"Considerations for prenatal counselling of patients with cardiac rhabdomyomas based on their cardiac and neurologic outcomes."

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Abstract
Cardiac rhabdomyomas are benign cardiac tumours with few cardiac complications, but with a known association to tuberous sclerosis that affects the neurologic outcome of the patients. We have analysed the long-term cardiac and neurological outcomes of patients with cardiac rhabdomyomas in order to allow comprehensive prenatal counselling, basing our findings on the records of all patients seen prenatally and postnatally with an echocardiographic diagnosis of cardiac rhabdomyoma encountered from August, 1982, to September, 2007. We analysed factors such as the number and the location of the tumours to establish their association with a diagnosis of tuberous sclerosis, predicting the cardiac and neurologic outcomes for the patients. Cardiac complications include arrhythmias, obstruction of the ventricular outflow tracts, and secondary cardiogenic shock. Arrhythmias were encountered most often during the neonatal period, with supraventricular tachycardia being the commonest rhythm distur...

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Development of renal and iliac aneurysms in a child with generalized infantile myofibromatosis

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Abstract Infantile myofibromatosis is a rare disorder characterized by the formation of tumors in the skin, soft tissues, bone, and viscera. We report the case of a 3-week-old girl who presented with severe hypertension due to generalized infantile myofibromatosis including renal involvement. The infant was treated by chemotherapy and showed progressive regression of the tumors. However, her evolution was marked by the development of aneurismal dilations of the renal and iliac arteries as observed in fibromuscular dysplasia. We discuss the possibility of a link between these two mesenchymal disorders.

Keywords Infantile myofibromatosis · Fibromuscular dysplasia · Renovascular hypertension · Aneurysm · Mesenchymal disorder

Introduction

Infantile myofibromatosis (IM) is rare, but represents the most frequent cause of fibrous tumors in pediatrics [1]. The disease commonly occurs at birth or in infancy. Its clinical presentation includes a solitary form, a multifocal form with lesions limited to the skin, soft tissue and bone, and a generalized form with visceral involvement. Although the solitary form is associated with spontaneous regression in more than 50% of the cases, the prognosis of the generalized form is particularly poor with a mortality rate greater than 75%, often caused by respiratory failure [2].

We report here a case of severe systemic hypertension in an infant with generalized IM including renal involvement. The child was treated by chemotherapy and showed
progressive regression of the myofibromatosis tumors. However, her evolution was marked by the development of aneurysms and stenosis of the renal and iliac arteries, as typically observed in fibromuscular dysplasia (FMD). We compare the two mesenchymal diseases and discuss their uncommon association in our patient.

Case report

A Caucasian 3-week old girl was referred for a cardiac systolic murmur and failure to thrive. The infant was full-term with no perinatal problems. There was no familial history of systemic hypertension, or cardiac, renal or vascular disease. In addition to the murmur, the clinical examination revealed severe arterial hypertension (maximal systolic pressure 170 mmHg, maximal diastolic pressure 110 mmHg), and the presence of a small purple nodule on the right thigh. The initial ultrasound showed non-obstructive myocardial hypertrophy, right nephromegaly with central hyperechogenicity, and a left paravertebral mass extending from L2 to L4 (27×19×31 mm) in contact with the vascular renal pedicle. The right renal vessels were anatomically normal, but displayed a high resistivity index. The blood flow in the surrounded left renal artery was significantly decreased. Biological analyses demonstrated serum urea nitrogen at 14 mg/dL, creatinemia at 0.4 mg/dL, and a normal ionogram (Na⁺: 135 mmol/L, K⁺: 4 mmol/L, HCO₃⁻: 26.5 mmol/L, Cl⁻: 100 mmol/L, Ca²⁺: 10 mg/dL). The glomerular filtration rate (GFR) calculated according to the Schwartz formula was 68 mL/min/1.73 m² and the MAG3 Tc-99 m scintigraphy demonstrated reduced function of the right kidney (30% of global renal function). Plasmatic renin activity and aldosterone level were 31 ng/mL/h (normal: 8–17 ng/mL/h for this age) and 4.7 nM (normal: 0.9–3.6 nM) respectively. The child was treated with esmolol and nicardipine followed by a combination of propranolol and enalapril. An extended radiological workup (abdominal magnetic resonance imaging, chest computed-tomography, and skeletal survey) confirmed the paravertebral mass and revealed the presence of lung and bone lesions localized in the ribs, in the D2 and D4 vertebrae, in the left humerus, and in both femurs. A surgical biopsy of the thigh nodule was performed. The pathological examination suggested the diagnosis of IM with hyalinized acellular zones in contact with spindle cells disposed in whorls or short fascicles. Immunohistochemistries demonstrated the myofibroblastic origin of the cells with positive staining for vimentin and alpha actin, but negative staining for desmin, CD99, and S-100 protein. The patient was treated by chemotherapy according to the European Paediatric Soft Tissue Sarcoma Group recommendations (vinblastine 0.2 mg/kg and methotrexate 1 mg/kg once a week). The IM lesions progressively regressed. However, the evolution was marked by the occurrence of aneurysms on both renal arteries (right: 8×20 mm, left: 9×12 mm) and on the right common iliac artery (13×17 mm) after 4 months of treatment. Subsequent monitoring showed progressive atrophy of the left kidney associated with stenosis of the left renal artery that ultimately prevented the detection of the left aneurysm. The renal function of the child gradually worsened. After 12 months of treatment, when the chemotherapy was stopped, the GFR evaluated by EDTA Cr-51 isotopic clearance was 21.7 mL/min/1.73 m² and the

