Solitary Renal Myofibromatosis: An Unusual Cause of Infantile Hypertension

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ABSTRACT. Introduction. Renovascular disease accounts for the vast majority of cases of infantile hypertension with complications resulting from umbilical arterial catheterization predominating in the neonatal period and fibrodysplastic lesions of the renal artery predominating outside the neonatal period. We report a previously undescribed cause of renovascular hypertension: solitary renal myofibromatosis.

Case Report. A 9-month-old male infant was transported to the intensive care unit at Children's Hospital in Denver, Colorado, for evaluation and treatment of a dilated cardiomyopathy and severe systemic hypertension. The child was full-term with no perinatal problems. Specifically, the child never required umbilical arterial catheterization. He was well until 6 months of age when his parents noted poor weight gain. At 9 months of age, he was evaluated at the referral hospital for failure to thrive. On examination he was noted to have a blood pressure of 170/110 mm Hg, but no other abnormalities. A chest radiograph showed cardiomegaly. Laboratory studies demonstrated normal electrolytes, blood urea nitrogen, and creatinine. However, urinalysis demonstrated 4+ protein without red blood cells. An echocardiogram showed severe left ventricular dilatation with an ejection fraction of 16%. On admission the child was noted to be cachectic. His vital signs, including blood pressure, were normal for age. The physical examination was unremarkable. Serum electrolytes, blood urea nitrogen, and creatinine were normal. Echocardiographic studies suggested a dilated hypertrophic cardiomyopathy. He was started on digoxin and captopril. Subsequently, he demonstrated episodic hypertension ranging from 170/90 to 220/130 mm Hg. A repeat echocardiogram 24 hours after admission demonstrated a purely hypertrophic cardiomyopathy. Verapamil and nifedipine were added to the treatment regimen in an effort to better control the blood pressure without success. Urine and blood for catecholamines and plasma renin activity, respectively, were sent and treatment with phentolamine instituted because of a possible pheochromocytoma. A spiral abdominal computerized tomographic scan revealed a markedly abnormal right kidney with linear streaky areas of calcification around the hilum and also an area of nonenhancement in the posterior upper pole. The adrenals and the left kidney were normal. Doppler ultrasound revealed a decrease in right renal arterial flow. The urinary catecholamines were normal and surgery was scheduled after the blood pressure was brought under control by medical treatment. At surgery, tumorous tissue and thrombosis of the renal artery were found in the right upper pole. A right nephrectomy was performed. Pathologic examination of the kidney showed the presence of a diffuse spindle cell proliferation in the interstitium of the kidney. The angiogenic/angiocentric character of the proliferation was demonstrated in several large renal vessels. The lumen of most vessels was narrowed and some vessels were totally occluded with recanalization and dystrophic calcifications observed. Immunostaining of the tumor demonstrated strong desmin and vimentin positivity and minimal actin positivity in the spindle cells. Mitotic activity was not noted in the spindle cell process. These pathologic changes were consistent with a diagnosis of infantile myofibromatosis (IM). The child’s preoperative plasma renin activity was 50 712 ng/dL/h (reference range, 235–3700 ng/dL/h).

