

Supplementary data

Chronological overview

Time after onset	Figure, stage	Observations, findings, laboratory values	Imaging	Interventions, drugs
1 m	Fig. 1, prior to stage Ia	Recurrent limp at the age of 9 years and 3.6 months Height 132 cm (14th p), body weight 31 kg (43rd p), BMI 17.8 kg/m ² (70th p). Abduction 35°, int./ext. rotation 20-0-35°. Vit. D 65.8 ng/mL	Contrast MRI 6 weeks after start of symptoms	1000 IU vit. D, 500 mg Cacium-Sandoz Forte daily
2 m	Fig. 2, early stage Ia	Cyst, small subchondral fracture	Radiographs and MRI	
4 m		Abduction 40°, int./ext. rotation 40-0-30°		
5 m	Fig. 3, stage Ib	Cyst, subchondral fracture > 50% → Salter-Thompson group B	Radiographs and contrast MRI	60 mg denosumab s.c. at 5.2 months
7 m		Cyst resolved	MRI	
9 m		Vit. D 50.3 ng/ml. Bone alkaline phosphatase 23.5 µg/L (normal 14–102)		
10 m		Abduction 40°, int./ext. rotation 45-0-35°. LLD -4 mm		
11 m	Fig. 4, stage IIb	Beginning of loss of containment	MRI (PD- weighting)	
1 y	Fig. 5, stage IIIa	Moderate extrusion, major anterior flattening	Radiographs	
1 y, 1 m	Fig. 6	Abduction 40°, int./ext. rotation 45-0-20°		20° varus osteotomy
1 y, 2 m		Scanty callus formation		Radiograph 6 weeks postop.
1 y, 7 m		Consolidation of osteotomy		Radiographs 6 months postop.
1 y, 8 m		Abd. 40°, int./ext. rot. 30-0-50°. LLD -1.5 cm		Plate removal 7 months postop.
2 y	Fig. 7, stage IIIb	Advanced re-ossification	MRI 11 months postop.	
2 y, 1 m	Fig. 8, almost stage IV		MRI	1000 IU vit. D
2 y, 8 m				Head hypertrophy: 11% increase in MD, 36% increase in volume
4 y, 3 m		At 13 years and 7 months, height 152 cm (9th p). No restraints		

p: percentile; BMI: body mass index; SC: subcutaneous injection; LLD: leg-length discrepancy; PD: proton density; MD: maximum diameter of femoral head.

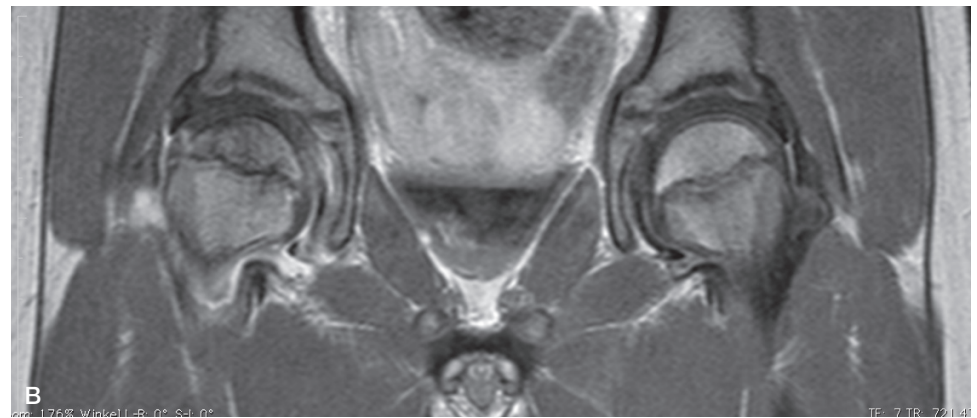
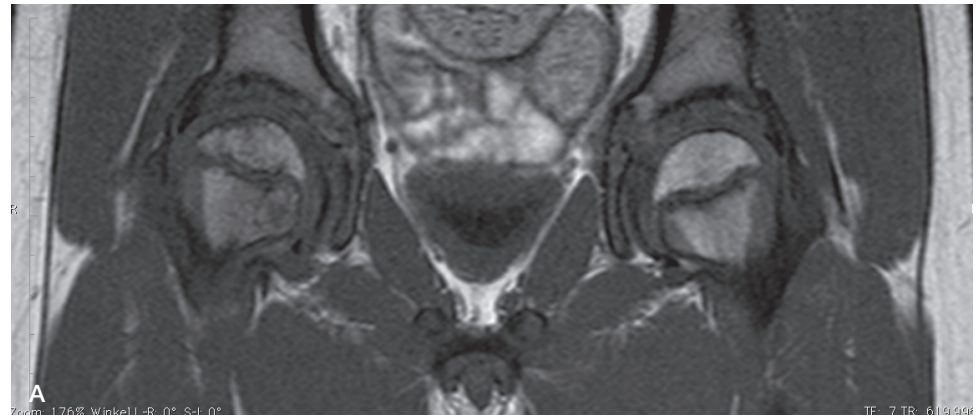


