Multicentric non-visceral infantile myofibromatosis causing hip contracture

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Infantile myofibromatosis is a rare mesenchymal tumor in infancy and childhood, thus infrequently encountered by clinicians.[1,2] In general, three subgroups are differentiated: solitary; multicentric; and multicentric with visceral involvement.[1–3] The solitary form is usually cutaneous with dermal involvement and extension into the underlying subcutis, muscle or bone(s).[1,2] Sometimes other solitary sites are affected.[4] In the multicentric subgroups several soft-tissue and bone sites may be involved alone,[1,3,5,6] or concomitantly with lung, cardiac, gastrointestinal or even central nervous system involvement (multicentric with visceral involvement).[7,8] The prognosis for solitary and non-visceral multicentric forms is excellent, whereas more than half of the infants with visceral involvement die from the disease and its complications.[1,3,6–8] Many of the lesions without visceral involvement stabilize and may undergo spontaneous regression within 1 or 2 years.[1,3,7] Here we report on a full-term newborn girl who presented with the benign form of multicentric non-visceral infantile myofibromatosis that caused significant contracture of the left hip, a complication not reported hitherto.

Case report

The girl was born to a 28-year-old mother (gravida 5, para 3) at 39 weeks after an uneventful pregnancy by normal vaginal delivery in a peripheral hospital. Amniotic fluid was slightly stained with meconium, premature rupture of membranes was not reported. APGAR score was 8/9/10, birthweight 2660 g (5th percentile), length 50 cm (50th percentile), and head circumference 33.5 cm (50th percentile). The parents and the other siblings were not affected by any cutaneous, musculo-skeletal or neoplastic disorders.

After delivery the neonate was transferred to St Franziskus Hospital Ahlen because of being small for gestational age, mild respiratory distress, transient hypoglycemia, suspicion of early-onset sepsis and the presence of several s.c., partially mobile, firm nodules on the trunk, arms, left hip and legs. Early-onset sepsis was confirmed, and i.v. antibiotic treatment with ampicillin and gentamicin for 7 days was initiated. Hypoglycemia resolved after i.v. administration of glucose, and there were no further respiratory problems. Coincidently, mildly elevated concentrations of galactose were found on newborn mass tandem spectrometry screening, which was due to a heterozygous reduction of uridine diphosphatase-galactose (UDP)-galactose epimerase activity without any clinical significance.

Clinical examination of the nodules showed multiple painless, partially mobile, s.c. nodules in proximity to bones, but without clear connection to these. The nodules were approximately 1.5 cm in diameter, located on the trunk, back, arms, left hip and legs. Due to the location of a nodule close to the left hip, a marked flexion contracture of this hip was present (Fig. 1). This was demonstrated on ultrasound of the hip, on which a typical nodule with a partially anechoic center surrounded by a thick tissue wall could be visualized close to the joint (Fig. 2), infiltrating the ligaments and capsule and thereby causing the contracture. The same ultrasound features could be seen in other subcutaneous nodules. Repeated ultrasound exams of the brain, heart, liver, spleen, kidneys and intestine did not show any involvement of visceral organs. Chest X-ray did not show any signs of lung involvement, and no connection of the soft-tissue tumors with or involvement of the bones could be demonstrated on X-ray (pictures not shown).

To determine the nature of the nodules, an open biopsy was taken from two infrascapular tumors (Department of Paediatric Surgery, Hamm, Germany). During operation the nodules appeared closely connected to muscle tissue, firm and of flesh-like color. A tentative histological diagnosis of infantile myofibromatosis was made by the local pathology specialist, which was confirmed by the German reference center for soft-tissue tumors (Institute of Pathology, University of Jena, Germany). The specimens (Fig. 3) showed characteristic nodular and multinodular proliferation. Within the nodules there was a zoning phenomenon. In their periphery, plump and spindle-shaped myofibroblasts were arranged in fascicles or whorls, without significant cellular atypia. In the center of the nodules there were less well differentiated spindle-shaped cells, typically arranged around thin-walled blood vessels. The tissue was immunopositive for smooth-muscle actin and vimentin.

The patient recovered soon from surgery and was discharged from hospital in good clinical condition. New nodules did not develop throughout the whole period, and an involvement of internal organs could not be demonstrated at the time of discharge. Because of the possibility of newly developing lesions, clinical and ultrasound controls were scheduled every 3–4 months.

