

Supplementary Materials

Table S1. Epidemiological and clinical data, laboratory and radiological findings, treatment and outcome of the selected papers in the narrative review

Author Year	# cases	Median age (months)	Male (%)	Comorbidity (%)	Clinical manifestations (n, %)	Laboratory data (n, %)	Radiological findings	Therapy Vitamin C	Outcome Timing (%)
Ceglie et al 2018 [18]	3	29	100%	0	Musculoskeletal: 3 (100%) -leg pain/refusal to walk 2 -limping, arthritis 1	Anemia: 2 (67%) Vitamin D Δ : 2 (67%) Folate Δ : 1 (33%) Hypoalbuminemia: 1 (33%)	RX osteopenia, Frankel's lines, Trummerfeld zone 1 widening of the anterior rib ends at costochondral junctions, Frankel's lines 1 MRI inflammatory alterations of the soft tissue and cortical bone 1	IV followed by oral 2 (67%) Oral 1 (33%)	Recovery 1 month (100%)
					Cutaneous: 1 (33%) -petechiae 1				
					Mucous: 2 (67%) -gingival swelling 2				
					Malaise/anorexia: 2 (67%) Poor nutritional status 2 (67%)				
Chalouhi et al 2020 [45]	3	36	33%	0	Musculoskeletal: 3 (100%) -leg pain/refusal to walk 3	-	RX osteopenia, Frankel's lines, Trummerfeld zone 1 vertebral osteopenia 1 normal 1 MRI metaphyseal symmetric bone-marrow signal changes of long bones 1 multifocal symmetric bone-marrow signal anomalies at the metaphysis, subperiosteal collections, periosteal reaction 1	Oral: 3 (100%)	Recovery (100%)
					Cutaneous: 1 (33%) -inflammatory hair follicles 1				
					Mucous: 2 (67%) -hyperemic gums 1 -conjunctival bleeding 1				
					Irritability: 3 (100%) Malaise/anorexia: 2 (67%) Fever: 1 (33%) Poor nutritional status 1(33%)				
De Ioris et al 2016 [5]	4	-	-	100% cerebral palsy 3 Rett's S. 1	Musculoskeletal: 3 (75%) -leg pain 3 -arthritis 2	Anemia: 2 (50%)	-	Oral: 4 (100%)	Recovery 3 months (100%)
					Cutaneous: 3 (75%) -petechiae, ecchymosis 3				

					Mucous: 3 (75%) - gingival swelling 3 - gingival bleeding 2 Irritability: 3 (75%)				
Fortenberry et al, 2020 [49]	5	120	100%	100% autism 5 cerebral palsy 1 ADHD 1	Musculoskeletal: 5 (100%) - leg pain/refusal to walk 3 - limping 2 - arthritis 1 - leg edema - back pain Cutaneous: 4 (80%) - petechiae 4 - ecchymosis 2 - perifollicular hemorrhages 1 Mucous: 4 (80%) - gingival swelling 4 - gingival bleeding 4 - epistaxis 1 Fever: 3 (60%) Hyperreactivity: 1 (20%) Anorexia: 1 (20%)	Anemia: 2 (40%) Vitamin D Δ: 4 (80%) Vitamin B12 Δ: 1 (20%) Vitamin B1 Δ: 1 (20%)	RX osteopenia 2 normal 1 MRI enhancement of the margins of sacrum and ilium, the posterior iliac bones, and the pelvis apophyses 1	Oral 3 (60%) IV followed by oral 1 rectal 1	Lost at FU 3 (60%) Improvement at discharge 2 (40%)
Golriz et al 2016 [3]	32	132	59%	100% TIRO 20 BMTR 3 Autism 3 DD 1 fructose intol. 1 neglect 1	-	-	RX Frankel line 3; Trummerfeld zone 3 MRI increased T2 signal in the bone marrow of metaphyses, periosteal reaction and edema at femurs and tibias 3 soft tissue edema 2	-	-
Gulko et al 2014 [47]	4	48	100%	100% autism 2 Asperger's 1 DD 1	Musculoskeletal: 4 (100%) - leg pain/refusal to walk 4 - arthritis 1 Cutaneous: 2 (50%) - petechiae 1 - ecchymosis 1	High inflammatory markers: 2 (50%) high CRP 1 high ESR 1 Vitamin D Δ: 1 (25%)	RX normal 1 physeal widening with Frankel's lines 3 small metaphyseal fracture 1 MRI multifocal symmetric signal abnormality	Oral: 4 (100%)	Improvement 4 (100%)