Figure 1. Initial MRI 6 weeks after the start of symptoms, revealing Perthes' disease on the right. A. Coronal T1-weighted image, 4-mm slice. Irregular decrease in the epiphyseal signal, faint roof sign, and cartilage hypertrophy. B. Contrast MRI, 4-mm slice. Perfusion impairment could be seen in the right epiphysis. Significant synovitis. Prior to stage Ia.



Figure 2. First pelvic radiographs at 2.3 months. A. AP view showing Perthes' disease on the right with increase in Waldenström's distance, a faint metaphyseal radiolucent band, and start of extrusion (cf. Figure 2 in the main text with position of the right head in relation to the white Ombrédanne-Perkins line (Ombrédanne 1923, Perkins 1928). No sclerosis. B. This Lauenstein projection shows minor anterior flattening, more evident metaphyseal involvement, and a subchondral fracture enhanced by gas, which was also visible in simultaneous MRI. Early stage Ia.

Figure 3. Coronal T1-weighted contrast MRI, 2-mm slice, 5.2 months after onset. Lack of perfusion in the center, small area of hyperperfusion laterally. Epi-metaphyseal cyst (postero)medially, showing enhancement and a central low signal—probably representing a sequestrum. Interestingly, an MRI done 6 weeks later revealed that the cyst had resolved. Marked synovitis. Simultaneous radiographs still showed no sclerosis of the epiphysis, but a slight reduction in epiphyseal height and some anterior flattening. Stage Ib. 2 days later, denosumab was administered.

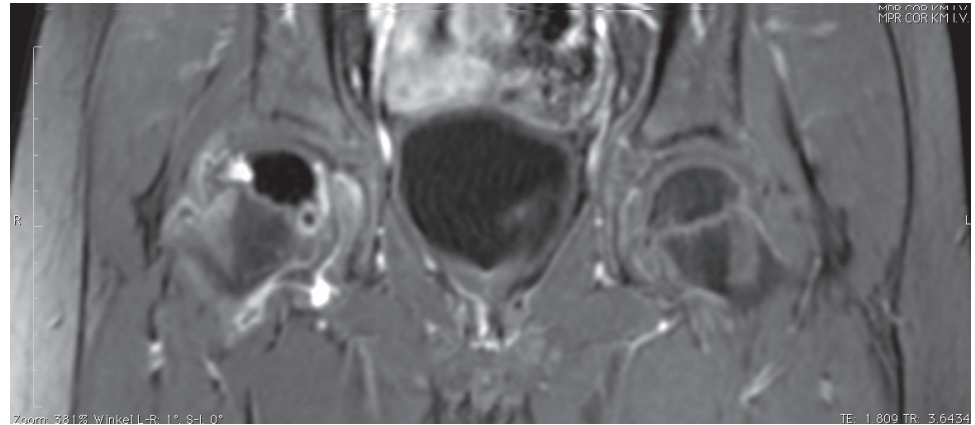


Figure 4. Coronal proton density-weighted fat-suppressed MRI, 3-mm slice. 11.5 months after onset and 6.3 months after injection of denosumab. Advanced resorption of necrotic bone: Coxa magna with evidence of extrusion. Flattening of the head by thickened cartilage of the acetabular roof and slight indentation by the acetabular rim. Concomitant labrum lift. Severe synovitis. The MRI morphology reflects the start of loss of containment. Stage IIb.

