Personalised therapy for pedatiric patients in rheumatology suffering from chronic non-bacterial osteomyelitis

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Introduction

Chronic Non-bacterial osteomyelitis (CNO) is an inflammatory disorder affecting the bones in children and adolescents not caused by infection. A severe form of this condition is Chronic Recurrent Multifocal Osteomyelitis (CRMO), which typically leads to symmetrical inflammatory lesions, widespread severe and chronic pain. As a result, this reduces the quality of life and may interfere with a child's psychological development; CNO is usually diagnosis of exclusion. Initial treatment usually begins with nonsteroidal anti-inflammatory medications (NSAIDs); however, this may not be enough to alleviate the symptoms in some patients; hence second, third line therapy is sometimes required (pamidronate and biologics).

Objective

The aim of our study was to analyse a personalised treatment for patients suffering from CNO/CRMO and input data into Chronic Non-Bacterial Osteomyelitis International Registry (CHOIR), through Research Electronic Data Capture (REDCap).

Material and methods

We assessed sixteen patients who had been seen by the rheumatology team at University Hospital, Olomouc. Data were collected from their first visit and throughout their follow-up appointments, which included clinical, laboratory, and imaging data (X-Ray, Localised MRI and Whole Body MRI), severity of the condition, medications, and their response to treatment.
We focused on number of active lesions, patient derived measurements; VASB (visual analogue scale for pain); VASR (Parent/patient assessment of overall well-being (10cm visual analogue scale));

Material and methods continued

CHAQ (Childhood Health Assessment Questionnaire), and VASL (Physician's global assessment of disease activity (10cm visual analogue scale)). The comparison was done using Wilcoxon test for dependent samples and Mann-Whitney U-test for independent samples. The value of $p < 0.05$ was adopted as the level of statistical significance.

Results

A total of 16 patients were analysed. Thirteen (81%) of them were females and 3 (19%) were males. For each patient the number of lesions were assessed from baseline till the latest visit. Out of the 16 patients, 15 (94%) patients had an improvement in their number of lesions (Fig. 1 Fig.3).
Abbreviations:NA=Not Applicable; NDY=Not Done Yet

Fig. 1 Active Lesions and Pain Score (source:own)

	sex	age	Number of Active Lesions (imaging: MR)						Pain Score							
			Initial Assessment		Latest Assessment		Change (resolution of lesion(s))	Involvement of the Vertebrae: 1present 0absent	VASL		VASB		VASR		CHAQ	
			Date	Lesion(s)	Date	Lesion(s)			Initial	Latest	Initial	Latest	Initial	Latest	Initial	Latest
1	F	16	29.05.20	12	13.10.22	5	7	0	0	0	0	0	0	0	0	0
2	F	11	6.10.22	6	13.1.23	3	3	I	0	0	0	0	0	0	0	0
3	M	11	27.01.22	6	3.8.22	2	4	0	51	19	5	10	51	20	1.25	0.375
4	F	15	23.12.21	5	6.1.23	3	2	0	29	23	0	5	64	44	0.5	0
5	F	9	26.1.22	11	7.12.22	4	7	I	15	0	25	17	39	29	0	0.25
6	M	20	14.1.21	3	2.12.21	2	1	1	30	0	30	5	10	5	0.125	0
7	F	3	3.3.21	6	16.3.22	2	4	0	NA	0	50	0	13	0	1.5	0
8	F	11	1.9.21	7	22.3.23	4	3	1	0	0	2	0	0	0	0.25	0
9	F	9	14.05.20	5	11.11.22	4	1	0	0	0	0	0	0	0	0.125	0
10	F	13	18.04.18	4	10.03.22	2	2	1	40	0	1	0	42	1	0	0
11	F	14	27.08.20	4	08.03.23	2	2	I	50	0	89	0	90	0	2.125	0
12	M	17	07.01.21	15	29.09.22	12	3	I	60	0	24	0	60	0	0.625	0
13	F	15	02.11.21	7	01.09.22	4	3	I	NA	NA	14	21	2	21	0	0
14	F	9	25.10.22	1	NDY	NDY	-	0	NA	NA	50	29	49	29	0	0
15	F	11	27.01.22	1	30.08.22	2	+1	0	5	0	18	10	41	0	0.250	0
16	F	11	12.01.22	1	02.03.22	0	1	0	0	0	70	0	0	0	0	0

Patient 15 was the only patient that did not improve, a whole-body MRI will be done in 6-9 months after baseline. Patient 5 was on NSAID but worsened in December 2022 after infection. MRI revealed new sites and she was started on pamidronate immediately. All data were expressed as median, minimum, and maximum value, mean and standard deviation.

