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FRI0284

RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF LARGE VESSEL VASCULITIS: EVIDENCE TO GUIDE THE MANAGEMENT OF GIANT CELL ARTERITIS

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Background: The latest EULAR recommendations for the management of large vessel vasculitis (LVV) were published in 2009 (1). Since then, imaging has become a reliable diagnostic tool and new therapeutic options are available for giant cell arteritis (GCA), supporting the need to update the recommendations.

Objectives: To analyse the current evidence for the management (diagnosis/monitoring and treatment) of LVV to inform the 2018 update of the EULAR recommendations.

Methods: A systematic literature review (SLR) dealing with diagnosis/monitoring and treatment strategies for LVV, respectively, was performed. Medline, Embase and Cochrane databases were searched from inception until 31st December 2017. Evidence on imaging was excluded in light of recently published EULAR recommendations (2). We reviewed data relevant to GCA. Level of Evidence (LoE), was assessed in accordance with the 2009 Oxford Centre for Evidence-based Medicine.

Results: We identified 283 papers from the SLR. The implementation of a fast-track approach to diagnosis significantly lowered the risk of permanent visual loss compared to historical cohorts (Level of evidence – LoE 2b). The SLR confirmed the efficacy of prompt initiation of glucocorticoids (GC). There was no high-quality evidence on the most appropriate starting dose, route of administration, tapering and duration of GC (LoE 4). Patients with GCA are at increased risk of dose-dependent GC-related adverse events (LoE 3b). The addition of methotrexate (MTX) (LoE 1a) or tocilizumab (TCZ) reduced relapse rates and GC requirements (LoE 1b). There was no consistent evidence that anti-platelet agents given at the time of GCA diagnosis prevented future ischaemic events (LoE 2a). There was little evidence to guide monitoring of patients with GCA.

Conclusion: Results from a SLR confirmed the importance of a prompt diagnosis and rapid initiation of GC therapy. Patients with GCA are at an increased risk for GC-related comorbidities. MTX and TCZ can reduce GC exposure and relapse rates. There are yet no high-quality data to guide monitoring and duration of treatment in GCA.

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FRI0286

CUTANEOUS POLYARTERITIS NODOSA: A SUBSET OF SYSTEMIC PAN OR A DISEASE APART?

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Background: Cutaneous Polyarteritis Nodosa (cutaneous PAN) is a rare form of necrotizing vasculitis involving predominantly medium and small arteries. It is limited to the skin. The clinical course is mostly chronic, however it has a more favourable prognosis than systemic PAN. Cutaneous PAN may be preceded by infection, drugs intake or may reflect underlying inflammatory or autoimmune disease. The diagnostic criteria are controversial and in some cases overlapping with those of systemic PAN. Cutaneous PAN is limited to the skin, but occasionally patients present extracutaneous symptoms, namely: myalgia, arthralgia or multineuritis

Objectives: To describe the clinical manifestations of cutaneous PAN, emphasizing the extracutaneous manifestations, as well as comorbid associations.

Methods: Retrospective study (1989-2018) of patients with cutaneous PAN seen in a tertiary center: referral area 800.000 inhabitants. All the cases were reviewed regarding epidemiological, clinical, electromyographic, histopathological and laboratory findings. Infections and comorbid diseases were also reviewed.

Results: Twenty-three cases were recruited: 8 male (34.78%) and 15 female (65.22%) patients. Mean age at onset: 47 years (range 18-76). Mean follow-up period :105 months (range 12-380). Cutaneous manifestations included: subcutaneous nodules (95.65%), ulcers (52.17%), livedo *reticularis* (60.87%), livedo *racemosa* (8.70%), *atrophie blanche* (39.13%) and purpura (4.34%). Cutaneous PAN most commonly occurred on the legs (100%), followed by the thighs (47.83%), the upper limbs (39.13%) and the trunk (17.39%). The most frequent extracutaneous symptom were asthenia (78.26%). Extracutaneous manifestations, limited to the same area of cutaneous lesions, were myalgia (60.87%) and paraesthesia (56.52%). An electromyography was performed in 14/23 patients and mononeuritis multiplex was observed in 7 patients. Only one patient progressed to systemic PAN, with development of renal disease 12 month after the diagnosis. The following infections were identified: hepatitis C (2), tuberculosis (1), *Streptococcus pyogenes* (1) and rickettsia (1). Comorbid diseases included: autoimmune hypothyroidism (2), cutaneous psoriasis (1), recidivant polychondritis (1), adult onset Still's disease (1), ulcerative colitis (1), pulmonary idiopathic fibrosis (1) and acute myeloid leukaemia (1). Glucocorticoids were used at medium-high doses (20-40 mg/day) in 20 patients as induction therapy, and NSAIDs at full doses in the remaining 3. Thirteen patients (56.52%) developed relapsing forms. Of this, 12 patients (52%) needed associated immunosuppressive treatment to prevent relapse. The most widely used immunosuppressant was methotrexate, followed by mycophenolate or azathioprine.

