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CASE REPORTS

Renovascular hypertension in neurofibromatosis, type I

Carmen CIOFU[a], MD, PhD, Eliza CINTEZA[b], MD, PhD,
Roxana DARABONT[c], MD, PhD, Bogdan POPA[d], MD, PhD,
Ioan CERNATESCU[e], MD, PhD, Emil LAPADAT[f], MD, PhD,

[a]Chief Department in IOMC "Alfred Rusescu", Bucharest, Romania;
[b]University of Medicine and Pharmacy "Carol Davila", 2nd Pediatrics Department, IOMC "Alfred Rusescu", Bucharest, Romania;
[c]Internal Medicine and Cardiology, University of Medicine and Pharmacy "Carol Davila", Cardiology Department, University Hospital Bucharest, Romania;
[d]Chief Department Angiography, Emergency Clinic Hospital, Bucharest, Romania;
[e]University of Medicine and Pharmacy "Carol Davila", 2nd Pediatrics Department, IOMC "Alfred Rusescu", Bucharest, Romania;
[f]Emergency Clinic Hospital, Bucharest, Romania

ABSTRACT

Pediatric renovascular hypertension is an uncommon, but important clinical problem. The authors present a typical case of neurofibromatosis type I, NF 1, (multiple café au lait spots, axillary and inguinal freckles, Lisch nodes, short stature, moderate mental retardation and positive family history) in an adolescent girl (17) with secondary renal hypertension. The diagnostic renal angiography identified a 95% right renal arterial stenosis at the origin. Angioplasty and stenting were not recommended and the surgical correction has to be done. The arterial hypertension is on good control under conservative medical treatment. This seems to be the first reported case from Romania presenting this very rare association of NF 1 and renal arterial stenosis in children.

Keywords: neurofibromatosis type I, hypertension, renal artery stenosis

INTRODUCTION

Neurofibromatosis type I (NF 1), the most common of hamartomatosis, is an autosomal dominant condition affecting 1/3000 people. The clinical elements for diagnosis are represented by 2 or more of the following: six or more café au lait spots larger than 5 mm in prepubertal children and larger than 1.5 cm in postpubertal individuals, two or more neurofibromas of any type or one plexiform neurofibroma, multiple axillary or inguinal freckles, a distinctive osseous lesion, optic glioma, iris hamartomas (Lisch nodules), first-degree relative with NF1. Vascular disease is an underestimated complication of NF 1.

The presence of the arterial hypertension in a patient with NF 1 can be a consequence of the proximal renal artery stenosis in a small number of cases. This association was mentioned for the first time in 1967 by Diekmann et al.[1] Vasculopathy in NF 1 is well known and includes renovascular hypertension, occlusive cerebrovascular disease and visceral ischemia.[2] Under the age of 30 the vasculopathy is a cause of death more frequent in neurofibromatosis than in general population. The life expectance

in NF1 is smaller with 20-25 years compared with the normal population.[3] In a meta analyze study done in 1993 the cardiovascular abnormalities, associated in NF1, were estimated at 2.3% and the vascular abnormalities under 1% from all cases.[4]

NF1 (OMIM 162200) is caused by mutation of the neurofibromin gene (gene map locus 17q11.2)[1], with decreased level of the gene product and putative tumor suppressor function. Other consequences are fibrous proliferation of the intima or media, and rarely of the adventitia. Neurofibromin is expressed in blood vessel endothelial and smooth muscle cells.[5] These lesions are, usually, at the origin of the artery, and they may be bilateral.[6] ❑

CASE REPORT

We present the case of an adolescent girl, H.M., 17 years, living in a shelter for children. The father, the paternal grandmother, and two sisters were diagnosed with NF 1. The mother and the brother are healthy. The girl was first diagnosed with NF 1 and mental retardation in a pediatric neurology clinic.

