Kawasaki disease complicated by renal artery stenosis

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Abstract

We report the case of a child who developed severe renovascular hypertension six months after acute Kawasaki disease. The hypertension was well controlled with enalapril, but there was a gradual decrease in function of the affected kidney. The lesion, an ostial stenosis of the right main renal artery, was not amenable to percutaneous balloon angioplasty, so was treated with bypass surgery. Vasculitis is an important cause of renovascular hypertension in children. This case highlights the importance of regular blood pressure monitoring in children with a history of systemic vasculitis.

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Keywords: renal artery stenosis; mucocutaneous lymph node syndrome; renovascular hypertension; vasculitis

Kawasaki disease (KD) is a multisystem vasculitis of the medium sized vessels. The acute phase of the disease is characterised by high fever, rash, erythema and oedema of the extremities, cervical lymphadenopathy, mucositis, and non-purulent conjunctivitis. A number of other abnormalities may also occur including sterile pyuria, aseptic meningitis, and arthritis. Clinical criteria to establish the diagnosis have been published elsewhere.

The most feared complication of KD is coronary artery aneurysm, which can lead to vascular occlusion and myocardial infarction. Extracoronary vascular lesions have also been reported. Renal artery involvement with stenosis leading to hypertension has been raised as a theoretical possibility, but is not generally considered a potential sequela of KD.

We report the case of a 2 year old girl who, six months after acute KD, was incidentally discovered to have severe hypertension. Investigations revealed stenosis of the right main renal artery.

Case report

An 18 month old white girl presented in January 1997 with a three day history of fever, incompletely relieved by acetaminophen (paracetamol), and a diffuse maculopapular rash. One day prior to presentation, she developed mild neck pain and stiffness, bilateral conjunctival injection without discharge, and mild rhinorrhoea with cough.

The vital signs on presentation were: temperature 38.0°C; heart rate 180 beats per minute, respiratory rate 28 per minute, and blood pressure (BP) 95/48 mm Hg. The rash was more intense in the creases and diaper area. Neck stiffness was also noted. There was no cervical lymphadenopathy. Laboratory investigations were normal with the exception of an increased erythrocyte sedimentation rate (48 mm/h), a slightly depressed serum albumin (32 g/l), and a cerebrospinal fluid white blood cell count of 12 per mm³; platelets were 280 × 10⁹/l.

The following morning her lips and tongue became red, and she had developed some swelling of the hands and feet, with mild palmar and plantar erythema. The temperature had continued to spike to 39–40°C and desquamation was seen in the diaper area. Kawasaki disease was diagnosed, and treated with intravenous immunoglobulin and acetylsalicylic acid. The fever resolved. During hospitalisation the BP was normal (85/50 to 100/60 mm Hg).

All bacterial and viral cultures were negative. The electrocardiogram (ECG) and echocardiogram were normal. Three weeks later, there was desquamation involving one finger. The echocardiogram remained normal. There was a mild thrombocytosis (482 × 10⁹/l).

Almost six months after the acute episode, she was readmitted with wheezing associated with a viral upper respiratory tract infection. The BP was noted to be consistently increased, with readings ranging from 125/70 to 154/86 mm Hg. There was no evidence of congestive heart failure. Serum electrolytes, urea, creatinine, urinalysis, ECG, and echocardiogram were all normal. Plasma renin activity was increased at 4.50 ng/l/s (normal range 0.21–1.06). Blood pressure returned to normal within 10 days of treatment with captopril.

A dimercaptosuccinic acid (DMSA) scan revealed normal parenchyma bilaterally, with a differential function of 42% on the right and 58% on the left. Although a diethylenetriaminepentaacetic acid (DTPA) scan after one small oral dose of captopril was normal, a second study two weeks later on a higher dose of captopril showed significant reduction in flow and function of the right kidney (cortical transit time increased from 2.0 minutes at baseline to 11.0 minutes). Renal angiogram performed two months later revealed severe stenosis of the right renal artery at its origin (fig 1). Differential renal vein renins obtained in the recumbent position were as follows: right renal vein 20.56 ng/l/s, left renal vein 13.03 ng/l/s. These results suggested that the hypertension was a result of the right renal artery stenosis and would be amenable to surgical intervention.

