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SP0074 DIAGNOSIS OF CEREBRAL VASCULITIS

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Among all forms of vasculitis, perhaps that affecting the CNS (CNS-V) poses the greatest challenge in diagnosis given the lack of any non invasive high specificity test, the complex and extensive list of mimicking conditions, its inaccessibility for biopsy and its genuine rarity. The diagnosis still requires the presence of an unexplained neurologic sign or symptom(s) following an exhaustive evaluation, evidence of vascular involvement (by direct or indirect angiography) or biopsy and most importantly the meticulous exclusion of all those conditions capable of producing mimicking clinical, radiographic or histologic findings that would confound accurate diagnosis. Despite these challenges CNS-V has been increasingly reported due to a combination of increased diagnostic awareness and advances in diagnostics. Two of these major advances will be discussed including the use of direct vascular wall imaging to differentiate vascular inflammation from spasm or atherosclerosis and the use of next generations sequencing to identify infectious etiologies and obviate the use of biopsy. Clinical examples will be presented.

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

How to manage and treat childhood onset lupus? A multidisciplinary point of view

SP0075 CASE PRESENTER: CHILDHOOD ONSET OF NEUROLUPUS

Eve Smith. *Alder Hey Children's NHS Foundation Trust, Paediatric Rheumatology, Liverpool, United Kingdom*

Background: In the series of talks 'How to manage and treat childhood onset lupus? A multidisciplinary point of view' the first talk focuses on achievement of the initial diagnosis of Lupus within the childhood period, including some potential pitfalls and how these can be avoided. Initial and ongoing treatment within the childhood period, alongside paediatric specific therapeutic considerations will be discussed. The role of the multidisciplinary team of doctors, nurses, physiotherapists, occupational therapists, psychologists and sub-specialists will be highlighted. The impact of the diagnosis on the child, family, education and social activities will also be described. This talk will be followed by a subsequent talks following the patient through transition and into adulthood.

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SP0076 CASE PRESENTER: TRANSITION OF NEUROLUPUS PHASE INTO ADULTHOOD

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Childhood-onset SLE (cSLE) accounts for approximately 20% of all SLE cases and is often regarded as one of the most complex rheumatic diseases. With the increase of five-year survival rate of cSLE patients to over 95%, there is a growing number of adolescents and young adults (AYA) transferring from pediatric to adult care. Even in the best-case scenario, there is often considerable challenges regarding this transition. Hence, it is not surprising that morbidity, mortality and disease activity in cSLE, as well as in many other chronic illnesses and conditions, worsen during or just after the transition. The reasons for these deteriorations are numerous, with most prominent arising from the nature of the disease and changes during the tumultuous period of adolescence, but also the differences between pediatric and adult clinical and healthcare settings. Besides, the AYA patients with chronic conditions often feel they are not well prepared for the transition to adult care, while the adult rheumatologists commonly report concerns about assuming the responsibility of patients with the pediatric-onset disease. Some of these concerns are probably motivated by increased vulnerability of AYA patients with cSLE, who are more likely than their adult counterparts to develop lupus nephritis and neuropsychiatric manifestations, as well as other organs involvement and atherosclerosis. Moreover, due to the severity of the disease, patients with cSLE are treated more aggressively, accumulating more drug-related toxicity than patients with adult-onset SLE, which results in significant SLE-related damage and complications such as osteoporosis during the childhood. On the other hand, there is decreased medication adherence in AYA, further complicated by the neurocognitive and memory impact of the disease, as well as high rates of comorbid depression and anxiety. Some additional problems in cSLE patients at transition age are sexuality, fertility, and pregnancy. All this makes patients with cSLE require specialized and multidisciplinary care at the transition, that is capable of addressing medical, psychosocial, educational and vocational needs.

This presentation will be part of the comprehensive session discussing distinct features of the SLE during the different phases of life. It will emphasize specific challenges of the transition from pediatric to adult care, with the use of a compelling clinical case as an example.