![Fig. 1](a) Coronal and b sagittal renal angiography showing aneurysmal dilatations of the right renal, the right common iliac, and the right internal iliac arteries (white arrowheads). The left renal artery is not visualized. The right renal artery shows a proximal stenosis (black arrowheads). The distal vascular pedicle is completely disorganized and the kidney is mainly perfused by a thin superior branch (open arrowhead)
MAG3 Tc-99 m scintigraphy revealed a deterioration of left renal function (relative uptake of 14.9%). At this time, radiological examinations showed the persistence of a small residual mass (diameter 10 mm) on the paravertebral left side, but neither bone nor lung lesions were observed. No other vascular lesions were detected. Ten months later, an angiography detected an additional aneurysm of the internal iliac artery and a stenosis of the proximal renal artery (Fig. 1). Downstream of the aneurysm, in the renal pedicle, the vessels were completely disorganized and the kidney was mainly perfused by a thin superior arterial branch. At that time, the child had biological signs of mild renal insufficiency (blood urea nitrogen 54 mg/dL, creatinine 0.58 mg/dL), hyperparathyroidism (PTH 128 μg/mL, phosphorus 5.3 mg/dL) with normal calcemia (9.98 mg/dL) under alfacalcidol, and moderate anemia (hemoglobin 9.9 g/dL). Her urine analyses were normal. Based on the risk of aneurysm rupture, surgical repair with insertion of a prosthetic graft of the iliac artery was performed. An attempt at revascularization of the right kidney was also performed, but led to a deterioration of the right function. The pathological examination of the iliac adrenal vessels showed important intimal thickening with a poorly cellular stroma and fragmentation of medial elastic tissue. Currently, the patient is being treated by hemodialysis and is waiting for a renal transplant.

Discussion

Infantile myofibromatosis is a mesenchymal disorder characterized by the nodular proliferation of spindle cells that are intermediate between fibroblasts and smooth muscle cells and are organized in fascicles or short bundles. In the solitary and the multifocal forms, the nodules are usually limited to the skin, soft tissues, and bone, but the generalized form involves several organs such as the lungs, heart, liver, adrenal, thyroid, gastrointestinal tract, and kidneys. The etiology of IM is unknown. Familial cases have been described with autosomal-dominant and recessive inheritances [3]. Renal myofibromatosis has been identified to be an unusual cause of infantile hypertension [4, 5]. As suggested by the increased levels of renin and aldosterone in the plasma of our patient and as demonstrated in a previous patient, IM may induce systemic hypertension by the development of a fibrodysplastic lesion and thrombosis of renal blood vessels [4]. The involvement of small blood vessels is common in IM. Vessels show intimal hyperplasia with intravascular proliferation of tumor cells and potential obliteration [4, 6]. However, vascular damage of large blood vessels is less frequent. Lesions of the pulmonary vein and other large veins have been described occasionally [7, 8]. Wright et al. have reported a patient with multifocal IM who subsequently developed several aneurismal dilations of the arterial system including the thoracic and abdominal aorta, carotid, iliac, and lower limb vessels. In this latter case, as in our patient, pathological examination of the vascular lesions showed marked intimal thickening with fragmentation of medial elastic tissue, suggesting the diagnosis of FMD [6]. FMD is a fibrous non-atherosclerotic and non-inflammatory disease of the medium and small-sized arteries characterized by vascular dilation and stenosis. It involves mainly the renal and internal carotid arteries although lesions of other arteries have been reported. Contrarily to IM, it typically affects women between 15 and 50 years [9]. FMD also occurs in pediatrics and constitutes the most frequent cause of renovascular hypertension in infants and children [5, 10]. FMD is not associated with tumor formation and rarely results in renal failure [9]. Its cause remains unknown, but epidemiological studies suggest that some environmental and genetic predisposing factors might play a role. It has been associated with cigarette smoking, history of hypertension, and familial history of FMD [9]. Microscopic findings include vascular wall fibroplasia, disruption of the elastic membrane and formation of small saccular aneurysms [10]. Medial fibroplasia is the most common dysplastic lesion, but intimal dysplasia occurs in approximately 10% of FMD and is more often seen in children [11]. The development of arterial aneurysms and vascular lesions mimicking FMD in a child with IM is uncommon and intriguing. We acknowledge that this evolution may be underestimated because of the poor prognosis of generalized IM. We also admit that no conclusion can be drawn from a single case and that this association could be a coincidence. However, this report, in addition to the case described by Wright et al., raises the question of a link between IM and FMD [6]. We hypothesize that both diseases actually result from the same myofibroblastic disorder that could have proliferative or dysplastic expression and that could be enhanced either by early or by late factors to lead ultimately to IM or FMD.

In conclusion, this report suggests that IM, as the symptom of a generalized mesenchymal disorder, might cause extensive vascular lesions, including aneurismal dilatation and stenosis, and that repeated radiological vascular explorations should be regularly performed in children with this disease.

References