					-hyperkeratosis 1 Mucous: 2 (50%) -gingival swelling 1 -gingival bleeding 1	Vitamin A Δ: 1 (25%)	at metaphyses with bone marrow enhancement 1 multifocal symmetric low signal on T1 and high signal on T2 at metaphyses; periosteal reaction; bone marrow enhancement 1 low signal on T1 and high signal on T2 at metaphyses 1 low signal on T1 and high signal on T2 at metaphyses; periosteal reaction; bone marrow enhancement 1		
Kitcharoen sakkul et al 2014 [50]	3	5	67%	67% DD 2 autism 1	Musculoskeletal: 3 (100%) -leg pain/refusal to walk 3 Cutaneous: 1 (33%) -hyperkeratosis 1 Mucous: 2 (67%) -gingival swelling 2 -gingival bleeding 2 Poor nutritional status: 1 (33%)	High inflammatory markers: 1 (33%) ESR 30 mm/h Vitamin D Δ: 2 (67%) Vitamin A Δ: 1 (33%)	RX Diffuse osteopenia, metaphyseal sclerotic lines 1 Frankel's lines in distal femur and proximal tibia 1 osteopenia and growth arrest lines in distal femurs and proximal tibias 1 MRI Normal 1 Bone marrow edema with bilateral enhancement of distal femoral and proximal tibial metaphyses, edema of the periosteum and muscle 1	Oral: 3 (100%)	Lost at FU: 1 (33%) Improvement 2 (67%)
Ma et al 2015 [4]	7	96	100%	100% DD 7	Musculoskeletal: 7 (100%) -leg pain/refusal to walk 7 -upper limb pain 1 Cutaneous: 5 (71%) -petechiae, ecchymosis 5 -perifollicular rash 1 Mucous: 5 (71%) -gingival swelling 5 -gingival bleeding 5 -epistaxis 1	High inflammatory markers: 2 (29%) ESR 44-30 mm/h CRP unspecified-1.8 mg/dl Vitamin D Δ: 5 (71%) Vitamin B1 Δ: 2 (29%)	RX Widening and irregularity of bilateral distal femoral and proximal tibial physis 1 Normal 1 upon review, widening of the physis and Frankel's line 1 non-specified alterations 4 MRI Bone marrow signal abnormalities at distal femur 1	Oral: 7 (100%)	Recovery 1-2 months (100%)

					Malaise: 2 (29%) Poor nutritional status: 1 (14%)	Vitamin B6 Δ: 2 (29%) Vitamin A Δ: 1 (14%)	Epiphyseal signal and diffuse infiltrative marrow process in femur and tibia metaphyses, edema and enhancement in soft tissues 1 Symmetric marrow edema and metaphyseal enhancement at femurs, tibias and fibulas; synovial enhancement and myositis 1 Bone marrow T2 hyperintensity and enhancement of the femoral metaphyseal, pelvis 1 Non-specified alterations 1		
Pan et al 2021 [48]	9	72	78%	67% autism 4 hydrocephalus 1 tuberous sclerosis 1	Musculoskeletal: 7 (78%) -leg pain/refusal to walk 7 -limping 7 -limb edema 4 Cutaneous: 6 (67%) -petechiae, ecchymosis 6 -perifollicular hemorrhage 2 Mucous: 4 (44%) -gingival bleeding 3 -epistaxis 1 Malaise: 2 (22%) Fever: 1 (11%) PH: 1 (11%) Poor nutritional status: 1(14%)	high inflammatory markers: 5 (55%), median ESR 22 mm/h median CRP 1.1 mg/dl Anemia: 5 (55%) Vitamin D Δ: 5 (55%) Vitamin B6 Δ: 2 (22%) Vitamin B9 Δ: 2 (22%) Vitamin B1 Δ: 1 (11%) Vitamin A Δ: 1 (11%) Vitamin K Δ: 1 (11%)	RX Normal 2 Frankel's lines 6, Osteopenia 2, Wimberger ring 2, Trummerfeld zone 4, subperiosteal hemorrhage 2, Pelkan spur 1 MRI increased signal and enhancement of the femoral, tibial, fibular metaphysis with bone marrow edema adjacent to the greater trochanter apophysis, osteitis of the femur 3	Oral: 6 (67%) IV followed by oral: 3 (33%)	Recovery 1-11 months (100%)
Ratageri et al 2005 [44]	3	12	100%	100% infantile tremor syndrome	Musculoskeletal: 2 (67%) -leg pain 2 Poor nutritional status: 3(100%)	Anemia: 3 (100%)	RX Frankel's lines 3	Oral: 3 (100%)	Improvement (100%)