She underwent an unsuccessful percutaneous balloon angioplasty of the right renal artery. Although BP control remained ad-
Equate on an angiotensin converting enzyme inhibitor, follow up DMSA seven months later showed deterioration in function of the right kidney from 42% to 34% (see table 1). This led to revascularisation surgery. A segment of internal iliac artery was used to bypass the area of stenosis. This vessel did not look entirely normal grossly, a piece was sent for pathological examination. Microscopic evaluation revealed evidence of remote necrotising vasculitis (fig 2).

The patient has been followed for one year postoperatively and has remained normotensive without any antihypertensive medication.

Discussion
Essential hypertension in childhood is rare, so all hypertensive children should be thoroughly investigated. Renovascular disease accounts for 8–10% of all cases of paediatric hypertension, with either extrinsic compression of renal arteries or intrinsic renal artery disease. Disease may be unilateral, or in up to 70% of cases, bilateral. Table 2 details aetiological possibilities for intrinsic disease. Although fibromuscular dysplasia is by far the most common cause (70%), the importance of preceding vasculitic disease should not be underestimated. In a UK study of 54 children with renovascular hypertension, five (9%) had a preceding non-specified vasculitis. KD is one of the most common childhood vasculitides, leading to inflammation and sometimes aneurysmal dilatation of medium sized vessels. Although any medium sized vessel in the body can be involved, investigation and follow up of affected children is directed mainly towards detection of coronary lesions. Renal artery aneurysms have been reported in association with KD in the past, and the possibility of hypertension as a complication has been raised. Despite this, the only reports of renovascular hypertension in association with KD of which we are aware resulted from abdominal aortic aneurysms.

Our patient clearly had normal BP at the time of onset of her KD. She showed none of the clinical stigmata of neurofibromatosis, eliminating this as an aetiological possibility. The location of the stenosis argues against fibromuscular dysplasia, as these lesions are usually multiple and located more distally, in branches of the main renal artery. Evidence of past necrotising vasculitis seen in the internal iliac supports the assertion that the renal artery disease was related to KD.

The angiogram did not reveal aneurysmal dilatation of the artery, but rather stenosis.

<table>
<thead>
<tr>
<th>Table 2 Causes of intrinsic renal artery disease*</th>
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<tbody>
<tr>
<td>Cause</td>
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<tr>
<td>Fibromuscular dysplasia</td>
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<tr>
<td>Neurofibromatosis 1 (15%)</td>
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<tr>
<td>Vasculitis (9%)</td>
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<td>Thrombosis</td>
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<td>Embolus</td>
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<td>Atherosclerotic</td>
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*Of stenosis. As this vessel did not look entirely normal grossly, a piece was sent for pathological examination. Microscopic evaluation revealed evidence of remote necrotising vasculitis (fig 2).

The patient has been followed for one year postoperatively and has remained normotensive without any antihypertensive medication.
Unfortunately, this diseased segment was not examined at operation, so no information regarding its gross or microscopic appearance is available. Several possibilities exist which may explain the development of this stenosis. Sasaguri and Kato have described both massive thrombus formation within an aneurysm and notable intimal proliferation. The possibility that healing of the necrotic vessel wall involved fibrotic scarring susceptible to scar contraction should also be considered. The fact that our patient did not respond to percutaneous balloon angioplasty may support the latter.

Although renovascular hypertension appears to be a rare complication of KD, the potential morbidity of untreated severe hypertension is significant. Our patient had received the standard follow up for KD in our institution, which focuses primarily on coronary artery complications. As there was no evidence of sequelae she was returned to her primary care physician for routine well child follow up. Her hypertension was fortuitously discovered during an episode of wheezing, but may have gone undetected much longer had she not come to medical attention for this reason. Perhaps more frequent BP monitoring should be part of the routine follow up of all children with KD.