Discussion. The causes of systemic hypertension in infancy are many although renal causes are by far the most common. Renal arterial stenosis or thrombosis accounts for 10% to 24% of cases of infantile hypertension. Renal artery thrombosis is usually a consequence of umbilical arterial catheterization, which can also lead to embolization of the renal artery. Renal artery stenosis may result from fibrodysplastic lesions (74%), abdominal aortitis (9%), a complication of renal transplantation (5%), and renal hypoplasia (3%). IM of the solitary type has never been reported as a cause of systemic hypertension. In our patient the IM caused both fibrodysplastic lesions and thrombosis of the renal artery, which led to severe systemic hypertension. IM is one of the myofibroblastic diseases of infancy and has three clinicopathologic expressions—solitary, multifocal, and generalized. The solitary and multifocal forms are usually limited to the skin, soft tissues, and bone. There is little morbidity and virtually no mortality in these forms of the disease. The generalized form, in addition to skin and bone involvement, may involve multiple visceral organs including the lungs, kidney, heart, liver, adrenals, thyroid, and the gastrointestinal tract. This form of the disease is the least common, usually presents in the first 6 months of life, and is associated with a high morbidity and mortality with death occurring as a result of lung involvement and respiratory failure. To our knowledge, solitary involvement of a viscera without involvement of skin, soft tissues, bone, or other visceral organs has never been reported. All three forms of IM share a distinctive microscopic appearance of interlacing fascicles of spindle cells. These interlacing fascicles sometimes blend into compact bundles with a fibrohyalin stroma in the same tumor. Origination around the blood vessels, or angiocentricity, is usually present in all types of lesions. The blood vessels involved in these lesions show intimal hyperpla...
Hypertension is rare in infants with a reported incidence as low as 0.2% in healthy newborns to as high as 8.9% in premature infants discharged from the nursery. Renovascular disease accounts for the vast majority of cases of infantile hypertension with complications resulting from umbilical arterial catheterization predominating in the neonatal period and fibrodysplastic lesions of the renal artery predominating outside the neonatal period. We report a previously undescribed cause of renovascular hypertension: solitary renal myofibromatosis. Infantile myofibromatosis (IM), one form of a spectrum of fibroblastic-myofibroblastic tumors in children, has been described as having only skin or bone involvement. Infantile myofibromatosis (IM), one form of a spectrum of fibroblastic-myofibroblastic tumors in children, has been described as having only skin or bone involvement. The solitary and multiple forms of these tumors usually undergo spontaneous regression. In this child we were unable to demonstrate evidence of multifocal myofibroblastic lesions. He seemed to have had a solitary myofibroblastic lesion in the right kidney which led to renal artery stenosis and thrombosis. This produced the renin-related hypertension, which responded only to tumor removal by nephrectomy. He is now growing and developing normally and his cardiomyopathy has resolved. He is presently normotensive and taking no medications. To date he has had no new or recurrent myofibroblastic lesions.

Conclusion. This case demonstrates that IM can present with solitary visceral organ involvement. The absence of involvement of soft tissues, skin, or bone makes clinical diagnosis of IM nearly impossible when a single visera is involved in isolation. A biopsy will be needed to make a diagnosis, and surgery may be needed depending on the organ of involvement and the clinical consequences. Pediatrics 1999;103(5). URL: http://www.pediatrics.org/cgi/content/full/103/5/e66; hypertension, myofibroblast, myofibroblastic disease, fibrosis, renal vascular disease.

ABBREVIATION. IM, infantile myofibromatosis.

The causes of systemic hypertension in infancy are many. The most common causes are renovascular disease, coarctation of aorta, polycystic kidney disease, renal parenchymal disease, congenital adrenal hyperplasia, neural crest tumors, pheochromocytomas, drugs, and toxins (steroids, cocaine, etc). Among these, renal causes (vascular and parenchymal) are the most common. Renal arterial disease accounts for 10% to 24% of cases of infan tile hypertension. This is usually in the form of renal arterial

sia leading to obliteration of the blood vessels. From these findings it has been postulated that IM is the result of a multifocal proliferation of mesenchymal or myofi broblast-like cells in the walls of blood vessels. These cells share morphologic and immunohistochemical characteristics of both fibroblasts and undifferentiated smooth muscle cells. There is usually no evidence of malignant characteristics in these cells. The solitary and multiple forms of these tumors usually undergo spontaneous regression. In this child we were unable to demonstrate evidence of multifocal myofibroblastic lesions. We report a previously undescribed cause of renal artery predominating outside the neonatal period. We report a previously undescribed cause of renal artery predominating outside the neonatal period.