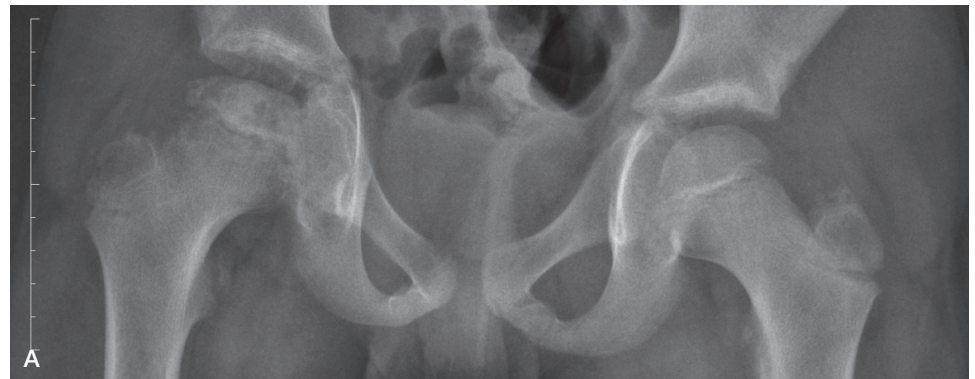
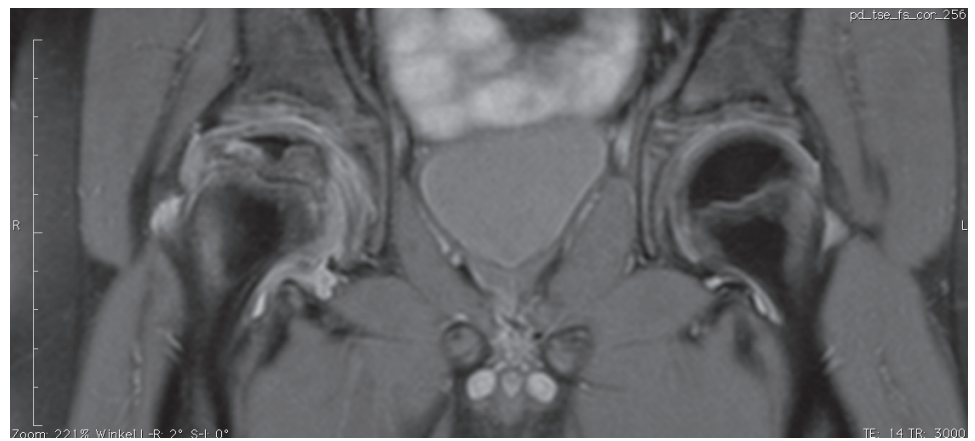


Figure 5. Pelvic radiographs taken 2 weeks later, 1 year after onset and 6.8 months after injection of denosumab. A. AP view showing coxa magna with an irregular bone texture of the epiphysis and a centrolateral density, with no circumscribed sclerotic fragments. Head unevenly rounded and moderately extruded. B. Bilateral Lauenstein projection showing major anterior flattening. Stage IIIa. A proximal varus osteotomy was performed 1 month later.

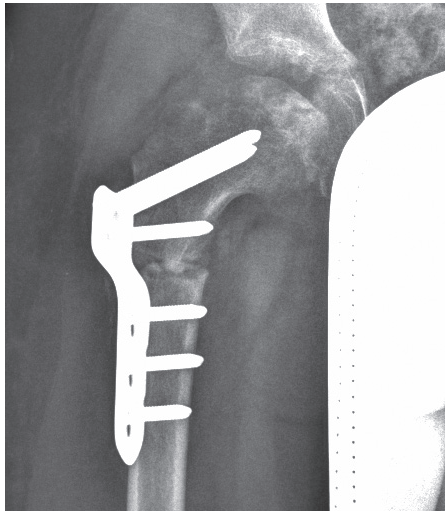


Figure 6. Radiograph taken 6 weeks postoperatively showing the varus osteotomy fixed with an angular stable pediatric LCP plate. Correction in varus of about 20° resulted in good containment. Head contour and bone texture were irregular. Scanty callus formation at the osteotomy.

