Objectives The aim of the study was to ascertain frequency of clinical manifestations in patients with CREST variant related to skin involvement in SSc.

Methods Since 1993 we have treated 184 patients with systemic sclerosis (SSc) at the Institute of Rheumatology in Belgrade. Within this group there were 51 (27.7%) – 49 females and 2 males, with complete clinical manifestations of CREST variant. Mean age of patients was 55.7 years and disease duration 10.9 years. Thirty-four patients (66.7%) had limited cutaneous SSc (lSSc) and 17 (33.3%) diffuse cutaneous SSc (dSSc).

Results Our results are in following Table 1:

Conclusion According our results, visceral involvement in systemic sclerosis does not depend on distribution of skin sclerosis. So we think that CREST variant of SSc can be classified as separate form of scleroderma.

AB0114 RAYNAUD'S PHENOMENON: CORRELATION BETWEEN CLINICAL MANIFESTATIONS AND NAILFOLD CAPILLARY MICROSCOPY

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Background

Objectives To determine the correlations between clinical characteristics and nailfold capillary patterns in patients with Raynaud's phenomenon (RP).

Methods Analysis of clinical and immunological features (RP: phases; time duration in years, symmetry, localization; skin and organ involvement, ANA tests) and nailfold capillary patterns were assessed in 150 patients referred for evaluation of RP during the period 1999–2000. Chi-Square and Fisher's tests were used for statistical analysis.

Results 142/8 female/male; mean age:42+ 15,6 years; RP duration:5,7 years. 47% of RP were referred without diagnosis, 5,5% as primary RP (pRP) and 49% as secondary RP (sRP): connective tissue diseases (CTD) in 73% of cases. Microangiopathic patterns detected were:38% normal, 25% functional (capillary pallor/hyperemia); 20% CTD pattern without specific capillary abnormalities of scleroderma (SSc), and 17% with SSc-pattern (? slow pattern? 7,6%; ?active pattern? 9,7%). Patients with slow pattern SSc were older than the patients with other patterns: mean average:53,8 years ($p < 0,05$). RP with uniphasic colour changes were observed principally in patients with normal or functional pattern and RP with biphasic colour changes in patients with SSc-pattern ($p < 0,02$). Significant association between ?slow? pattern SSc and anticentromere antibodies was detected ($p < 0,004$) and between ?active? pattern SSc and positive ANA test with nucleolar pattern. Anticentromere antibodies were detected in 9% of patients showing functional pattern with capillary pallor and ?active? pattern SSc was observed in 42% of positive Scl-70 antibodies patients. Sclerodermatous skin changes was associated with SSc-pattern and functional capillary pallor pattern ($p < 0,001$) and a higher proportion of soft tissue swelling in hands and organ involvement was detected in patients with ?slow? pattern-SSc.

Conclusion Functional pattern with capillary pallor showed a significant association with uniphasic RP, sclerodermatous skin changes and negative ANA test. Only 42% of patients with positive Scl-70 antibodies exhibited ?active? pattern.

AB0115 SCLERODERMA-LIKE CHANGES IN A DIABETIC PATIENT: A CLINICAL CASE

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Background Diabetes mellitus is a metabolic systemic disease that can be associated, particularly when glucose metabolism control is poor, with skin changes and sometimes finger contractures of the hands that clinically resemble scleroderma. Distinction between the two different conditions is important, because they have distinct therapeutic approach and prognostic.

A 55 year-old white woman came to our Unit because of skin changes and articular contractures. She had diabetes mellitus since a gestation eleven years ago and was being followed in the Endocrinology department for this reason. Her disease had been resistant to antidiabetic oral treatment and was complicated with a severe polyneuropathy in glove and stoking pattern. Control of glucose metabolism was poor and she was being taught to start insulin therapy. She had been also diagnosticated of an autoimmune tiroiditis and recent arterial hypertension. We observed a thin woman with yight shiny skin over her fingers and unreducible contractures of some of them in both hands. The skin of her distal legs was bilaterally swelled and sclerotic too. She refered a Raynaud fenomenon, which we weren't able to provoke with cold water. There were no other musculoskeletal findings or symptoms suggesting CREST or systemic disease beyond diabetes. Her ANA and anti-DNA were negative, as was anticentrome antibody and Scl70. The hand x-rays showed neither calcifications nor erosions. A capilaroscopy was performed, showing some megacapillaries and structural disorganisation. No avascular areas were found. We concluded, in face of the analytic results, that this was a scleroderma-like manifestation of diabetic cheiroarthropathy and not systemic or limited scleroderma. The changes seen in the capilaroscopy could be due to the cheiroarthropathy itself.

Objectives

Methods

Results

Conclusion

AB0116 TREATMENT OF SYSTEMIC SCLEROSIS WITH ANTI-TNF-ALPHA ANTIBODIES. A CASE REPORT

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Background In february 1999 a 39 year old woman developed progressive swelling of the hands, arthralgias, Raynaud's phenomenon, dyspepsia and reduced physical strength.

For this reasons, positive ANA's (no anti topoisomerase I antibodies, pathologic oesophagus manometry and clinical signs of lung involvement including typical skin lesions (thickening, necrosis, erythema anulare, etc.) systemic scleroderma was diagnosed.

In the course of disease DMARDs such as penicillamin and cyclophosphamide showed no efficacy over a period of 18 months. Relatively high doses of methylprednisolone (up to 250 mg/d; not below 20 mg/d) were needed to reduce the clinical signs of the disease.

In december 2000 anti-TNF-alpha-antibody therapy (infliximad) was started in a dosage of about 5 mg per kg body weight.