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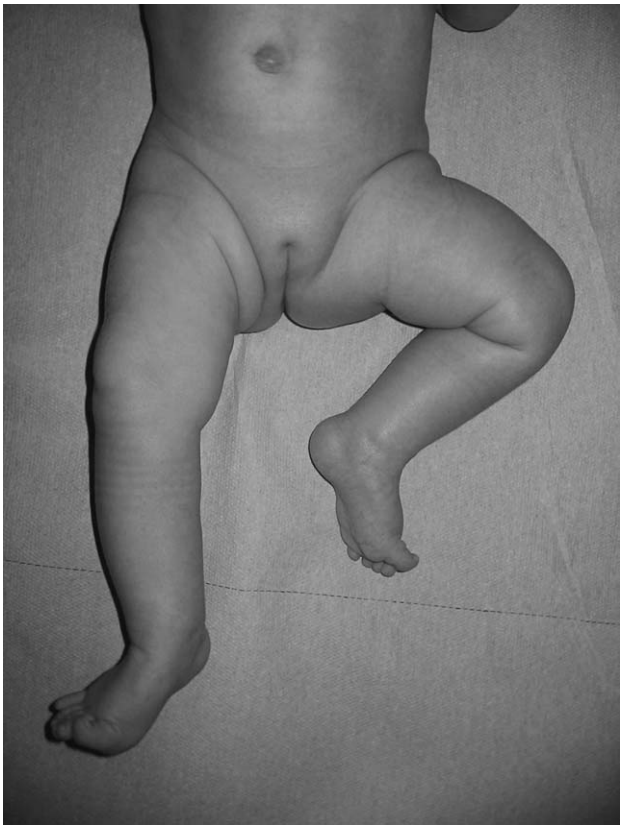

Fig. 1 Marked flexion contracture of the left hip at the age of 3 months (comparable to the clinical picture at birth).

After 12 months no additional lesions were found, and almost all lesions have disappeared completely or diminished in size. For treatment of the flexion contracture of the left hip, the patient was referred to a pediatric orthopedic department, where a conservative treatment approach was chosen. After 12 months the hip contracture had improved considerably. Flexion and adduction were freely possible, only abduction and extension involved some residual impairment. No nodule could be found on clinical and ultrasound examination (picture not shown). The left leg was a few millimeters shorter. On hip X-ray only mild dysplasia was present, therefore it was decided to continue with the conservative treatment for the present time.

Discussion

Infantile myofibromatosis is one of the more common fibrous proliferation disorders in infancy, but is still rare and thus little known among clinicians.[1–8] Although initially described some five decades ago as congenital fibrosarcoma, this disease entity was reclassified as congenital generalized fibromatosis in 1954, when it was recognized that these spindle cell tumors lacked malignant potential.[3] A systematic review of a large number of cases in 1981 resulted in recognition of the myofibroblastic nature of the tumor, and it was then named 'infantile myofibromatosis'.[2] Its etiology is unclear. A small number of reports have both implicated an autosomal dominant and autosomal recessive inheritance pattern, hence a thorough family history is essential.[1,3]

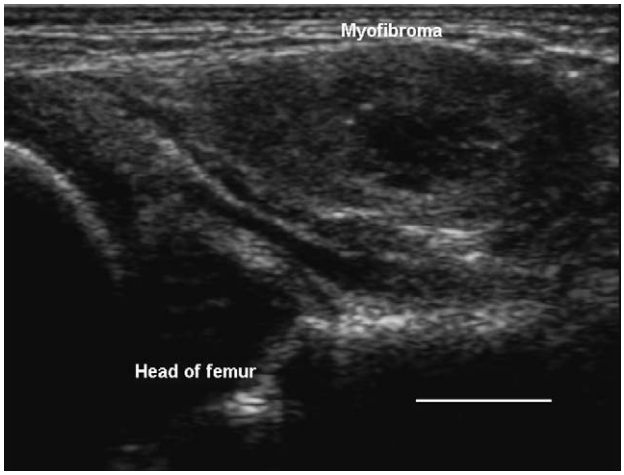

Fig. 2 Ultrasound image of the left hip region after birth: nodule 2.0 × 1.0 cm in diameter, central part partially anechoic, thick surrounding tissue wall, embedded in muscle tissue, no bone involvement of the hip, but infiltration of adjacent ligaments and capsule structures. Bar, 1 cm.

