Case report

A rare case of neonatal-onset infantile myofibromatosis with metastatic recurrence in adulthood

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Abstract

Infantile myofibromatosis (IM) is a rare mesenchymal disorder, typically observed during infancy and characterized by the development of myofibroblastic tumors within skin, muscle, bone or viscera. In most cases, spontaneous regression of the lesions occurs before the age of four, however therapeutic tools such as surgery and chemotherapy sometimes need to be implemented. Metastatic recurrence of this condition is very rare. We report the case of a newborn infant with multicentric IM involving the skin, intestinal tract and bone, who required long-term symptomatic treatment. Spontaneous regression was noticed at the age of four but twenty years later she presented with a complete spontaneous right pneumothorax revealing cystic pulmonary metastases of IM. There have been very few reports of metastatic recurrence of IM in adulthood and this unique presentation underlines the need for long-term follow-up of these patients to detect and prevent possible complications.

Keywords: *infantile myofibromatosis; recurrence; visceral involvement; metastasis*

Introduction

Infantile myofibromatosis (IM) is the most common fibrous tumor in infants and children under the age of two. However, it remains a very rare condition characterized by congenital benign myofibroblastic tumors of the skin, subcutaneous skin, striated muscles, bones and viscera. These lesions may be solitary or multicentric with or without visceral involvement.

The course of the disease depends on the initial presentation: spontaneous regression is expected with good prognosis in case of solitary lesions (limited to the skin and subcutaneous skin) whereas patients presenting with multicentric lesions (with bone and/or visceral involvement) suffer from a poor prognosis with high morbidity and mortality. There have been very few reports of adult onset so far, and metastatic recurrence in adulthood also seems to be very rare.

We report the case of a patient with late metastatic recurrence of IM in adulthood, developing after spontaneous regression of a multicentric type of IM with initial neonatal onset.

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Case report

We report the case of a full-term female newborn, born at 39 weeks of gestation, with no family history of IM. No perinatal event was

reported and clinical examination showed no abnormality.

At seven days of age, she was hospitalized for intractable emesis associated with a shock-like state. Laboratory results showed inflammatory syndrome with an elevated C-reactive protein (126 mg/L). Bacteriological urine and cerebrospinal fluid culture test results were negative. Abdominal ultrasound showed a swelling in the right adrenal lodge and chest X-ray revealed an unexpected abnormality in the right lung.

Her condition was stabilized after broad spectrum antibiotherapy was introduced and she was then transferred to the regional maternity hospital two days later to perform complementary exams.

At the age of nine days, clinical examination showed a lump in the right upper quadrant as well as a right costal swelling. A second abdominal ultrasound confirmed a vascularized adrenal mass and she was transferred to the Department of Pediatric Oncology with suspicion for neuroblastoma.

At ten days of life, clinical examination found a cutaneous nodule in the right axilla (measuring 1 cm in size), a subcutaneous nodule under the xiphoid process (measuring 3 mm in size) and a cutaneous nodule on the left hand.

Complementary examinations were performed. MIBG scintigraphy, catecholamine urinary excretion, bone marrow aspiration and bone marrow biopsy yielded normal results and neuroblastoma diagnosis was ruled out. A chest CT scan showed three thoracic masses (in the right costo-vertebral sulcus, in the right axilla and the right costo-phrenic angle). A biopsy of the axillary nodule was performed and histological analysis confirmed the diagnosis of infantile myofibromatosis.

As spontaneous regression was expected and given the absence of vital organ involvement, no aggressive treatment such as chemotherapy was undertaken and medical care consisted of symptomatic treatment with close follow-up.

Concerning her visceral involvement, she underwent a digestive endoscopy due to laboratory parameters showing low proteinemia. Several polyps were found in the gastrointestinal tract. Biopsies confirmed the diagnosis of IM, complicated with a protein-losing enteropathy and she thus received high-protein parenteral nutrition along with IV immunoglobulin. Five months later, when the patient was about to be discharged, a control endoscopy showed a tremendous decline in the number of polyps and pathological analyses of the biopsies were negative for IM. Parenteral nutrition was gradually stopped and enteral nutrition was subsequently increased, with good tolerance (no recurrence of vomiting and normalization of protein count).

Concerning her bone involvement, a standard skeleton X-ray first revealed several bone lesions (involving the skull, thighbone, pelvis, chest, and spinal column). MRI confirmed two vertebral collapses of T8 and T11 (*vertebra plana*). A corset for spine support was designed in order to avoid pathologic fracture and neurological complications. These lesions remained stable for the rest of the hospitalization period.

Concerning her cutaneous involvement, a spontaneous regression of the initially described cutaneous nodules was observed, while two new nodules occurred, which were localized under the left eyebrow and in the left hand palm.

The patient was discharged at the age of 6 months, with close monitoring of nutritional status and bone involvement (corset and physical therapy).

At the age of 7 months, the patient's general health was stable with well-tolerated enteral nutrition and weight gain. Clinical examination found a gradual regression of the nodule of the left hand palm. The nodule under the left eyebrow remained stable until the age of 9 months, when a decrease in size was noticed. A digestive endoscopy showed a unique polyp of the right colonic angle and MRI showed persistence of T8 and T11 vertebral collapses. The rest of the clinical examination was normal and no neurological disorder was found.

At the age of 1 year, clinical examination was unchanged (stability of the nodule under the left eyebrow, normal neurological exam). A digestive endoscopy yielded normal results and MRI showed a minimal bone regeneration. At the age of two, MRI revealed a satisfactory

vertebral bone repair and the corset was allowed to be removed.