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SP0077 CASE DISCUSSANT

Brigitte Bader-Meunier. *Hôpital Necker, Pediatric Immunology and Rheumatology, Paris, France*

Background: Padiatric-onset systemic lupus (pSLE) is a severe multisystem autoimmune condition which mostly manifests after the age of 10 years. It is mainly a polygenic disorder, but a mutation in a single gene may predispose to the development of SLE (« monogenic lupus »). We will describe some unusual presentations which may lead to a delayed diagnosis or misdiagnosis and provide clues for the diagnosis of monogenic lupus.

Objectives: To discuss the difficult diagnosis and pitfalls in pSLE

Results: The most common initial manifestations of pSLE are cutaneous, musculoskeletal, renal, hematologic, and fever. However, atypical symptoms may reveal the diagnosis or occur during the course of SLE. In a French retrospective study¹, thirty-two percent of children had atypical symptoms, mainly including abdominal involvement in 26 patients, which lead to negative laparotomy for presumed appendicitis before the diagnosis of SLE could be established. Abdominal pain was related to lupus pancreatitis or peritonitis. The diagnosis of pSLE should be systematically searched for in a teenager who presents with unexplained mood disorders, psychosis or depression, which may reveal pSLE. In a patient

with a suspected diagnosis of neuropsychiatric pSLE, underlying factors including infections, hypertension, metabolic abnormalities or adverse effects of medication should be excluded before considering a luovus-related neurological involvement². Finally, the diagnosis of pSLE should be also considered in case of severe complications such as macrophage activation syndrome or alveolar hemorrhage. Monogenic SLE should be suspected in early-onset SLE (< 5-year-old) and mainly comprise complement deficiencies, genetic overproduction of interferon- α , B-cell apoptosis defects and rare inherited immunodeficiencies. Each of these conditions is associated with specific features : 1) Primary complement defects are associated with recurrent pyogenic or neisserial infections 2) type-1 interferonopathies are often associated with spasticity, cerebral calcifications, encephalopathy, skin ulcers and chilblains, and, in some cases, with a growth delay (spondylenchondrodysplasia) 3) B-cell apoptosis defects (mutation in *PRKCD* gene) is associated with a lymphoproliferative disease. A proper diagnosis of SLE must therefore be based upon a complete family medical history as well as on clinical evaluation with details history of both present and past illnesses, analysis of growth chart as well as laboratory tests for SLE. The search for auto-antibodies towards nuclear antigens is a key step in the diagnosis strategy, keeping in mind that antinuclear antibodies are not specific for SLE. Screening for complement deficiencies via CH50, AP50, C3 and C4 is recommended in order to facilitate adequate treatment of comorbidities including infections² in pSLE patients².

Conclusion: The diagnosis of pSLE should be suspected in teenagers with acute unexplained symptoms, especially in case of abdominal pain or neuropsychiatric involvement. A monogenic predisposition to SLE should be considered in early-onset SLE, especially in patients with SLE family history, consanguinity, recurrent infections, and/or encephalopathy with spasticity.

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SP0078 CASE PRESENTER: LONGSTANDING NEURO LUPUS IN ADULT LIFE

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Background: Juvenile-onset systemic lupus erythematosus (SLE) poses significant challenges for paediatric and adult rheumatologists. Longstanding disease in adult life carries the sequelae of the protracted course of the disease, as well as of the various treatments received.

Objectives: To present a didactic case of long-standing SLE of childhood onset, with the purpose to familiarise the audience with the multifaceted aspects of the disease, following transition from adolescence into adulthood.

Methods: Report of an illustrative juvenile-onset SLE patient after transition in adulthood.

