THU0547

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA IN PEDIATRIC RHEUMATOLOGY PRACTICE: LARGE SERIES EXPERIENCE OF THE SINGLE CENTER

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Background: Fibrodysplasia Ossificans Progressiva (FOP), also known as a "second skeleton disease" is extremely rare (1: 2000000) and disabling genetic disorder, caused by mutation of ACVR1 gene, a bone morphogenetic protein receptor. Among medical specialties there are no certain, capable to provide not only diagnostics, but also all medical maintenance (assessment and monitoring of extent of damages, the differentiated drug treatment, rehabilitation, contact with adjacent experts). It would be reasonable if the rheumatologist carried out a role of the main attending physician for the patient with FOP. It seems to be a lot of similarities between rheumatic diseases, especially spondyloarthritis (SpA) and FOP in the pathophysiology, clinical manifestation and the therapy approach.

Objectives: to present the single-center experience of the FOP patients and to identify similar symptoms in FOP and rheumatic disease.

Methods: The analysis of the large series of patients with FOP, who observed in the rheumatologic clinic.

Results: Our single center experience includes 26 patients with FOP. All 26 patients (13 male and 13 female) had 3 basic FOP clinical manifestations. In 23 patients molecular-genetic tests were performed and typical mutation (Arginine 206) occurred in 22 cases and one had an extremely rare mutation (Glicine 328). 22 (85%) patients had common for FOP massive heterotopic ossifications. 3 of them had formed heterotopic ossification through the X-ray negative stage to visible changes. Among typical phenotypic stigmas were: great toe malformation; thumbs malformation; peripheral osteochondromas; cervical spine abnormalities. Majority of the cases presented some similarities to SpA manifestations: ankylosis of the apophysal joints and vertebral bodies mostly in cervical spine; X-ray/CT evidence of the sacroiliitis in all patients, who were examined (n=8). Because of severe body deformity or metal details after previous surgery intervention there were no possibility to perform MRI in most patients, but we confirm typical sacroiliitis with extended bone edema on MRI in 3 patients. Recurrent episodes of the large joints synovitis were present in 5 patients. 4 patients demonstrated gradually formation of great toe ankylosis during the follow-up observation. The involution and decreasing of new FOP nodes associated with non-steroidal anti-inflammatory drug intake and/or glucocorticoids therapy were occurred in all patients.

Clinical features	Male	female	Total N of patients
Sex ratio	13	13	26 (1:1)
Age of initial manifestations (years)	<1	8	1
	1-9	6	8
	≥10	0	3
Great toe malformation	13	12	25 (96%)
Thumbs malformation	2	3	5 (19%)
Cervical spine abnormalities	12	9	21 (81%)
Peripheral osteochondromas	8	7	15 (58%)
Massive heterotopic ossifications	12	10	22 (85%)
CT/X-Ray/MRI picture of sacroiliitis	2 (of 2)	6 (of 6)	8 of 8 (100%)

Conclusion: Appearance of the similarities in FOP and SpA manifestation and the therapy approach could identify FOP as a potential rheumatic disease. Clinical observation of FOP patients could provide the important information for rheumatologist about insufficiently explored process of new bone formation.

Disclosure of Interests: None declared

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THU0548

ASSOCIATIONS BETWEEN: MARKERS OF BONE TURNOVER AND RADIOLOGICAL FINDINGS IN CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Although many children attending pediatric rheumatology departments are diagnosed with low bone mineral density on the basis of clinical imaging, it is difficult to determine which patients have the higher risk of developing osteoporosis as the secondary disease. Recently performed studies involving rheumatological patients have proposed

numerous serological indicators for better evaluation of the disease activity. These include markers of bone turnover, among others: bone alkaline phosphatase and osteoprotegerin (which are more specific for bone formation) and also beta isomerized carboxy terminal telopeptide of type I collagen, also known as Beta-Crosslaps (which is considered as an indicator of bone resorption).

Objectives: The main objective of the study was to evaluate the clinical usefulness of measuring serum concentrations of the selected markers of bone turnover in juvenile idiopathic arthritis (JIA) patients and assess their potential significance in prevention of osteoporosis in these children.

Methods: Study involved 59 children previously diagnosed with JIA (mean age at diagnosis: 9.0±4.3 years, mean age at study baseline: 12.7±3.9 years). All patients underwent Dual X-Ray Absorptiometry (DXA) examinations in order to assess bone mineral density. Wrist radiographs were also taken for evaluation according to the Steinbrocker classification. The presence of abnormalities in these tests was chosen as the criterion to divide patients into subgroups to perform group comparisons for the serum levels of markers of bone turnover: bone alkaline phosphatase, osteoprotegerin and Beta-Crosslaps.