After four perfusions (weeks 0, 2, 6, 10) clinical improvement (healing of skin necrosis, reduced dyspepsia and dyspnoea, increased general feeling, reduced VAS from 80 to 20, increased opening of the mouth, increased movement of the hands and fingers) permitted a slow reduction of the daily steroid dose.

Objectives ./.

Methods ./.

Results ./.

Conclusion This is a case with positive therapeutic onset of infliximab (remicade) in a case with systemic sclerosis.

FRI0184 ANGIOTENSIN-CONVERTING ENZYME AND ANTI-ANGIOTENSIN-CONVERTING ENZYME ANTIBODIES IN SYSTEMIC SCLEROSIS

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Background

Objectives To investigate the levels of angiotensin-converting enzyme (ACE) and anti-angiotensin-converting enzyme antibodies (ACEab) in patients with systemic sclerosis (SSc).

Methods Thirty five patients with systemic sclerosis, age $50,0 \pm 11,7$ (mean $\pm$ SD), range 27–71 years, were included in the study. Duration of disease ranged from 1 to 20 years, means $7,0 \pm 5,2$. Thirteen pts had diffuse systemic sclerosis (dSSc), twenty two had limited systemic sclerosis (lSSc). Ten healthy subjects were selected as controls. Spectrofluorimetry for detection of ACE and ELISA for ACEab were used.

Results We revealed the two-fold lower levels of ACE in SSc pts compared with controls ($0,022 \pm 0,021$ vs $0,044 \pm 0,028$; $\delta = 0,012$). There were no differences in ACE values observed between the dSSc and lSSc groups ($0,019 \pm 0,017$ and $0,024 \pm 0,024$ respectively). The lowest levels of ACE were found in SSc pts treated with inhibitors of ACE ($0,013 \pm 0,010$), but was not statistically different from those of untreated SSc pts. In SSc pts, a positive correlation was detected between the levels of ACE and erythrocyte sedimentation rate ($r = 0,505$; $p = 0,019$), fibrinogen ($r = 0,578$; $p = 0,015$), titers of antinuclear antibodies ($r = 0,529$; $p = 0,029$).

The levels of ACEab in SSc pts were similar to those of the control group ($0,180 \pm 0,190$ and $0,208 \pm 0,057$, respectively). However, the ACEab levels in pts with dSSc were significantly higher than those in lSSc pts ($0,29 \pm 0,24$ vs $0,14 \pm 0,16$; $p = 0,041$). Comparable to lSSc group impaired results were also seen in pts treated with ACE inhibitors ($0,1642 \pm 0,1093$). The ACEab levels positively correlated with ANA titers only in dSSc pts ($r = 0,835$; $p = 0,019$). There was no relation between the ACE and ACEab levels neither in SSc pts nor in controls.

Conclusion ACEab can be involved in pathogenesis of SSc and further investigation is needed.

FRI0185 AUTOLOGOUS STEM CELL TRANSPLANTATION INTERNATIONAL SCLERODERMA TRIAL

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Background Autologous hemopoietic stem cell transplantation (HSCT) is emerging as a potential therapy for severe rheumatic autoimmune diseases, including systemic sclerosis. Phase I/II studies involving 65 patients with progressive SSC and organ involvement proved the feasibility of HSCT and demonstrated significant longterm effects on skin score, but with considerable toxicity including a treatment-related mortality of 12%. These results must be viewed against current data on morbidity and mortality (5-yr survival 50%) for this patient category. At the recent EBMT/EULAR consensus meeting, the concept for a randomised, controlled trial was approved to investigate whether the longterm benefits of HSCT outweigh the risks. As a result the ? ASTIS Trial? (Autologous Stem cell Transplantation International Scleroderma Trial) has now been launched.

Objectives To compare efficacy and safety of HSCT versus monthly intravenous pulse-therapy cyclophosphamide in patients with diffuse systemic sclerosis and heart, lung or kidney involvement at risk for premature mortality. The goal of both treatments is to prolong survival by arresting or retarding the disease process. It is postulated that HSCT has superior efficacy, which needs to be balanced against potentially higher toxicity.

Methods The ASTIS Trial is an international, multicenter, prospective, controlled, randomised, phase III study in selected patients with early diffuse SSC and major organ involvement. The ASTIS Trial is conducted under the auspices of EBMT/EULAR (Basel, Switzerland). The investigational treatment arm (HSCT) comprises the following consecutive steps: mobilisation of hematopoietic stem cells with i.v. cyclophosphamide (2×2 gr/m²) and filgrastim (10 ug/kg/day), leukapheresis and selection of CD34⁺ stem cells, conditioning with i.v. cyclophosphamide (200 mg/kg) and rbATG (7.5 mg/kg), followed by reinfusion of autologous stem cells. The control treatment arm consists of 12 monthly i.v. pulses cyclophosphamide (750 mg/m²).

The primary endpoint is event-free survival during the study period of 2 years, events defined as the development of persistent major organ failure (heart, lung, kidney) and death. Secondary endpoints include treatment-related mortality, toxicity, skin score, SHAQ, and quality-of-life. Side studies include evaluation of immune reconstitution in blood and fibrotic activity in skin. It is intended to enrol 200 patients in 3 years.

Results

Conclusion The ASTIS Trial is the first randomised study to evaluate the potential clinical benefits of HSCT versus conventional therapy in severe rheumatic autoimmune disease. The study will address whether a short period of intense immune suppression differs from chronically given, more moderate immune suppression, both qualitatively and quantitatively. Given the low incidence of severe forms of systemic sclerosis, and the efforts needed to conduct the study, international collaboration is mandatory.

FRI0186 CIRCADIAN PROFILE OF SERUM MELATONIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background Melatonin (MT) is secreted by the pineal gland and a circadian rhythm of MT secretion is related to light-darkness exposure. MT has been found to influence immune and endocrine functions and is a free radical scavenger. Immune