Infantile myofibromatosis of the iliac bone

Case report

A 13-year-old female presented a limping of the left lower limb, which appeared 2 months before. Clinical examination showed a painless and non-febrile stiffness of the hip. Past medical history was remarkable by the resection of a subcutaneous retroauricular myofibromatosis infantile tumor at age of 2 months, the presence of numerous naevi on the trunk, congenital hydrocephalus and macrocephalus. The patient denied pain, weight loss and visual change. Hematological examination revealed no abnormality.

Plain radiograms showed a well-defined osteolytic lesion with a sclerotic rim without periosteal reaction in left iliac bone (Figure 1). A computed tomography scan revealed a well-circumscribed hypodense lesion measuring 4 x 4 x 2 cm with slight expansion and erosion of internal and external cortex of the iliac bone (Figure 2). On magnetic resonance imaging, the lesion was polycyclic, iso-intense on T1-weighted images and hyper-intense on T2-weighted images. Contrast enhancement was intense (Figure 1).

Open biopsy first and total resection second was performed through Smith Petersen approach. Bone defect was filled by a piece of autologous ipsilateral iliac crest. Macroscopically, the tumor was soft, red-brown, well defined (Figure 3). On histopathologic examination, the lesion consisted of interlacing fascicles of spindle cells with eosinophilic cytoplasm looking like normal smooth muscle (Figure 3). Hyalinized collagen fibers were seen in the stroma, accompanied by parts of myxoid changes. Blood vessels...
were present. Focal atypical nucleus and few round epithelioid cells were seen. Immunohistochemical study showed that many cells were diffusely positive for PS100 (Polyclonal Latin Dako), smooth muscle actin (clone 1A4 Dako) and focally positive for CD34 (clone Qbend 10 Beckman Coulter). Staining was negative for desmin (clone D33 Dako), GFAP (polyclonal Dako) and caldesmone (clone h-CD Dako). Cellular proliferation rate was 1%, without mitoses, necrosis or anaplasia. The cells were also examined for chromosomal aberration. Karyotype was normal, despite a translocation t(9;16) was found on the first retroauricular tumor.

Finally, the diagnosis was a new localization of infantile myofibromatosis, occurring 12 years after the first one. Total body MRI was realized to search for further localizations and showed two odontogenic tumors localized on the 13 and 43 teeth. They were totally resected and the diagnosis of keratocystic lesions, which were not related to IM.

The presence of a congenital macrocephalus, numerous naevi on the trunk, two myofibromatosis infantile tumors in childhood, two odontogenic keratocysts and conjunctival lesions oriented the medical team toward a diagnosis of Gorlin syndrome, which was not confirmed by the genetic test.

At both 1 year and 3 years follow-up, we observed on X-ray no signs of recurrence and partial reconstruction of the iliac bone. The clinical examination showed normal range of motion of the hip and absence of limping.

Discussion

First described by William and Schrum in 1951 (8), who wrote about a “congenital fibrosarcoma”, infantile myofibromatosis was better identified by Stout in 1954 (3) who coined the definition of “congenital generalized fibromatosis” to describe disseminated nodular lesions in neonates, largely composed of collagen-forming spindle cells and involving variously multiple tissues. Subsequently, many names have been given to this entity until 1981, when Chung and Enzinger (2) used the “infantile myofibromatosis” term to emphasize the microscopic resemblance of the lesion to smooth muscle tissue and its frequent occurrence in both newborns and older infants based on their series of 61 cases. Although relatively rare, IM represents 35% of the soft tissue tumors present at the time of birth with an incidence of IM in newborns of 1/400,000 (9, 10). In 89% of patients, IM occurs
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with the 2 first years of life and affects 61% of cases from birth to 5 months of life (2). Solitary lesions, like the majority of fibrous tumors of childhood, are more common in boys with a sex ratio F/M from 1/5 to 1/8 whereas multicenter types are more frequent in girls (11). Bone lesions are uncommon in the solitary type and only 4 other localizations have been reported: distal tibia (Inwards et al.) (12), distal ulna (Kindblom and Angervall) (13), proximal femur (Yamamoto et al.) (14) and lumbar vertebrae [interspinous ligament of L2/L3 (15) and a lytic lesion of the 2nd lumbar vertebra (16)]. To our knowledge, localization in the iliac bone has never been reported before. This localization was responsible of a limping of to a flexum of the hip in our patient. Fortunately, there was no articular lesion and no deformation of the acetabulum.