The patient came to the physician for occipital headache, lasting for several days. Before this episode she reported other episodes of occipital headache in the morning, perspiration and facial flush. The physician diagnosed arterial hypertension (140/100; 160/80; 139/75 mmHg, all values being over the 95 percentile for age, sex and height – in this case 125/82 mmHg), and sent her to IOMC "A. Rusescu" for investigations.

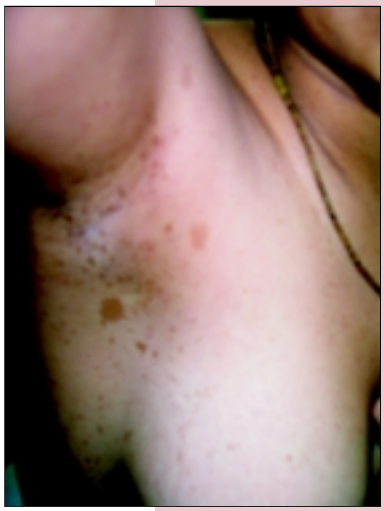

FIGURE 1. Axillar freckles and café au lait spots

Clinical examination reveals a 17 years girl, Tanner IV, weight 48 kg, height 143 cm (under the 5 percentile for age and sex), BMI (body mass index) 23,48, with multiple café-au-lait spots (a number of 15 maculae), (fig.1), 2-6 cm diameter, rounded, all over the body, freckles on the face, thorax, axillar (fig.1) and inguinal, heart rate 93/min, paraombilical systolic murmur, low intellect (IQ73). Blood pressure was measured at the arms and legs: right arm 138/93mmHg, left arm 141/91 mmHg, right leg 143/104 mmHg, left leg 160/102 mmHg.

The electrocardiography was normal.

Ophthalmologic examination diagnosed Lisch nodes and transitory mild spasm on the retinal arteries.

The biological investigations were normal, except a mild increased level of the erythrocyte sedimentation rate and C reactive protein. The abdominal echographic examination showed a normal aspect of the suprarenal glands. The Duplex ultrasound examination of the kidneys was diagnostic. At the origin of the right renal artery, there was aliasing of the color flux and the spectral Doppler signal was much dispersed. The peak systolic velocity was 190cm/s, (fig.2), which allows us to assert a haemodynamicaly significant stenosis[7,8] and the right intrarenal flow was flattened, with a "parvus et tardus" pattern, (fig.3), characteristic for a high degree stenosis (>80%)[9,10]. The Doppler appearance of the left kidney was normal.

At the angiography, a 95% right renal axial stenosis appeared, at the origin of the vessel, (fig.4). It was 2.5 cm long from the origin of the right renal artery. The other arteries (abdominal aorta, left renal artery, celiac artery, mesenteric arteries, and periphery arteries) were normal. The nephrogram and the pielogram were of normal aspect on both sides.

The diagnoses in this case are neurofibromatosis, type I, secondary arterial hypertension, right renal artery stenosis. Short stature and mental retardation are characteristics of the NF 1.

Other alternative causes for arterial hypertension in NF 1 are essential hypertension (rarely of this group of age), aortic coarctation (exclu-

ded), pheocromocitomas (excluded on the base of clinical manifestations and abdominal echographic examination), and intracranial hypertension due to the neurofibromas (excluded on the absence of the intracranial hypertension signs – clinical and ophthalmologic examination). The association of mental retardation, cardiovascular anomalies and short stature in this case can suggest the NF 1 microdeletion syndrome (a more severe phenotype)[11], but the evidence can be made only by genetic studies.

Conservative medical treatment was initiated with two antihypertensive drugs (beta-blocker and angiotensin converting enzyme inhibitor (ACEI) with a good response and than limited at ACEI. The curative treatment includes angioplasty, stenting or surgery. The cardiologists recommend the surgical treatment being the best in this case. ❑

CONCLUSION

1. This case illustrates one of the very rare causes of arterial hypertension (1/3000 NF1 incidence, and from this subpopulation group < 1% has renal artery stenosis).
2. It is no evidence of another form of vasculopathy or nervous tumors associated in this case.
3. The NF 1 microdeletion syndrome in this case can be confirmed only by genetic studies.
4. The arterial hypertension is under control with medical treatment, in this teenager girl, but the surgical curative treatment has to be done.
5. This case is probably the first case of NF 1 with renal artery stenosis reported in Romania, which underwent a complex and modern investigation.