Results: A 25-year old lady was diagnosed with SLE at the age of 9, due to generalised tonic-clonic seizures (status epilepticus), photosensitive rash and positive serology for SLE (ANA, anti-dsDNA, low complements). She was treated with high-dose glucocorticoids and cyclophosphamide with a good neurologic response. At the age of 15, she developed hematuria and nephrotic proteinuria; a kidney biopsy was compatible with class IV lupus nephritis (LN), with few crescents. She received mycophenolate mofetil (MMF), again with glucocorticoids, with complete response at 12 months. After entering adulthood, 5 years later, at the age of 21, she had a severe renal flare with recurrence of nephrotic proteinuria and active urinary sediment. A second kidney biopsy was performed, which showed histologic transformation into mixed class IV + V LN, and increase in chronicity index. Readministration of MMF failed to provide at least partial response; to this end, high-dose intravenous cyclophosphamide was administered, again with no response after 6 months. Finally, the patient was treated with rituximab, in combination with MMF, which managed to achieve partial remission, with proteinuria levels ~ 1.5 gr/day and normal renal function. Sixteen years following her initial diagnosis, apart from her ongoing renal inflammation, our patient has suffered significant side-effects from long-term glucocorticoid therapy and her quality of life is significantly affected.

Conclusion: This case illustrates the formidable challenges faced by both patients and treating physicians, for a patient diagnosed with SLE in childhood and had frequent flares during transition into adulthood and later in adult life.

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15:30:00 – 17:00:00

Radiographic progression in arthritides: still valid or a tale from the past!?

SP0079 STRUCTURAL DAMAGE PROGRESSION IN RA – DOES IT STILL MATTER WITH IMPROVED MEDICAL AND NON-MEDICAL TREATMENTS

Désirée van der Heijde. Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands

The distinction between symptomatic and disease modifying drugs is based on inhibition of structural damage and preservation of physical function. Radiographs of hands and feet are typically used to assess structural damage in RA. They provide a good representation of overall damage of all joints and bone erosions and joint space narrowing can be assessed reliably. Structural damage is the consequence of inflammation and is related to permanent loss of function and other outcomes important to patients such as work and quality of life. In cohorts of RA patients followed in the eighties of the twentieth century, the average progression rate was about 7 units of the modified Sharp score. This was still the case in the control arms of the RCTs in the nineties and early zeros. However, in recent trials the progression in the control arms is reduced to around 1 unit per year. There are several reasons for this reduced progression observed in clinical trials. First, the duration of placebo is limited to a maximum of 12-16 weeks for ethical reasons. Consequently, there is only restricted time to develop radiographic damage. Second, more frequently an active comparator is used instead of placebo. Third, there is better overall standard of care. Fourth, inclusion of patients with less severe disease in RCTs. Moreover, some speculate that there is a trend to a milder form of RA, however this is hard to proof. For all these reasons, it is essential to enrich the population with patients with a higher chance of showing radiographic progression over the (short) period of the RCT To enhance the probability of proving a reduction in radiographic progression. These factors include ACPA/RF-positivity, erosive disease and elevated CRP.

It is frequently asked if a reduction of the mean progression of 1 unit in the control arm to the mean progression of 0.5 unit in the treatment arm is clinically relevant. However, clinical relevance cannot be based on mean progression scores due to the skewness of the progression: many patients do not show progression, while a minority show (major) progression. A reduction in the likelihood of (significant) progression by treatment A over treatment B could already provide more useful information. Moreover, people tend to relate the '1 unit' to the maximum score of 448 units of the scale. Though, it is important to realise that a patient with a score of 50 already has major damage and that RA is a chronic disease with many patients suffering for many years. But true clinical relevance of structural damage needs to be established in observational cohorts over longer follow-up times.

Despite the limited radiographic progression in the control arms of RCTs, it was possible to show the disease modifying effect by inhibition of structural damage progression for csDMARDs (mainly MTX), all bDMARDs and tsDMARDs currently on the market.

Disclosure of Interests: Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge

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SP0080 STRUCTURAL DAMAGE PROGRESSION IN AXSPA

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Structural damage in axial spondyloarthritis (axSpA) develops usually first in the sacroiliac joints and later in the spine. While development of structural damage in the sacroiliac joints is mostly relevant for diagnosis and classification (non-radiographic versus radiographic axSpA), structural damage in the spine has a relevance for the long-term outcome of the disease. Structural damage in the spine and inflammatory activity are two major determinant of functional status and spinal mobility in axSpA.

Structural damage in the spine in axSpA is mostly attributable to the process of new bone formation (development of syndesmophytes resulting in bony ankylosis) occurring in the areas affected by inflammation. Advanced ankylosis of the