In multicenter IM, skin, subcutaneous tissue, muscle and bone are the most commonly involved sites. In bone localizations, X-ray usually shows multiple lesions in the metaphyseal region of bones which can result in pathological fractures. Bone lesions radiologically appear as well-defined osteolytic area with or without sclerotic rim. In our case, CT scan showed a hypodense lesion with erosion of both lateral and medial cortex of iliac bone, suggesting that IM can be very aggressive and locally destructive although it is usually considered as a benign tumor. On MRI, IM lesions are usually isointense or hypointense on T1-weighted images and hyperintense, as in our case, on T2-weighted images. Contrast enhancement is usually intense (17, 18).

The usual size of IM tumors varies from 1 to 3 cm. They have a red-brown coloration and rubbery consistency. Microscopically, our case demonstrated features of IM with characteristic interlacing fascicles of spindle-shaped cells intermediate in appearance between fibroblasts and smooth-muscle cells in a fibro-myxoid matrix. The tumor cells have usually an eosinophilic cytoplasm; the proliferation rate and the atypia are poor. The mitotic activity is normal or minimally increased (2, 10, 12, 19).

Immunohistochemically, the cells observed in IM stain for smooth muscle actin, vimentin, HHF-35 and desmin is not always present, as in our case (20). CD34 positive evokes diagnosis of IM, showing the presence of vascular spaces in the tumor. Negative reactions are expected for S100 protein, epithelial membrane antigen and keratin.

In the differential diagnosis, congenital or infantile desmoid-type fibromatosis, fibrosarcoma, fibrous histocytoma, leiomyosarcoma, neurofibromas, osteoblasts mass and fibrous dysplasia must be considered. All those lesions have specific histological, immunohistochemical and ultrastructural features and different natural histories.

Familial IM is rare and the inheritance pattern of IM is unclear. In literature, conflicting evidences exist with regard to the inheritance pattern of IM. Some familial cases point to an autosomal recessive, while others indicate an autosomal dominant pattern with variable penetrance and genetic heterogeneity has been suggested as well.

In our case, as reported in 2004 (21), cytogenetic and fluorescence in situ hybridization analyzed revealed that the first retroauricular IM presented an unbalanced whole arm translocation between chromosomes 9 and 16, which was not present in the second IM tumor of the iliac bone.

The overall prognosis of the solitary IM and multicenter without visceral involvement forms of IM is excellent. No death has been reported in cases of multicenter type with single visceral involvement whereas the multicenter type with multiple visceral involvements has poor prognosis with mortality.
rates between 80% and 100% due to cardiopulmonary and gastrointestinal involvement (22). The treatment is determined by the localization of the lesion. Spontaneous regression has been described in literature.

Few cases of recurrence have been also described; Kindblom and Angervall (13) reported an IM of the ulna, which recurred twice after curettage. Recurrence rates for excised tumors range from 10 to 31% and recurrence has been reported up to 15 years from initial presentation (2, 7). In our case, the patient has presented a new localization, which was never described, 12 years after the excision of the first IM tumor. The recurrence of the tumor and the full clinical context oriented us to a genetic background; however, Gorlin syndrome has not been confirmed.

Therefore, facing a child with IM, a biopsy should first confirm the diagnosis. Secondarily, investigations must look for evidence of visceral involvement. This includes a full body IRM, which showed in our case two keratocysts odontogenic but no other IM synchronous lesion. In the solitary form, complete surgical excision is required. In the multicenter type, excision is required if a vital function is affected. Spontaneous regression has been described, which suggest that observation with close follow-up can be an option (23, 24).

Adjuvant chemotherapy has been described for the multicenter disease (25).

In summary, solitary osseous infantile myofibromatosis is a rare benign mesenchymal disorder. Total surgical resection is the treatment of choice, associated to an excellent prognosis. However, recurrence can happen even long time after the first resection, and new localization is possible, as in our case. This suggests close follow-up and clear information on the risk of recurrence to the parents and the family doctor, even if a total resection has been performed.

Disclosure

No conflicts.

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