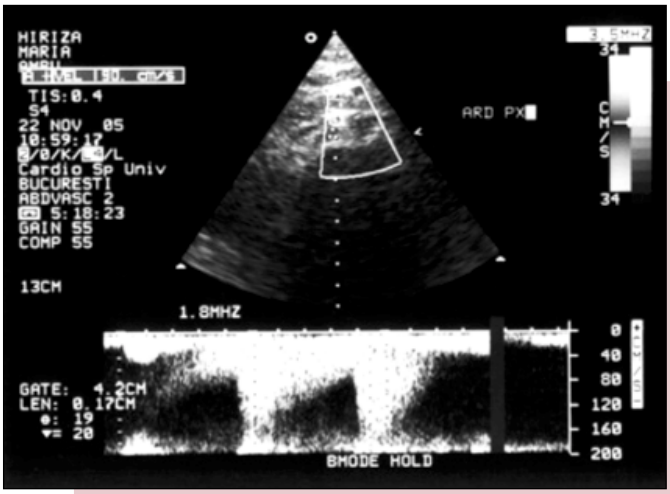

FIGURE 2. Doppler right renal artery stenosis in the proximal segment, at the origin

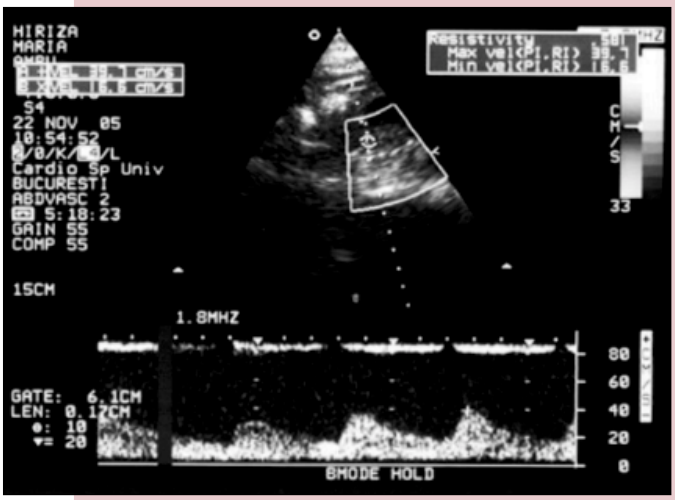

FIGURE 3. Flattened intraparenchymal flux on the right side.

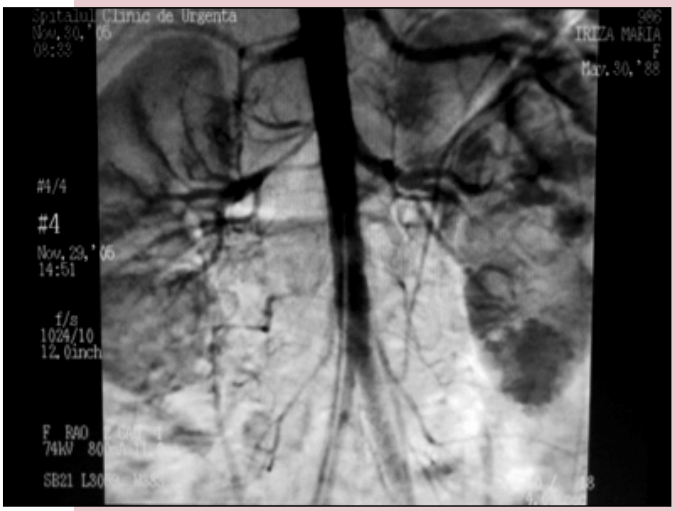

FIGURE 4. Right renal artery stenosis, 95%, 2.5 cm, at the emergence of the right renal artery

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