Ratanachu-E et al 2003 [53]	28	29	60%	7% cerebral palsy 2	Musculoskeletal: 25 (100%) -leg pain/refusal to walk 25 -limping 24 -arthritis 13	Anemia: 19 (68%)	RX Frenkel's lines 28, osteopenia 22, Pelkan spur 9, Winberger ring 8, subepiphyseal infarction 4, epiphyseal separation 2	Oral: 28 (100%)	recovery 1-4 weeks (100%)
					Cutaneous: 1 (4%) -Petechiae 1				
					Mucous: 12 (43%) -gingival bleeding 12				
					Fever: 5 (21%) PH 2 (7%) Poor nutritional status 12 (43%)				
Rubino et al 2020 [46]	4	42	100%	50% cerebral palsy 1 autism 1	Musculoskeletal: 4 (100%) -leg pain/refusal to walk 4 -arthritis 2	High inflammatory markers: 4 (100%) median ESR 76 mm/h median CRP 2.3 mg/dl Anemia: 2 (50%) Vitamin D Δ: 3 (75%)	RX Frankel's lines 3, Trummerfeld zone 3, osteopenia 2, Pelkan spur 1 MRI multifocal metaphyseal alterations 4	Oral: 4 (100%)	Recovery 2- 4 weeks
					Cutaneous: 3 (75%) -petechiae, ecchymosis 3				
					Mucous: 4 (100%) -gingival bleeding 3 -gingival swelling 1				
					Irritability: 3 (75%) Poor nutritional status 1 (25%)				
Singh et al 2015 [75]	48	-	-	100% malnutrition 48	-	-	RX typical scurvy alterations 48 (Winberger ring 41, Frankel's line 41, pencil-thin cortex 36, corner sign 21, Pelkan spur 12, Trummerfeld zone 2)	-	-
Swed-Tobia et al, 2019 [52]	3	7	67%	100% Autism 3	Musculoskeletal: 3 (100%) -leg pain/refusal to walk 3 -knee contracture 1	High inflammatory markers: 2 (67%) Anemia: 2 (67%)	RX normal 3 MRI Intramedullary edema of vertebrae sacrum, sacroiliac joints, acetabulum, pubis, femurs 1	IV followed by oral: 3 (100%)	Improvement few days (100%)
					Cutaneous: 3 (67%) -petechiae, ecchymosis 3				

					Mucous: 3 (67%) -gingival bleeding 3		Intramedullary edema of right femur and pubis with a periosteal reaction, muscle reaction 1		
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ADHD: Attention Deficit Hyperactivity Disorder; BMTR: bone marrow transplant recipient; CRP: C reactive protein; DD: developmental delay; ESR: erythrocyte sedimentation rate; FU: follow-up; IV intravenous; MRI: magnetic resonance imaging; ND: neurological diseases; PH pulmonary hypertension; RX: radiograph; TIRO: transfusion iron related overload; Δ : deficiency