Neurofibromatosis associated with hypertrophic cardiomyopathy

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ABSTRACT

نستعرض في هذا المقال شاباً عمره 18عاماً ويعاني من ورم ليفي عصبي من النوع1، كما أنه مُصاب باعتلال عضلة القلب الضخامي مع حركة أمامية انقباضية للوريقة الأمامية للصمام المترالي. أشار المدروج بأن التدفق البطيني يصل إلى 85 ملم زئبقي وذلك نتيجة لتضيق تحت الصمام الأبهري مع وجود خلل انبساطي للبطين الأيسر. وتمت الإشارة إلى إمكانية وجود علاقة سببية بين هذين المرضين أو أن حدوث هذا الشيء كان مجرد صدفة.

We present a case of an 18-year-old boy with neurofibromatosis type 1 and hypertrophic cardiomyopathy with systolic anteward movement of the anterior leaflet of the mitral valve. Gradient in the left ventricular outflow was 85 mm Hg secondary to subvalvular aortic stenosis with left ventricular diastolic dysfunction. The possibility of a coincidence, or a causal relationship of these 2 conditions is mentioned.

Saudi Med J 2010; Vol. 31 (8): 935-936

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Received 11th April 2010. Accepted 28th June 2010.

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Neurofibromatoses are genetic disorders of the nervous system that primarily affect the development and growth of neural tissues. There are 2 main distinct forms that have been recognized on clinical, and genetic grounds these are; designated neurofibromatosis type 1 (NF1), and neurofibromatosis type 2 (NF2). There are also other syndromes classified as different types of neurofibromatoses with some similar features as NF1.[1,2] Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disease with heterogeneous phenotypic expression, and a diverse clinical course, characterized by both sudden death, and disabling symptoms related to heart failure.[3] The HCM has been reported in association with neurofibromatosis.[4] In this study, we present an 18-year-old boy with NF1, and hypertrophic obstructive cardiomyopathy with progressive aortic stenosis requiring surgical treatment. We want to report rare cardiac involvement and discuss possible association between neurofibromatosis and HCM.

Case Report. The patient is an 18-year-old boy, who has been followed-up in the dermatology clinic since 5 years of age. On physical examination, there are multiple symetrical flat areas of skin hyperpigmentation ("café-au-lait spots") with rounded edges with predominance on his face, neck, and upper trunk (**Figure 1**). Dysmorphic facial features include hypertelorism, thick lips, large ears, and prominent mandible. Multiple, small, and skin-colored nodules projecting above the skin level are present on his body. He was referred to the Cardiology clinic for heart murmur. On auscultation there was loud, systolic-diastolic murmur with maximum on the heart base. The electrocardiography revealed first degree atrioventricular block, incomplete right bundle branch block, and left ventricular hypertrophy, while the chest x-ray showed aortic cardiac shape. Echocardiography confirmed HCM with systolic anteward movement of the anterior leaflet of the mitral valve (**Figure 2**). There was mild degree of valvular pulmonary artery stenosis with a gradient of 27 mm Hg. Gradient in the left ventricular outflow was 85 mm Hg, secondary to subvalvular aortic stenosis with left ventricular diastolic dysfunction. Initially, second-degree aortic stenosis has been progressive over time. Because of progressive aortic stenosis, aortic valvuloplasty, and septal myectomy have been carried out. The gradient in the left ventricular tract dropped after surgery to 15 mm Hg, and aortic insufficiency disappeared. The physical condition of the

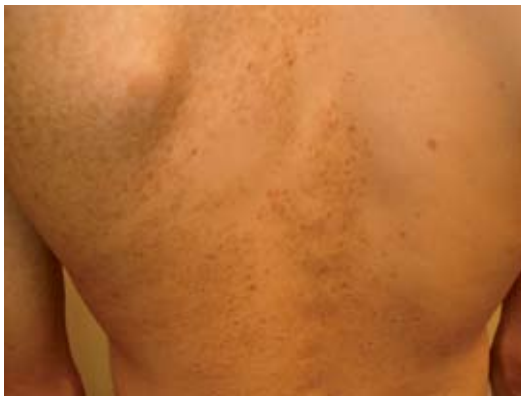

Figure 1 - Skin hyperpigmentation and neurofibromas.

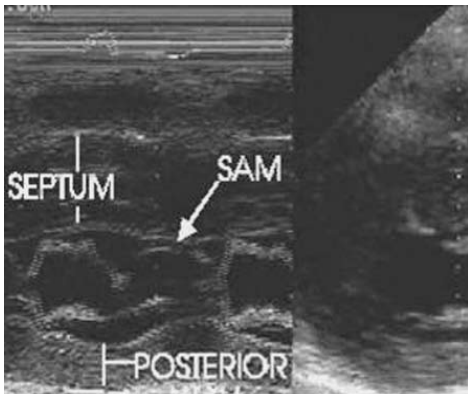

Figure 2 - Hypertrophic cardiomyopathy. SAM – systolic anteward movement of the anterior leaflet of the mitral valve.

patient improved significantly after surgery, and he is currently being followed-up in the cardiology clinic.

Discussion. Neurofibromatosis type I (von Recklinghausen syndrome) is a genetically inherited disease with formation of nerve tissue tumors (neurofibromas), which may be asymptomatic, or can cause symptoms by local tissue compression. The disorder affects all neural crest cells (Schwann cells, melanocytes, endoneural fibroblasts). Hypertrophic cardiomyopathy is a genetic cardiac disease with heterogeneous phenotypic expression and a diverse clinical course characterized by both sudden death, and disabling symptoms related to heart failure. Approximately 50% of hypertrophic cardiomyopathies are inherited as autosomal dominant disorder, sometimes associated with neuroectodermal syndromes, such as neurofibromatosis, and pheochromocytoma.[4] The HCM is one of the common causes of severe arrhythmias, and sudden death.[5] The left ventricular outflow tract gradient has been prominent and quantifiable feature of HCM.[6] However, the long-term effect of the subaortic gradient on clinical outcomes continues to be a source of uncertainty. Cardiac involvement can cause significant problems of patients with neurofibromatosis, but there is still not enough information. In one study, cardiac abnormalities have been found in 13 of 48 young patients (27%) with NF.[7] Two patients had septal to posterior left ventricular free wall ratio greater than 1.5, suggesting HCM.[7] On the other hand, in another report,[8] none of 2322 patients with definite NF1 had HCM. The etiology of HCM is unknown, although genetic factors are almost certainly involved. In addition, there is increasing evidence, both clinical and experimental, of an abnormality in catecholamine metabolism. Reports of abnormal catecholamine metabolism in neurofibromatosis have led to the suggestion that there is an etiological link between the 2 diseases and abnormalities of catecholamine metabolism, and nerve growth factor in neurofibromatosis can cause secondary ventricular hypertrophy with septal involvement.[9]

In conclusion, patients with neurofibromatosis can develop cardiomyopathy with potentially progressive course. Based on clinical experience, and bibliographic data we recommend that persons with NF should be followed-up in the Cardiology clinic and echocardiography should be carried out early, with any changes on electrocardiogram, or thoracic x-ray. In the case of HCM, it is necessary to follow-up these patients, as they may need surgical treatment.

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