Histopathology of myofibromas (Fig. 3) is characterized by typical features as described in the present case report. In addition, frequently there is intravascular subendothelial growth; and mitotic activity (which usually is minimal to low) can be up to 10 per 10 high-power fields; both features do not signify malignancy. The tissue is immunopositive for smooth-muscle actin and vimentin, but immunonegative for S 100-protein and cytokeratins.[3,5–7,9]

To confirm the diagnosis, surgical biopsy is indicated to distinguish the disease from other entities such as dermoid, hemangioma, hemangiopericytoma, neurofibroma, metastatic neuroblastoma, fibrosarcoma, or rhabdomyosarcoma.[3,5–8]

As noted earlier, there are three clinical subgroups: solitary; multicentric without; and multicentric with visceral involvement.[1–3,5–8] The head and neck followed by the extremities and trunk are the most common sites of involvement.[5] Sixty percent

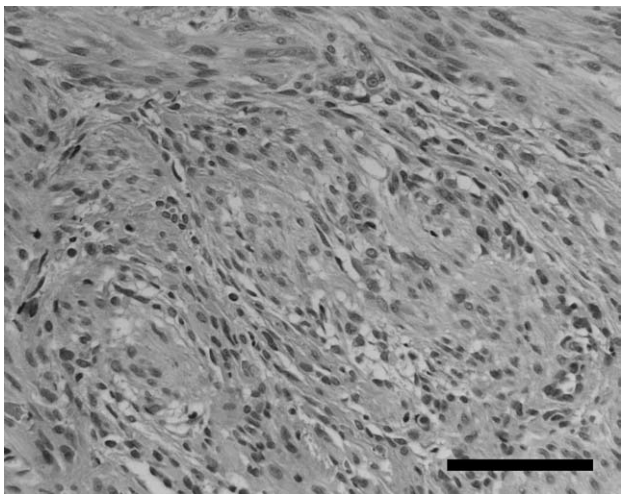

Fig. 3 Histopathological features (HE): myofibroblasts in a bundle-shaped structure, partially biphasic architecture. No cytological atypia. Bar, 100 μm.

of the patients have tumors at birth, but these can develop and progress also later in life.[1,3,9] The solitary form is usually cutaneous with dermal involvement and extension into the underlying subcutis, muscle or bone(s); it constitutes >50% of all cases and has a male preponderance.[1,6] The multicentric form without visceral involvement (approximately 30%), as diagnosed in the present patient, differs from this subgroup with regard to the number of nodules and a female preponderance.[1] The prognosis for solitary and multicentric forms without visceral involvement is excellent, and many of these lesions stabilize and may undergo spontaneous regression.[1,3,6] They can, however, cause severe complications if they are located close to sensitive sites such as the respiratory tract,[6] the eyes, joints or deep in muscles, where they present as torticollis.[3] Locations in long bones can cause fractures or growth impairment.[6] The present patient, who had a flexion contracture of the left hip, is to the best of our knowledge the first to be reported with this particular complication. The flexion contracture was due to infiltration of the ligaments and the capsule in the joint area, and was not caused by bone involvement. Due to the rare occurrence of this complication no clear guidance on the best treatment modality is available. A conservative approach was chosen because of the possible risk of recurrence after operation.[5] The satisfactory recovery justifies this approach. In some cases of other sites of involvement, complete surgical excision was performed,[4] but with a reported recurrence rate of approximately 10%.[3,5] In the majority of patients spontaneous regression can be awaited, which is common, in rare cases even in the multicentric form with visceral involvement.[1,3,6] Chemotherapy is most likely indicated only for patients with visceral involvement and severe manifestations,[3,10] because more than half of them have a poor prognosis and usually succumb to cardiopulmonary or gastrointestinal complications during the first months of life.[3,6,10]

Close clinical and imaging surveillance is indicated because some patients can develop new lesions later during their life.[1,3,5,8,9] Special attention needs to be paid to the examination of internal organs because their involvement indicates a poor prognosis. Ultrasound with its typical picture is a good option for imaging, but if in doubt then further techniques such as X-ray, CT scan and MRI are indicated.[9]

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