Conclusion: A long-term follow-up, with careful anamnesis and examination, including electromyography, is necessary to better characterize the cutaneous and extracutaneous manifestations of cutaneous PAN. The progression to systemic involvement is infrequent and cutaneous PAN has a more benign course from a clinical, and prognostic point of view.

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FRI0287

EFFICACY OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS TREATMENTS ACCORDING TO THE TYPE OF MANIFESTATIONS BASED ON ANALYSIS OF 636 PATIENTS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) represent the treatment cornerstone. So far, EGPA management has been based on conventional immunosuppressants, but GC-dependence remains frequent. Recently, therapies targeting B cells and interleukin-5 have been prescribed, but data on large cohorts are lacking.

Objectives: This study aimed to describe therapeutic management and efficacy of treatments in EGPA patients.

Methods: We set up a multicenter European cohort that included 636 EGPA patients. Treatments used, complete remission rates and vasculitis relapse-free survival were recorded. Complete remission was defined as absence of vasculitis relapse and prednisone dose <5 mg/d at last follow-up. Efficacy to treat GC-dependent asthma/ENT signs was defined as the absence of asthma/ENT symptoms and prednisone dose ≤7.5mg/d within the 6 months after initiation.

Results: For induction, cyclophosphamide (CYC) was the most frequently prescribed immunosuppressant (36.2%), more often in patients with FFS ≥1 (P<0.0001). GCs alone were used in 37.3%, azathioprine (AZA) in 14.4% and methotrexate (MTX) in 6.2%. No difference was found in the 10-years overall survival between patients with FFS=0, FFS=1 and FFS≥2.

Complete remission rates were similar between conventional immunosuppressants (CYC, AZA or MTX) and GCs alone. Vasculitis relapse-free survival was also similar between CYC, AZA or MTX and GCs alone. Similar results were observed for first vasculitis relapse treatments.

During follow-up, GC-dependent asthma and/or ENT manifestations were treated with AZA (40%), MTX (25%), mycophenolate mofetil (16%), rituximab (RTX) (21%), CYC (19%), cyclosporine (6%), omalizumab (5.9%) and mepolizumab (5.5%), allowing GC-tapering ≤7.5mg/in 23%, 31%, 17%, 43%, 5%, 71%, 25% and 50%, respectively. Conventional immunosuppressants were mostly used in first and second line, while eosinophil-targeted biotherapies were used in 4th or 5th lines.

Conclusion: In EGPA patients, the response to conventional immunosuppressants, in addition to GCs, is often disappointing compared to GCs alone, without clear benefit on complete remission rates and relapse-free

survival. In contrast, notwithstanding a small number of treated patients, eosinophil-targeted therapies seemed promising to treat asthma and/or ENT manifestations.

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FRI0288

OPHTHALMOLOGICAL MANIFESTATIONS AND ENDOTHELIN-1 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIS (SNV)

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Background: Inflammatory eye disease is described in 50% to 60% of patients with ANCA-positive vasculitis and in 10–20% of patients with polyarteritis nodosa, and for 8% to 16% of patients it is an initial manifestation [1,2]. Endothelin-1 (ET-1) as a potential participant in the local regulation of intraocular pressure, ocular blood vessel tone, and iris smooth muscle tone, suggesting that it may be an important mediator in the development of ocular pathologic conditions [3]. The lower ET-1 plasma levels were found in the optic neuropathy [4].

Objectives: to provide a more complete description of the ocular disease in patients with systemic necrotizing vasculitis (SNV), to evaluate the serum level of ET-1 in patients with SNV with and without eye involvement.

Methods: The study included 36 patients with SNV (polyarteritis nodosa - 8, ANCA - associated vasculitis - 28) and healthy controls (n=26). The 17 patients with SNV had ophthalmological manifestations. Clinical activities of patients were calculated according to the Birmingham Vasculitis Activity Score (BVAS). The serum levels of ET-1 (pmol/L) were determined by immunoassay analysis using the kits of Biomedica. The outcomes of this study were the differences in marker levels between SNV patients with and without eye involvement and healthy controls estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves (AUC).

Results: The ocular manifestation of patient with SNV included episcleritis (n=10), anterior uveitis (n=3), ischaemic optic neuritis (n=3) and occlusive retinal vasculitis (n=1). All patients had active disease (BVAS>11). There were no significant differences of BVAS, ESR and CRP between SNV patients with and without eye involvement. In 14% patients with SNV eye involvement was an initial manifestation. The level of ET-1 (M ± σ) in group of SNV patients with eye involvement (n=17) was 0.28 ± 0.13 and did not differ significantly from the control group (0.27 ± 0.10, p> 0.05). At the same time, in patients without eye involvement (n=19), it was significantly elevated (0.36 ± 0.34) compared with control group and with group of SNV patients with eye involvement (p < 0.001). ROC analysis showed that the AUC for ET-1 is 0.5±0.10 (p=0.98), which indicates not acceptable capacity for ET-1 differentiate groups of patients with ocular involvement and patients without ocular involvement (sensitivity - 59%, specificity - 57%).