The follow up was stopped at the age of four, as the only remaining lesion was the nodule under the left eyebrow, which had remained stable in the preceding years.

At the age of 22, the patient was admitted to the hospital for a complete spontaneous right pneumothorax. Chest CT scan showed bilateral cystic lesions with thin walls, some bullae-like lesions in the sub-pleural region and a restrictive ventilatory dysfunction. A thoracoscopic drainage and pleurodesis were performed, along with surgical biopsy of the parenchymal lung lesions. Histological analysis confirmed cystic pulmonary metastases of infantile myofibromatosis. Eleven months after surgical intervention, the patient remains asymptomatic and a new CT scan does not show any change in nodule size and number.

Discussion

IM was first described in the 50s: in his study « Juvenile fibromatoses » [1], Stout was the first to talk about « Congenital Generalized Fibromatosis» to describe multinodular tumors composed of collagen-forming spindle cells, involving superficial and muscular tissues as well as viscera and bones. Then, Chung et al suggested the term « infantile myofibromatosis» to emphasize the fact that these lesions show features of smooth muscle cells and fibroblasts, have a tendency of spontaneous regression and usually occur in children with a familial incidence in some cases [2].

IM is the most common fibrous tumor in newborns and infants. Clinical manifestation of IM occurs at birth in 50% of cases and in the first two years of life in 88% of cases [3]. IM is a rare mesenchymal disorder with an estimated prevalence of 1/150 000 births. It is characterized by solitary (myofibroma) or multiple nodules (myofibromatosis), which may present as purple to pink skin lesions, most usually painless except for adjacent nerve compression.

The exact etiology of this condition is still unknown, however familial cases have been described exhibiting autosomal and recessive transmission with incomplete penetrance and various expressivity. Recently, causative mutations in the PDGFRB gene (tyrosine kinase receptor for platelet derived growth factor which are stimulators for mesenchymal cells) and NOTCH3 gene (which is a positive stimulator of PDGFRB expression), have been discovered in affected families [4, 5].

Diagnosis is confirmed with histopathology, revealing peripheral spindle cells (myofibroblasts) proliferation, arranged in fascicles and surrounding polygonal cells. Necrosis and calcifications are also often noted in the central zone [2]. Immunochemistry is positive for actin and vimentin but negative for desmin, CD34 and S100 protein [3].

Tumors can be located in the skin, bone, muscle and viscera. Three varieties are described: solitary IM, multicentric IM without visceral involvement and with visceral involvement.

Solitary forms represent 80% of cases, mostly found in boys, described as a firm proliferating nodule or mass, more or less inflammatory, superficial, cutaneous or subcutaneous, principally located in the head, neck and trunk. Multicentric forms are more frequently found in girls. Skin, subcutaneous tissue, muscle and bone are the most commonly involved sites and spontaneous regression is most likely expected. On standard X-ray, bone involvement appears as an osteolytic lesion. Visceral involvement (i.e. central nervous system, lungs, intestinal tract) is usually revealed on gadolinium-enhanced MRI [3].

It is suggested that the underlying mechanism of tumor regression and growth is related to angiogenic stimulation and regression, both triggered by bFGF (basic Fibroblast-Growth-Factor) [6, 7].

No medical intervention is required when dealing with a soft tissue lesion as spontaneous regression is the expected evolution. Surgical removal can be performed for biopsy or for aesthetic purpose. High morbidity and mortality rates and uncertain prognosis are expected for patients with visceral involvement. Indeed, they may develop neurological, pulmonary, gastro-

intestinal and cardiac complications later in the course of disease, thus compromising vital prognosis. When entire removal is possible, surgery is the best treatment for solitary forms. In multicentric life-threatening cases, chemotherapy can be used whose gold standard regimen is vinblastine and methotrexate [8]. Other drugs such as alpha interferon or standard chemotherapy (vincristin, D-actinomycin and cyclophosphamide) may be used too [9]. Recent in vitro studies on Imatinib suggest that this molecule may trigger a response on cells expressing PDGFRB with mutations found in IM patients [10, 11]. Clinical trials testing this drug remain to be conducted on patients with IM.

Long-term clinical follow-up is advised, especially as late recurrence nodules have been reported (usually after incomplete resection or even in adulthood). Scheper *et al* [11] first reported a unique case of myofibromatosis with separate primary lesions at multiple sites involving the skin and oral cavity at the age of 2, 9, 12 and 23-year-old. All were surgically removed without local recurrences. Mashiah *et al* [9] emphasized the importance of long-term follow-up in multicentric form with the description of disease recurrence in the form of a single thyroid nodule, 30 months after spontaneous regression of confirmed IM subcutaneous nodules. The pathophysiological mechanisms underlying late IM recurrence remain unknown. Recently, Murray *et al* [12] reported the story of a 24-year-old woman, with PDGFRB mutation, who experienced late recurrences during her pregnancy (such as a lesion of the lower lip and a myofibroma histologically confirmed a few months later) after classical multicentric IM in infancy (skin, subcutaneous, bone and pancreatic masses) with spontaneous regression. Hormonal influence has been suggested by the authors to have led to the recurrence.

Conclusion

To our knowledge, the case we report is the first to describe a child with primary IM lesions involving the skin, intestinal tract and bone with spontaneous regression after 4 years of follow-up and presenting with pulmonary recurrences twenty years later in adulthood, in the form of cystic pulmonary metastases. This clinical picture is exceptional, but enables to underline the need for long-term follow-up in order to detect recurrences and prevent possible complications.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors have no conflicts of interest to declare

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