Bilateral renal artery stenosis in Kawasaki disease: a report of two cases

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ABSTRACT

We report two cases, a boy and a girl, who developed severe renal hypertension over sub-acute phase of Kawasaki Disease (KD). Paediatricians should be alert to consider preceding KD as potential source of secondary hypertension in young infants, and raised blood pressure should be regarded as a life-threatening complication in all KD children.

Introduction

We report two cases, which developed severe renal hypertension over sub-acute phase of Kawasaki Disease (KD) (1).

Case 1

A 16-month-old girl presented to our Department with an 8-day history of high fever, not responding to amoxicillin. Clinical examination was unremarkable, brachial blood pressure (bBP) 80/55 mmHg.

Nonetheless, negative culture and numerous leukocytes on urine analysis prompted to suspect urinary infection and to introduce cefixime. The day after admission, the girl, still febrile, presented bilateral non-exudative conjunctivitis, mucosal erythema and red lips. ESR resulted 122 mm/h (Westergren, normal value < 21), CRP 4.9 mg/dl (normal value < 0.5), white blood cells (WBC) 11.4 X 10^9/L, neutrophils 65%, haemoglobin (Hb) 10.5 g/dL, platelet count (PLT) 483 X 10^9/L, and other unremarkable blood work-up. Common bacterial and viral infections were excluded with culture and antibody titres. Electrocardiogram and two-dimensional echocardiography with echo-colour Doppler as well as abdominal ultrasound were unremarkable. Due to high persisting fever, conjunctivitis, mucositis, striking irritability, sterile pyuria, increased ESR, CRP, leukocytosis, mild anemia and thrombocytosis – PLT rose to 865 X 10^9/L-, incomplete KD was suspected and IVIG along with aspirin were given on 10^{th} day from the fever onset, resulting in a prompt defervescence. On the 14^{th} day, peeling of right hand digits appeared. The girl was discharged on aspirin (3 mg/Kg). A successive echocardiography excluded coronary involvement, and bBP was 90/55 mmHg. At the 3-week cardiac follow-up, coronary assessment was normal, but bBP resulted 140/85 mmHg on the left side, and 150/90 mmHg on the right, persisting over the following week. Serum electrolytes, creatinine, urea, and urinalysis were normal. PLT normalized, while Hb level was still 10 g/dL, with normal ferritin. Echocolordoppler of renal arteries revealed stenosis of right renal artery (max velocity 261 cm/sec) and of left renal artery (max velocity 286 cm/sec). Plasma renin activity was increased at 4.20 ng/l/s (normal value 0.28 -1.06). MR angiography confirmed bilateral renal stenosis, mainly affecting the left side, along with dilatation and artery wall abnormalities involving the left axillar artery (Fig. 1). A diethylenetriaminoepentaacetic acid (DTPA) and ortho-iodiohippurate (HIPP) scan revealed normal kidney parenchyma bilaterally, without functional impairment. Amlodipine (0.2 mg/Kg/day) was introduced. At the 6-month follow-up, no coronary alterations were detected, while renal stenosis and left axillar artery dilatation were unchanged. BBP was within normal range for age on both sides (80/60 mm Hg) on Amlodipine treatment.

Case 2

A 3 and a half-month-old infant was admitted to our Department with a fever lasting over 5 days (39°C), bilateral conjunctivitis, and dyspnoea. Clinical exam also revealed mucositis; bBP was 70/50 mmHg. ESR resulted 120 mm/h, CRP 22.1 mg/dL, WBC 16.8 x 10^9/L (neutrophils 75.2%), Hb 9.4 g/dL, and PLT 504 x 10^9/L. Culture and antibody titres excluded common bacterial and viral infections. ECG and two-dimensional echocardiography with echo-colour Doppler excluded cardiac abnormalities. Electroencephalogram showed diffuse slow waves. Cerebrospinal fluid analysis resulted unremarkable.

