INTERNATIONAL JOURNAL OF RESEARCH AND ANALYSIS VOLUME 4 ISSUE 6 ISSN 2347-3185 2017

LEOPARD SYNDROME-CATS BITE ON THE HEART

*ATUL JHA[1]

Case summary

14 yrs old deaf and mute girl had been symptomatic with compaints of recurrent vomiting and irregular menstrual cycles. While she was under evaluation, she was referred to our centre for evaluation of ECG abnormalities. On detailed history taking she was found to be dysmorphic, deaf and mute since birth. However the developement of other motor and sensory milestones had been normal and she could communicate rather well using sign language. She did not have any evidence of mental retardation. She did not offer any specific cardiac complaints except mild exertional dyspnoea. There was no similar symptom profile in the family although her father had died of 'some cardiac disease' at the age of 35 yrs.

On examination she had a BMI of 15.77 kg/m_2 with a weight and height of 31.35 kg and 141 cms respectively and thus had significant growth retardation. She had a triangular face with ocular hypertelorism, low set ears and unilateral ptosis. Multiple flat black brown macules, dispersed mostly on the face, neck, and upper part of the trunk, but sparing the mucosa were noted over her body. There was had bilateral sensori-neural hearing loss without any other focal neurological deficit. Cardiac examination showed that she was in sinus rhythm and normotensive. The apex beat was in the fifth intercostals space. There was a short systolic murmur in the left parasternal area without any abnormality of the first of second heart sound. Examination of the other systems was normal. The external genitalia were normal.

The ECG showed extreme North-West axis, a normal PR interval, left atrial enlargement with an incomplete RBBB. The chest X-ray showed slight cardiomegaly with a predominantly left ventricular apex and bilateral partially ossified cervical rib. An echocardiography was performed which showed a concentric left ventricular hypertrophy with an ejection fraction of 70%. There was systolic anterior motion of the mitral valve and a non obstructive HCM (Gradients and velocities). A skin biopsy was done which confirmed the diagnosis of lentigines.

She was diagnosed as a case of LEOPARD syndrome because of the presence of **L**entigines, **E**CG abnormalities, **O**cular hypretelorism, **R**etardation of growth and **D**eafness (sensori-neural) although she did not have any evidence of **P**ulmonary stenosis or **A**bnormalities of genitalia. She continues to be on our follow up for progression of the cardiac illness and has been referred for hearing aids.

[1] MBBS, MD

Discussion

Gorlin coined the term LEOPARD syndrome as a mnemonic and the characteristic spotted appearance that these patients have due to lentiginosis [1]. Our patient had lentiginosis, electrocardiographic abnormalities, ocular hypertelorism, retardation of growth and sensorineural deafness but did not have pulmonary stenosis or abnormalities of genitalia. She had hypertrophic cardiomyopathy, which although is not a part of the original mnemonic but has been frequently reported [2].

There is no definite pattern of inheritance that the disease follows but some authorities have described an autosomal dominant inheritance. Most of the cases are sporadic. It is postulated that the cells of mesodermal origin and gene products from a mutant neuroectodermal cell population interact which manifest as a multisystem involvement [3].

None of the family members of our patient had any symptom of this syndrome. There was a history of early cardiac death in the family (father) but in the absence of any more definite evidence we have not related it to the syndrome. The most common manifestations of LS are lentigines and ECG abnormalities. These lentigines are brown to black macules that are present on the face trunk and axilla. They are specifically absent on the mucosal surfaces. Although LS has been described without lentigines but presence of lentigines can help in differentiating LS from Noonan syndrome [4].Not only the pathogenesis but also pattern of PTPN11 mutation differs in the two conditions - suppression of PTP (protein tyrosine phosphatase) activity in LS and enhanced activity in Noonan syndrome [5].

Electrocardiographic abnormalities are frequent and present in about 50% of the cases. The most common patterns that are seen are axis deviation (Lt > Rt) and bundle branch block (mostly right). Ventricular hypertrophy is commonly seen on the ECG and is frequently biventricular. Other conduction abnormalities seen are S_{123}, paroxysmal atrial tachycardia and complete heart block. Our patient had an extreme axis deviation and a right bundle branch block. Most the electrocardiographic abnormalities are asymptomatic and patients frequently harbor a disease without any cardiac symptom [6]. Ocular hypertelorism and other facial dysmorphism are generally present from childhood and the parents frequently have this as a presenting complaint. Also the characteristic facial features make it easier to recognize.

Pulmonary stenosis (PS) is the only structural cardiac abnormality that forms a part of the mnemonic. PS is usually mild and is mostly valvular in nature. It is not known whether this manifestation is present since birth or develops later as it is seen in only 40% of the cases. However there is a possibility of PS developing with age and so it is prudent to follow these

patients. Hypertrophic cardiomyopathy (HCM) may involve either ventricle but is more common on the left side, specially the septal region [2].

Abnormalities of growth and gentalia are less common association. The commonest pattern of genital involvement is undescended testes with a small penis. Growth retardation is a common feature in these patients. Deafness is the least frequently reported of the mnemonic involving only 15% of the patients. Our patient however, had bilateral sensori-neural deafness which was present since childhood [4].

Patients of LS do not require any specific management. They may benefit from hearing aids and vocational training for future independence. The management of our patient would be on the lines of management of HCM. No drugs for the moment but initiation of calcium channel blockers or beta blockers to minimize LV flow gradient when obstruction develops.

Conclusion

It is important to understand that although LS is a multisystem affliction with protean manifestation the patients have a natural history similar to their cardiac illness. It is important to suspect a cardiac illness even in a cardio-wise asymptomatic patient of LS and follow-up the patient of LS for future development of such illness.