Results: According to the Steinbrocker classification, 10 (16.9%) patients were staged as class I or higher. These children had significantly lower serum levels of bone alkaline phosphatase (p=0.0333) than patients with no radiological changes on wrist radiographs. The non-zero Steinbrocker subgroup had also lower Total Body Less Head Z-Score results (p=0.010) than the remaining patients.

The DXA results, expressed as Total Body Less Head and Lumbar Spine Z-Score, disclosed low bone mineral density in 10 (16.9%) and 12 (20.3%) patients, respectively. There were no significant correlations between serum levels of markers of bone turnover and bone mineral density measurements. However, bone alkaline phosphatase and osteoprotegerin were negatively correlated with DXA muscle mass (r=-0.359 p=0.040 for bone alkaline phosphatase, r=-0.372 p=0.0392 for osteoprotegerin). Similar correlation was found for bone alkaline phosphatase and DXA fat mass (r=-0.418 p<0.01).

Although Beta-Crosslaps appeared to be the only marker of bone turnover significantly (p=0.0410) associated with Juvenile Arthritis Disease Activity Score 27-Joint Count (JADAS27), it was independent from radiological findings involved in the analysis. However, serum levels of Beta-Crosslaps were higher in patients evaluated in summer than in those assessed in winter (p=0.0464). Radiological findings were not season-variable.

Conclusion: Low serum concentration of bone alkaline phosphatase seems to be a risk factor for low bone mineral density and, by extension, for osteoporosis. Therefore it should be considered as an important laboratory test in JIA patients suspected of secondary osteoporosis. Clinical significance of osteoprotegerin and Beta-Crosslaps needs to be further investigated.

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THU0549

SURGICAL MANAGEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: A MONOCENTRIC EXPERIENCE OF 257 PROSTHESIS

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Background: Juvenile idiopathic arthritis (JIA) includes all forms of inflammatory arthritis, with onset before the 16th birthday, lasting more than 6 weeks. Although conservative management with nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs can be effective, a significant number of young adults affected by JIA requires a major surgical procedure, including different types of prosthetic devices.

Objectives: This article presents a monocentric experience of an interdisciplinary team of rheumatologists and orthopedic surgeons for JIA and the outcome of patients subjected to prosthesis implantation.

Methods: Data were collected through a retrospective analysis of 583 patients attending to our transitional care center for JIA between 1999 and 2018, in the context of a once-week rheumatologic counseling with the orthopedic surgeons. Descriptive statistics were used to evaluate the baseline and follow-up data.

Results: On a total of 257 prosthesis implantations, 137 were total hip prosthesis, 101 total knee prosthesis and 19 total ankle prosthesis. The 10-year implant survival rate was 97%, with good results in term of function and comfort for the patients. Complications were observed in 9% of

patients, including intraoperative fractures, periprosthetic joint infections and wound dehiscence. The majority of patients were treated with biologic therapy before surgery.

Conclusion: Prosthesis implantation in JIA patients is a complicated and difficult procedure, related to the management of the biologic therapy, the low quality of bone, the remarkable stiffness and deformity of the joints. Long-term results were good, even in patients with severe arthritis, showing drastic reduction of joint pain and an improvement of functionality. The risk of complications results to be modest compared to a great survival rate and a valid recovery of joint range of motion. The interdisciplinary team composed by rheumatologists and orthopedic surgeons for the all follow-up of these patients is a cornerstone to obtain the perfect schedule for prosthetic implantation.

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THU0550 MYCOPHENOLATE MOFETIL (MMF) IN DEFINED AND UNDEFINED INTERFERONOPATHIES

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Background: Type I interferonopathies are genetic disorders characterized by an up-regulation of type I interferon (IFN) activity. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. They are characterized by autoinflammation and varying degrees of autoimmunity or immunodeficiency. Some patients with a phenotype strongly suggestive for type I interferonopathy with a high IS, do not show any mutations in known type I interferonopathies related genes, being classified as undefined

Objectives: To evaluate the effect of mycophenolate mofetil (MMF) in patients with defined and undefined type I interferonopathy

Methods: 7 patients with type I interferonopathy followed at a Pediatric Rheumatology center, were included. Leucocyte (WBC) and platelet count, hemoglobin (Hb), CRP, ESR, serum amyloid A (SAA), autoantibodies, complement levels and IS, were assessed before and after 5-7 months of MMF treatment (600 mg/m² BID). IS was determined by qPCR (high scores >1.42)