Results continued

The change in number of active lesions was found to be statistically significant (p 0.001). Improvement in VASL was more prominent in group with vertebrae involvement (p=0.096).

Fig. 3 Number of Active Lesions (source:own)

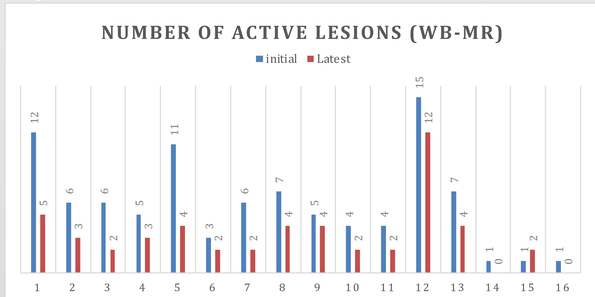
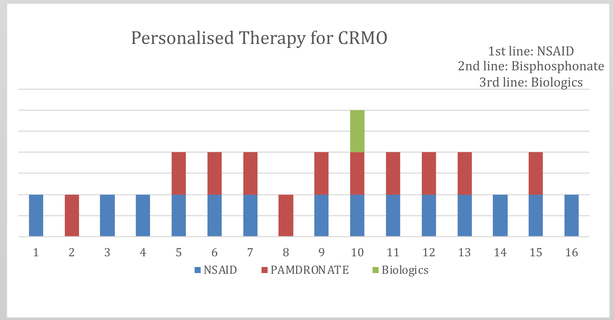


Fig. 2 Personalised Therapy for CRMO (source:own)



In the event of vertebrae involvement, pamidronate was administered every 3 months as first line treatment. Biologics used in patient 10 was Adalimumab.

Results continued

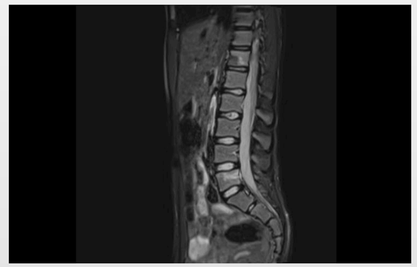


Fig. 4 Vertebral lesion; 13 year old female patient with multiple CRMO involvement including T12 and L5 vertebral lesions.

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Discussion

More data is required comparing patients on NSAIDs vs pamidronate alone. To draw conclusion and trends, a blind study consisting of two large groups: one with Pamidronate, the other group receiving placebo; but ensuring both groups consist of individuals with similar background for comparison. There are moral and ethical issues associated with such studies as few parents will want their child to be part of the placebo group. Hence CHOIR registry is collecting existing data and prospectively drawing conclusions. This is the most appropriate and ethical way to approach and analyse personalised therapy for patients with CRMO. In future research, biologics should also be analysed more in depth to see its efficacy.

Conclusion

The number of active lesions decreased significantly in our patients after therapy (NSAIDs, pamidronate and biologics).

References

1. Zhao Y, Oliver EY, Cooper MS, et al. The CRMO study group and the CARRA SVARD subcommittee consensus treatment plans for chronic nonbacterial osteomyelitis refractory to nonsteroidal anti inflammatory drugs and/or with active spinal lesions. *Arthritis Care Res (Hoboken).* 2018;70(8):1228-1237.
2. Hedrich CM, Hofmann SR, Pablik J, et al. Autoinflammatory bone disorders with special focus on chronic recurrent multifocal osteomyelitis (CRMO). Pediatr Rheumatol Online J 2013; 11:47.