the eyes and the palates of the audience.

The talk on 'Autoimmune syndrome induced by adjuvants' set the tone and pace for the second day of the conference. It was followed by talks on the Lupus nephritis in pregnancy, new modalities of Psoriasis therapy, biologics in JIA and the new drug Golimumab. We presented our posters in the post lunch session. Poster presentation included case reports about rare medical disorders and research studies. My college mate and I won the second and first prizes in medical students' poster category respectively under the guidance of Dr.Subramanian Nallasivan. The number of oral and poster presentations exposed the level of enthusiasm for research in the medical community.

Afternoon session began with an informative talk about Takayasu arteritis which covered right from the basics to the advanced and recent updates about the disease. We also had an oral presentation session and a debate about Belimumab where both the speakers provided excellent data and review regarding the drug. It also raised new and answered existing questions of the practitioners. We were fascinated to hear our guide Dr.Subramanian Nallasivan's lecture about 'Biosimilars in Rheumatology- Real life data brainstorming discussion about "why women" and from South Tamilnadu", which was also well received. The closing session was the rapid fire round that provided the essential pearls about various aspects of rheumatology and was a fitting end to the scientific session of the second day. The Gala dinner at Jalavihar, as it's called was filled with 'gala' and fun.

...(continued on Page 11)
The last day of the conference started with the talk on auto antibodies in general population. Diagnosis and therapy of large vessel vasculitis, myositis and MCTD received good response. Several talks on the management of osteoarthritis and role of molecular therapy provoked new thoughts among those gathered. More oral presenters showcased their mettle in research. Tips to publish research, career guidance and startups in rheumatological practice proved useful to the competitive and young part of the audience. The conference came to an end with the valedictory function. The curtains were brought down and the assembly dispersed with knowledge and memories looking forward to the next edition of SZIRACON. Thank you all.

By Yuva Vishalini Ravindran, Madurai, India.

E-mail ID: haileyjaden@gmail.com

VOA welcomes such coverage of your conferences, events in your country to interest fellow members across 29 APLAR family of nations.

Living with Arthritis - by Dulika Weerasinghe, Sri Lanka

Having being identified as a rheumatoid arthritis patient 12 years ago, my dreams were almost shattered.

For someone who is married and having a little daughter, I never knew this hereditary disease would pin me down. Being an IT Engineer and holding a managerial position in an IT company, I did not allow my sickness to take control of my life.

With the help of Myright and SRA of Sweden who has made Disability Organizations Joint Front (DOJF) their driving force in the battle against arthritis, I had the opportunity of being the 1st president of Association of Persons with Rheumatic Diseases (APRD) in 2013, which now conducts all related activities in Sri Lanka.

We with the help of College of Specialists in Rheumatology and Rehabilitation (CSRRSL) are working with 10 districts in Sri Lanka. 90% of these patients are women. It gives me a lot of courage and satisfaction when I know I am not alone.

Dulika Weerasinghe
(Bsc-MIS (Ireland), PGDBM(Col), Scrum Master(Scrum Alliance), MBA (Reading), Secretary (2015-2017) - Association of Persons with Rheumatic Disease)
CALL FOR ABSTRACTS

Abstract Submission Deadline Details
- All Abstracts must be submitted before June 30th, 2017
- The online submission system will be closed at 24:00 hours by June 30th, 2017.
- All Abstracts submitted after the deadline will not be accepted.
- For more information, kindly email abstract@aplar2017.com

REGISTRATION DETAILS

<table>
<thead>
<tr>
<th>Registration Category</th>
<th>Early Rate (Before June 30th 2017)</th>
<th>Late/Oasis Rate (After July 1st 2017)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delegate (Medical Doctor/Scientist)</td>
<td>650 USD</td>
<td>750 USD</td>
</tr>
<tr>
<td>Allied Health Professional/Trainee/Student</td>
<td>350 USD</td>
<td>450 USD</td>
</tr>
</tbody>
</table>

Early Bird Registration (Before September 1st 2017) - Late Registration (After September 1st 2017)

- MSUS Workshop: 475 USD - 950 USD
- MRI Workshop: 125 USD - 250 USD
- Review Course: 50 USD - 50 USD

APLAR 2017 is now themed “Women Rheumatologists First” granting a 30% discount to all women rheumatologists upon their registration to the congress.

For more information please visit: www.aplar2017.com

VoA invites YOU to write: On the broad canvas of Rheumatology, Medicine and Life
- Thought provoking Essay • Challenging case • Anecdote, Satire, Cartoon • Debate
- Travelogue • Events, News and Views • Letters, Suggestions, Complaints
- Please recommend advertisement / Sponsor a page by your National Society / drug company

Announcements by Member National Organisation .... FREE !!!!

Adverts / Events / Announcements:
- Full Page USD 350
- Half Page USD 250
- Quarter Page USD 150

Email: prakashpispati@vsnl.net ; prakashpispati@gmail.com

VoA ... its YOURS !

VoA: Editorial Team (in formation)

Editor-in-Chief: Dr Prakash Pispati.
Associate Editor: Gp Capt. Dr Shankar Subramanian,
Editorial Board: Dr Kevin Pile, Dr K Yamamoto, Dr Zhanguo Li, Dr D Danda, Dr Yue Yang
Design & Layout: Prakash Pispati, Tushar Prabhoo, Mumbai, India.
Secretarial: Ms. Christine Rebello

All material published in this e-Bulletin represent the opinions and views of the authors and not necessarily of APLAR or its editorial team. Material published in this e-Bulletin are intended for information, understanding and discussion only and should not be relied upon as recommending a specific diagnosis or treatment. APLAR and its Editorial team accepts no legal responsibility for any errors or omissions and make no warranty with respect to material contained herein. The Editorial team of this e-Bulletin does not guarantee or endorse any commercial product or service. Copyright, no articles or its part may be published without permission of the Editor-in-Chief. email: prakashpispati@gmail.com ; prakashpispati@vsnl.net Mumbai, India