Results: Patient 1 and 2 presented respectively with SAVI and Aicardi-Goutieres syndrome. The others were classified as undefined. In patient 1 (table), treated with JAK1/2 inhibitor, MMF was followed by decrease of inflammatory markers and resolution of lung involvement; in patient 2 to an increase in Hb and normalization of inflammatory markers. Among patients with an undefined phenotype the addition of MMF to low dose prednisone led to complete resolution of inflammation. A reduction of the antinuclear antibodies titre was observed in patients 2, 3 and 7 and a normalization of complement level in patients 3, 4 and 7. Patient 5 had normal inflammatory markers already before the beginning of MMF possibly due to previously administered immunosuppressive treatment. Despite all patients presented a significant improvement of clinical picture after 5 months of MMF treatment, the IS decreased only in 4/7 patients while it remain stable or increased in the others

	PI 1	PI 2	PI 3	PI 4	PI 5	PI 6	PI 7
Disease	SAVI (lung and skin involvement, systemic inflammation)	Aicardi Goutieres (neurological involvement, rash, fever)	Undefined (epilepsy, arthritis, skin involvement)	Undefined (recurrent fever, hypertransaminasemia, hemophagocytic lymphohistiocytosis)	Undefined (hemiplegia)	Undefined (epilepsy, arthritis, skin involvement)	Undefined (recurrent fever, lymphadenopathy, hypogammaglobulinemia)
Clinical improvement after MMF	Resolution of lung involvement	Resolution of fever and rash	Resolution of rash, arthritis, improvement of seizures	Resolution of fever, inflammation and hypertransaminasemia	Improvement of motility	Resolution of arthritis and skin involvement	Resolution of fever and lymphadenopathy
Gender	F	F	M	M	M	F	M
Age at onset (yrs)	3 (days)	2	4	7	4	6	16
WBC/mm ³	16/17.4	8,0/8.4	9,8/8.5	1,7/8.4	4,4/8.2	4,4/5.2	6,6/5.9
Hb g/dl	7,7/8.9	8,5/12.3	12,9/12.8	9,7/13	12,1/10.7	12/12.9	11,5/15.1
PLT/mm ³	950/766	680/320	194/181	56/161	358/421	381/390	218/323
ESR (mm)	44/40	49/9	38/10	7/6	2/5	24/8	3/3
CRP (mg/dl)	1,22/0.73	3,13/0.06	5,55/0.32	<0.05/<0.05	<0.05/<0.05	1,15/<0.05	8,34/0.98
SAA (mg/dl)	95,8/3,62	5,37/2.82	188/8.11	<1.89	<0.84/	4,19/0.78	/
C3	154/134	122/108	81/92	83/118	203/170	127/108	53/133

Abstract THU0550 – Figure 1

Conclusion: Our data suggest that mycophenolate mofetil might be an effective therapy in patients with type I interferonopathy leading to improvement of clinical and laboratory features thus allowing a glucocorticoid sparing

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THU0551 VACCINATION COVERAGE IN FRENCH CHILDREN WITH AUTO-INFLAMMATORY DISEASES : PRELIMINARY DATA FROM THE JIRCOHORTE

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Background: Autoinflammatory diseases (AID) comprise a large number of rare diseases that manifest as recurrent sterile inflammation or disproportionate infection-induced inflammatory symptoms. Vaccine relation to AID is complex: on one hand the susceptibility to infections vary with the treatment options of the patient, on the other hand the disease activity may be triggered by vaccination. Nevertheless, effective immunization is crucial in this population. Up to now very little is known about vaccination coverage in AID children.

Objectives: To determine vaccination coverage in French children with an autoinflammatory disease.

Methods: Patients between 2 and 18 years with autoinflammatory diseases followed at the French Reference Center for Auto-Inflammatory Diseases-Versailles Hospital and included to the Juvenile Inflammatory Rheumatism cohort (JIRcohort) network - an international multicenter prospective cohort for children with inflammatory and rheumatological diseases - were included in this retrospective monocentric observational study. Vaccination coverage of each disease and complete status of vaccination was assessed at the last out-patient visit, according to the national immunization program.

Detail of every vaccine received (number of doses and date of administration) were collected by a pediatrician from written immunization record (vaccination card). Demographic data, disease and medications used since diagnosis were also assessed. Patients with no available immunization record were excluded.

Results: 128 patients met the inclusion criteria. Sex ratio was 1.2 (70/58). Median age at the last out-patient visit was 8.4 years (2.5-17.9 years). 53 children (41%) presented periodic fever with aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome, 30 familial mediterranean