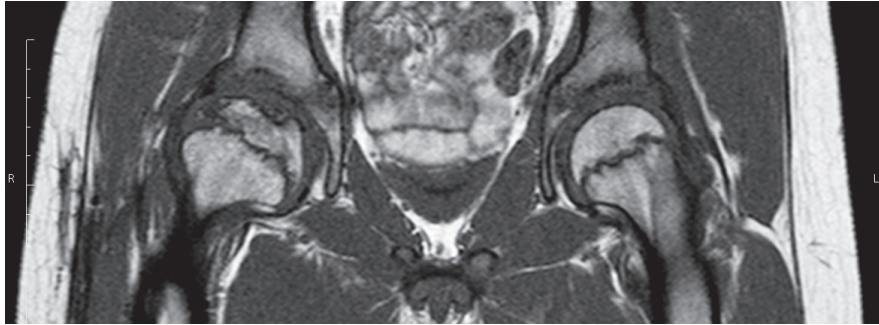


Figure 7. Coronal T1-weighted MRI, 3-mm slice. 11 months postoperatively, 2 years after onset. Persistent coxa magna. Head well rounded and well-contained with advanced epiphyseal re-ossification: stage IIIb.

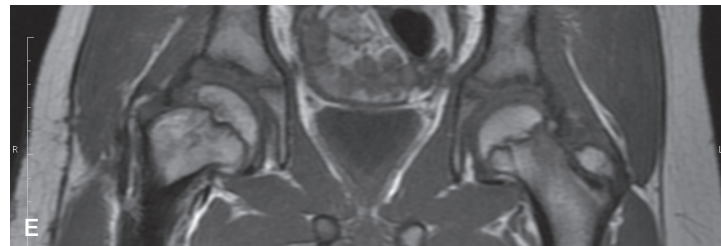
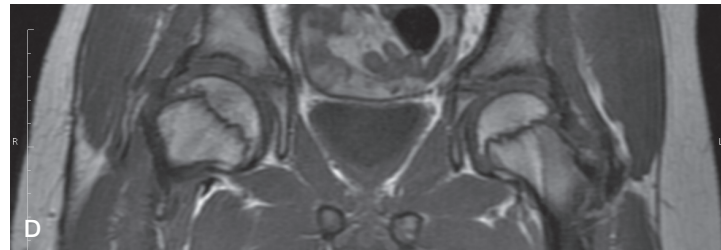
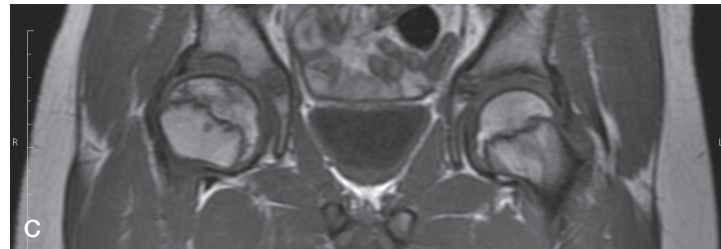
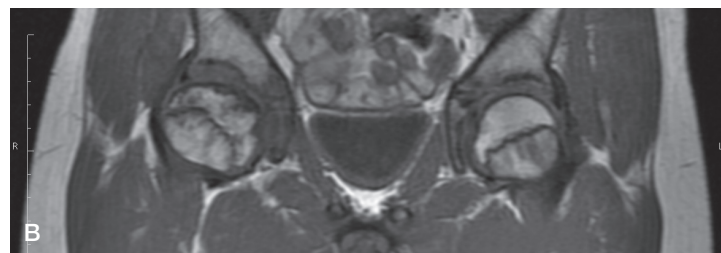
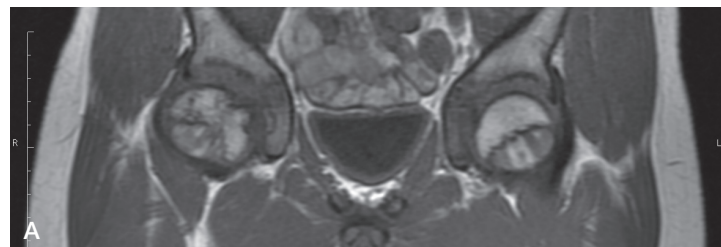


Figure 8. Coronal T1-weighted MRI (images 9–13, 4-mm slices) at 2 years and 8 months. Persistent coxa magna. Head almost spherical and well-contained. Labrum slanting downwards. No manifestation of physeal lesion. Almost complete healing.
 A. Image 9, far anteriorly. Advanced re-ossification. Physis halfway blurred (partial volume effect?).
 B. Image 10. Advanced re-ossification. No physeal lesion.
 C. Image 11. Complete healing. No physeal lesion.
 D. Image 12. Complete healing. No physeal lesion.
 E. Image 13. Advanced re-ossification. No physeal lesion. Nearly stage IV.