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Case Report

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Chronic thrombocytopenia and skeletal dysplasia in a 14-year-old girl with cystic fibrosis

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Abbreviations: CF: Cystic Fibrosis; SBDS: Shwachman-Bodian-Diamond Syndrome; PI: Pancreas Insufficiency; NOF: Non-Ossifying Fibroma

A 14-year-old Caucasian female with genetically confirmed diagnosis of cystic fibrosis (CF) (ΔF508/N1303K) and chronic exocrine pancreatic insufficiency (PI) presented with increasing pain of both knees. She developed a progressive chronic thrombocytopenia without any clinical symptoms (Table 1). Autoimmunological, rheumatological and infectiological causes were ruled out and the diagnosis of Shwachman-Bodian-Diamond Syndrome (SBDS) was established in 2009. Molecular genetic analysis detected a heterozygous missense-mutation in the SBDS-gene (c.127G>T for p.Val43Leu) of unknown clinical significance.

X-rays of both knees showed bilateral cystic structures of the distal femoral diametaphysis (Figure 1). Magnetic resonance imaging (Figure 2) supported the diagnosis of non-ossifying fibroma (NOF) without evidence of malignancy confirmed by histopathological results. A bone marrow biopsy was performed which excluded major complications of SBDS (myelodysplastic syndrome and acute myeloid leukemia). In consequence of the persisting pain despite analgesic treatment, curettage and spongioplasty of the bone lesions were performed. The pain resolved four weeks after surgical intervention while the asymptomatic thrombocytopenia further persisted.

The combination of exocrine PI, chronic thrombocytopenia and skeletal dysplasia represents the characteristic phenotype of SBDS and allows the clinical diagnosis without genetic confirmation [1,2]. The detection of mutations in the SBDS-gene may lead to an early diagnosis of SBDS before the full clinical spectrum is present. However, mutations in an homozygous status can only be found in approximately 90% of SBDS-patients [1,3].

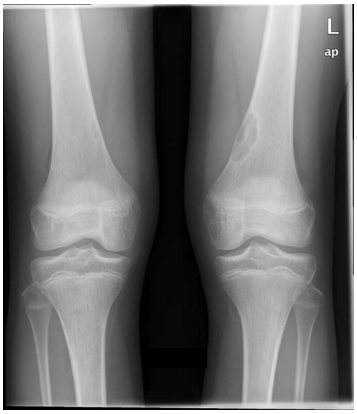

Figure 1. Hyperlucent lesions of the right and left femoral diametaphysis (X-ray a.p.) with thin sclerotic rims.

This case demonstrates the difficulties in establishing the diagnosis of SBDS especially in patients with other chronic diseases sharing similar symptoms (e.g. PI which was contributed solely to CF after birth). PI in SBDS can improve within the first years of life whereas in CF the PI is irreversible due to fibrotic changes in the organ.

Quarterly blood counts during the routine CF-visits were scheduled and with regard to haematological complications, annual bone marrow biopsies were recommended [1].

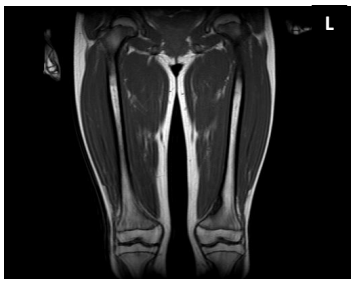

Figure 2. 3.8 cm x 1.2 cm measured, exentric lesion of the right and left femoral diametaphysis appearing hypointense in T1WI with peripheral low signal rims, which correspond to the sclerotic border (Coronal T1-weighted MRI-sequence).

Table 1. Blood count over the past years (2009 diagnosis of SBDS; 2014 non-ossifying fibromas) –annual lowest values are shown.

Year	Thrombocytes (/nl) (normal range: 150-400)	Leucocytes (x1E^3/l) (normal range:4.5-17.5)	abs. Neutrophils (x1E^9/l) (normal range: 1.5-9.9)	Hemoglobin (g/dl) (normal range: 11.5-15.0)
2009	88	4.05	2.44	11.4
2010	110	4.75	2.67	11.6
2011	80	3.92	1.97	12.5
2012	81	3.86	1.64	12.2
2013	79	3.79	0.48	12.7
2014	30	4.12	1.95	11.2
2015	71	3.40	1.67	12.2

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