Despite netilmycin and ceftazidime, on day 4 from admission, he, still febrile, developed cervical lymphoadenopathy, and a diffuse maculopapular rash involving all the body and the scalp. A

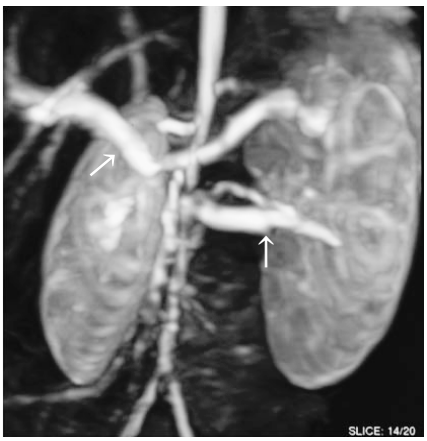


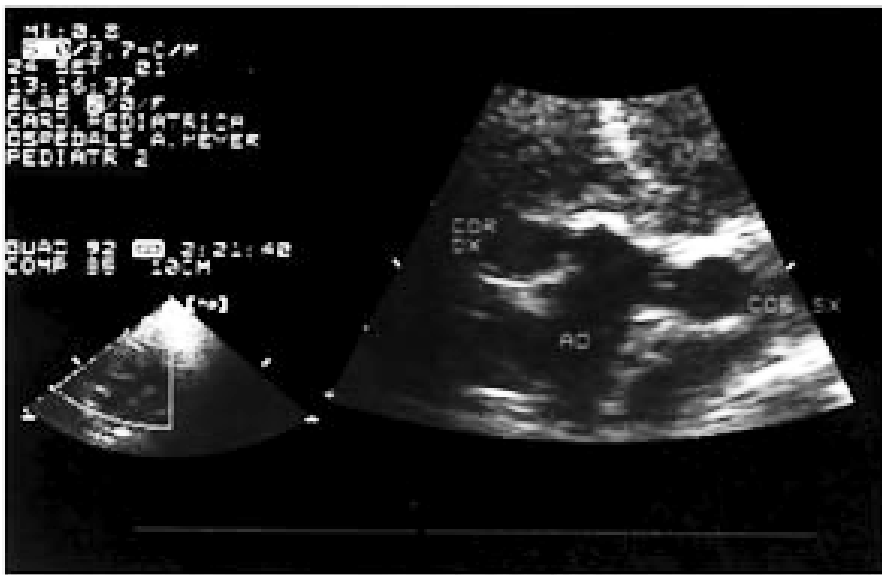
Fig. 1. MR angiography showing bilaterally arterial renal stenosis, principally affecting the left side.

new electrocardiogram showed inverted T waves, and echo-colour Doppler two giant aneurysms: left coronary diameter 13 mm, right coronary 11 mm, as well as a small area of hypokinesia/akinesia of the posterior ventricular wall. Captopril was then added
Due to high persisting fever, conjunctivitis, mucositis, rash, cervical lymphadenopathy along with coronary involvement, KD was suspected and IVIG with low molecular weight heparin were promptly given. Fever dropped during IVIG infusion and the patient dramatically improved. PLT rose to 1.200 x 109/L. The child was discharged on low dose aspirin, and heparin was substituted by warfarin. Three weeks later, two digits peeling on the right hand occurred. At one month, clinical evaluation was unremarkable, bBP was 160/90, laboratory tests were completely normalized. MR angiography showed mild bilateral renal stenosis, diffuse aneurysms of the right axillar, and iliac arteries (Fig. 2). Successive cardiac ultrasonographic studies revealed mild mitral regurgitation and diffusely hypokinetic left ventricle. Captopril was then discontinued and diltiazem (1mg/Kg) with furosemide (2mg/Kg) introduced. Functional kidney evaluations, including plasma renin activity, DTPA and HIPP scan, were within the normal range for age. At the 1-year cardiac ultrasonographic follow-up, the left ventricular function was improved with an ejection fraction of 49%; but mild mitral regurgitation along with basal and posterior hypokinesia persisted. BBP was normal for age. Giant aneurysms were always unchanged until 2 years and 8 months after the acute phase, when the child suddenly died of cardiac arrest. Necroscopy revealed diffuse medium sized vessel alterations involving coronary arteries along with axillar, renal and iliac arteries. Post-thrombotic changes on myocardial anterior wall were evident. No alterations were detected on cerebral vessels.