CASE REPORT

A 9-month-old male infant was transported to the intensive care unit at Children’s Hospital in Denver, Colorado, for evaluation and treatment of a dilated cardiomyopathy and severe systemic hypertension. The child was a term product of a 26-year-old woman without medical problems. There were no perinatal problems, and specifically, the child never required umbilical arterial catheterization. He was apparently well and thriving until 6 months of age when he developed respiratory syncytial virus pneumonia, from which he recovered without needing hospitalization. However, since that time his parents noted poor weight gain. At 9 months he was evaluated at the referral hospital for failure to thrive. On examination he was noted to have a blood pressure of 170/110 mm Hg but no other abnormalities. A chest radiograph showed cardiomegaly. Laboratory studies demonstrated normal electrolytes, blood urea nitrogen, and creatinine. However, urinalysis demonstrated 4+ protein without red blood cells. These results prompted an echocardiogram which showed severe left ventricular dilatation with an ejection fraction of 16%. No coarctation of the aorta was noted. A Doppler ultrasound of the kidneys was read as normal. At this point the patient was transferred to Children’s Hospital for further evaluation.

At Children’s Hospital, intensive care and urinary output were noted to be extremely thin, almost cathartic. He was afebrile, had a heart rate of 180 beats per minute, and blood pressure readings which were normal for age in all four extremities. The physical examination, including the eye grounds, was unremarkable. His blood chemistry including electrolytes, blood urea nitrogen, and creatinine were normal for age. A repeat echocardiogram was performed which confirmed the presence of a dilated hypertrophic cardiomyopathy. He was started on digoxin and captopril for treatment of a presumed postural dilated cardiomyopathy. Subsequently, he began to demonstrate episodic hypertension with blood pressures ranging from 170/90 mm Hg to 220/130 mm Hg. A repeat echocardiogram 24 hours after admission demonstrated a purely hypertrophic cardiomyopathy. The ejection fraction had improved to 26%. Verapamil and nifedipine were added to the treatment regimen in an effort to better control the blood pressure. However, the child’s blood pressure remained significantly elevated at 140/90 mm Hg to 190/110 mm Hg. Because of the seemingly sporadic nature of the hypertension, urine and blood for catecholamines and plasma renin activity, respectively, were collected, and treatment with phentolamine was instituted because of a possible pheochromocytoma. A spiral abdominal computerized tomographic scan revealed a markedly abnormal right kidney with linear streaky areas of calcification around the hilum and also an area of nonenhancement in the posterior upper pole (Fig 1). The adrenals and the left kidney were normal. Doppler ultrasound revealed a lucency in the right kidney with a suggestion of internal decrease in right renal arterial flow. The urinary catecholamines were reported to be within normal limits. Based on computerized tomographic findings, the differential diagnosis now included Wilms’ tumor, intrarenal neuroblastoma, or renal tuberculosis, and surgery was scheduled after the blood pressure was brought under control by medical treatment. At surgery, a large renal tumor was found to involve the upper pole of the right kidney. Thrombosis of the right renal artery was also noted. A right nephrectomy was therefore performed.

Pathologic examination of the kidney showed the presence of a diffuse spindle cell proliferation in the interstitium of the kidney. The previously described angiogenic/angiocentric character of the proliferation was demonstrated in several large renal vessels (Fig 2). The tumor of most vessels was narrowed and many were totally occluded with recanalization and dystrophic calcifications observed. There were similar vascular changes in the fatty tissue adjacent to the periaortic lymph nodes. Immunostaining of the tumor demonstrated strong desmin and vimentin positivity and minimal actin positivity in the spindle cells. Mitotic activity was not noted in the spindle cell process. These pathologic changes were consistent with a diagnosis of IM. His preoperative plasma renin activity was 50,712 ng/dL/h (reference range, 235–5700 ng/dL/h).