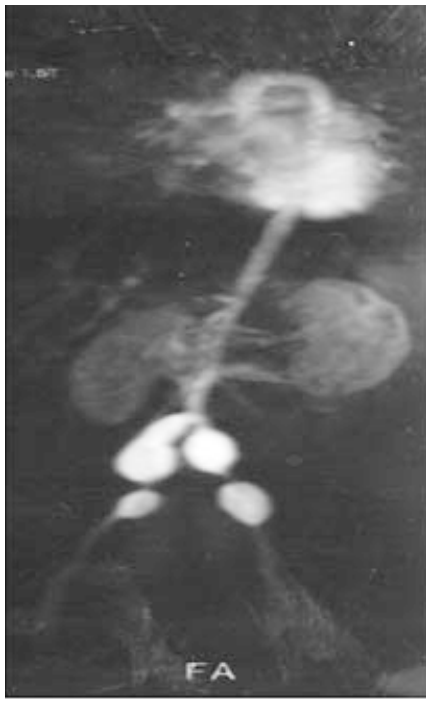
Discussion

Essential hypertension in childhood is rare; fibromuscular dysplasia is undoubtedly the most common cause, with reno-vascular diseases accounting for more than 10% of all cases (2).
Arterial hypertension, due to reno-vascular dysfunctions, is uncommon in children, and the majority of affected children do not complain of it at all or just of vague symptoms (3). In order to reduce high morbidity/mortality due to silent hypertension, BP monitoring should be part of the routine health assessment and follow-up of young children, especially those suffering from systemic vasculitides.
Despite being the second most common vasculitis in children, KD is not frequently considered cause of hypertension among intrinsic renal artery diseases (4). Beyond the coronary in-

Panel A



Panel B



Fig, 2. *Panel A*. Giant aneurysms. The left coronary diameter was 13mm and the right coronary diameter 11 mm. Apical five chambers view modified for coronary arteries. *Panel B*. MR angiography showing bilaterally arterial renal stenosis and diffuse aneurysms of iliac arteries.

volvement, KD is systemic vasculitis and kidney involvement, including tubulo-interstitial nephropathy and/or glomerular disease, can, even though rare, develop: several cases of acute renal failure have been reported during the course of KD (5-7)

Even though renal artery abnormalities may lead to hypertension over time (8, 9), renal vascular hypertension due to renal artery stenosis secondary to KD has been seldom reported, resulting more rare than renal insufficiency (10, 11).

In our two children, functional evaluations did not ever reveal findings suggestive of renal failure: hypertension resulted due to bilateral renal artery stenosis in both cases.

As previously reported (10, 11), our infants had clearly a normal bBP during the acute and sub-acute phase of disease, later developing a real hypertension. Conversely, in our patients MR angiography, a validated and useful technique for depicting peripheral vascular lesions in children (12), confirmed bilateral, and not monolateral, renal artery stenosis. Of note, our second case is the youngest reported KD with hypertension due to renal stenosis. In our cases, conversely to bilateral renal stenosis due to fibromuscular dysplasia, pharmacology option achieved a sustained control of hypertension, suggesting the different damage and a possible endothelial remodelling over a systemic vasculitis such as KD.

In conclusion, these cases should alert physicians to consider KD as potential source of secondary hypertension in young infants, and, beside coronary disease, raised BP should be regarded as a life-threatening complication in KD children.

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