DISCUSSION

The causes of systemic hypertension in infancy are many. The most common causes are renovascular disease, coarctation of aorta, polycystic kidney disease, renal parenchymal disease, congenital adrenal hyperplasia, neural crest tumors, pheochromocytomas, drugs, and toxins (steroids, cocaine, etc). Among these, renal causes (vascular and parenchymal) are the most common. Renal arterial disease accounts for 10% to 24% of cases of infantile hypertension. This is usually in the form of renal arterial...
stenosis or thrombosis. Renal artery thrombosis is usually a consequence of umbilical arterial catheterization which can also lead to embolization of the renal artery. Renal artery stenosis may result from fibrodysplastic lesions (74%), abdominal aortitis (9%), a complication of renal transplantation (5%), and renal hypoplasia (3%). Neurofibromatosis type 1 is sometimes (5%–25%) associated with fibrodysplastic lesions of the renal artery. IM of the solitary type has never been reported as a cause of systemic hypertension. In our patient, the IM caused both fibrodysplastic lesions and thrombosis of the renal artery, which led to severe systemic hypertension.

IM is one of the myofibroblastic diseases of infancy and has three clinicopathologic expressions—solitary, multifocal, and the generalized forms. The solitary and multifocal forms are usually limited to the skin, soft tissues, and bone. There is little morbidity and virtually no mortality in these forms of the disease. The generalized form, in addition to skin and bone involvement, may involve multiple visceral organs including the lungs, kidney, heart, liver, adrenals, thyroid, and the gastrointestinal tract. This form of the disease is the least common, usually presents in the first 6 months of life, and is associated with a high morbidity and mortality with death occurring as a result of lung involvement and respiratory failure. To our knowledge, solitary involvement of a viscer without involvement of skin, soft tissues, bone, or other visceral organs has never been reported.

All three forms of IM share a distinctive microscopic appearance of interlacing fascicles of spindle cells. These interlacing fascicles sometimes blend into compact bundles with a fibrohyalin stroma in the same tumor. This histologic variability is characteristic of IM. Although the anatomic site from which these tumors arise has not been ascertained, origination around the blood vessels or angiocentricity is usually present in all types of lesions. The blood vessels involved in these lesions show intimal hyperplasia leading to obliteration of the blood vessels. This has been best described in the lung vasculature. From these findings it has been postulated that IM is the result of a multifocal proliferation of mesenchymal or myofibroblast-like cells in the walls of blood vessels. These cells share morphologic and immunohistochemical characteristics of both fibroblasts and undifferentiated smooth muscle cells. There is usually no evidence of malignant characteristics in these cells. These tumors may undergo partial regression and dystrophic calcification. The solitary and multiple forms of these tumors usually undergo spontaneous regression.

![Fig 1. Computer tomography scans of the abdomen. Top: noncontrast view demonstrates linear areas of calcification (arrows) around the hilum of the right kidney. Bottom: contrast-enhanced view demonstrates areas of nonenhancement (arrows) in the posterior upper pole of the right kidney. Areas of calcification are again visualized.](http://www.pediatrics.org/cgi/content/full/103/5/e66)
In this child we were unable to demonstrate either by clinical examination or imaging studies specific evidence of multifocal myofibroblastic lesions. He seemed to have had a solitary myofibroblastic lesion in the right kidney which led to renal artery stenosis and thrombosis. This produced the renin-related hypertension, which responded to tumor removal by nephrectomy. Postoperatively he has shown steady improvement. He is now growing and developing normally and his cardiomyopathy has resolved. He is presently normotensive and taking no medications. To date he has had no new or recurrent myofibroblastic lesions.

CONCLUSION

IM can present with solitary kidney involvement causing severe hypertension. It is unusual that IM presents with isolated visceral involvement. The absence of involvement of soft tissues, skin, or bone makes clinical diagnosis of IM nearly impossible when a single viscera is involved in isolation. A biopsy will be needed to make a diagnosis, and surgery may be needed depending on the organ of involvement and the clinical consequences.

REFERENCES

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