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Holt Oram Syndrome.

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ABSTRACT

Holt Oram Syndrome, an autosomal dominant disorder is constellation of congenital heart diseases and skeletal abnormalities. Amongst the congenital heart defects ostium secundum type of atrial septal defect is most common. Electrocardiographic abnormalities include heart blocks and AV conduction defects up to variable extent. In addition to cardiac abnormalities skeletal abnormalities such as radial dysplasia or hypoplasia and other upper limb abnormalities have been reported. We are presenting a case 25 years old lady with Holt Oram syndrome presenting with cardiac failure.

Keywords: Holt Oram syndrome, atrial septal defect, skeletal abnormalities.

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INTRODUCTION

Holt Oram syndrome is inherited in autosomal dominant pattern. It is characterized by congenital cardiac defects and skeletal abnormalities. Amongst the congenital heart defects ostium secundum atrial septal defect is most common followed by ventricular septal defects and ostium primum atrial septal defect. Variable electrocardiographic abnormalities including heart blocks and AV conduction blocks have been reported. More complex cardiac lesions such as tetralogy of Fallot, endocardial cushion defects, and total anomalous pulmonary venous return are also noted in these subjects. Skeletal abnormalities include radial, carpal, metacarpal and upper limb dysplasia or hypoplasia.

CASE REPORT

A twenty five years old lady presented in medicine emergency department with symptoms of severe respiratory distress. She was having two live issues. During second delivery she developed complains of dyspnoea. Family history was unremarkable. Physical examination revealed elevated jugular venous pressure, hepatomegaly, bilateral pedal oedema. BP was 110/68 mm of Hg. She was having respiratory rate of 32/min with bilateral basal rales and oxygen saturation was 82% at room air. Cardiovascular examination revealed left parasternal lift, fixed splitting of the second heart sound, and a systolic murmur of grade IV/VI at left parasternal area. Chest X-ray PA view showed cardiomegaly mainly of right atrium and the right ventricle, levocardia and increased pulmonary vascular markings [Fig.1]. On musculoskeletal examination, she had an abnormally rudiment thumb. Plain radiograph of both hands revealed hypoplasia of first metacarpal bone of the left hand [Fig.2]. Electrocardiogram showed sinus bradycardia; first degree AV block and right ventricular hypertrophy with right axis deviation [Fig.3]. 2-D echocardiography showed ostium secundum atrial septal defect of 5 cm. Clinical diagnosis of Holt Oram syndrome was made in view of clinical presentation and investigations. The patient was managed well with medical treatment for heart failure and subsequently referred to cardiothoracic department for surgical intervention after stabilization.

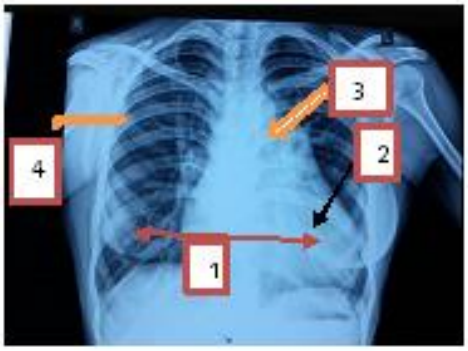

Figure 1: CXR showing cardiomegaly [1], prominent right ventricle [2], right atrial enlargement [3] and vascular prominence over upper lobes [4].

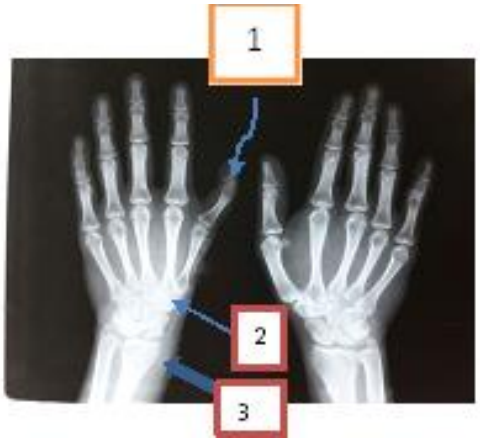

Figure 2: X ray showing hypoplasia of phalanges of thumb [1], carpals [2] and radius [3] of left hand.

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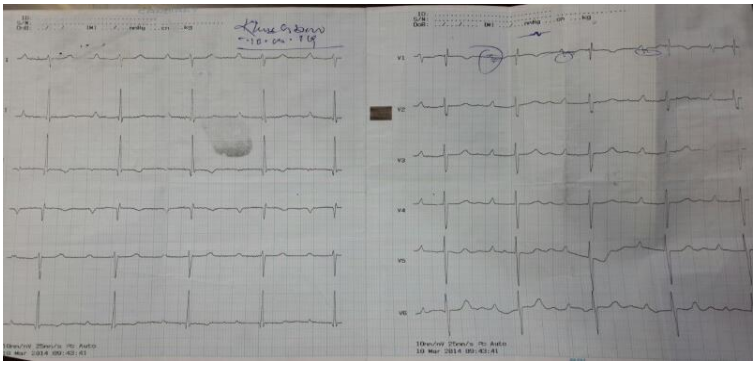

Figure 3: ECG showing sinus bradycardia and 1st degree AV block.

DISCUSSION

Holt-Oram syndrome (HOS) or atriodigital dysplasia or heart- hand syndrome is an autosomal dominant disorder caused by mutations on chromosome 12q24.1 that inactivate the TBX5 gene [1]. This syndrome was first described in 1960 by Mary Clayton Holt and Samuel Oram, who detected atrial septal defect in members of 4 generations of a family, though sporadic mutation and anticipation phenomenon has been reported [2]. The prevalence of HOS is approximately one per 100,000 births with 85% cases occurring due to mutations. The clinical features of HOS are dysplasia of upper limb, may range from minor radiographic abnormalities to phocomelia. The skeletal deformities are mainly digitalization of thumb, hypoplasia or dysplasia of radius, carpal and metacarpal bones [3].The skeletal abnormalities are rarely seen in lower limbs because mutated gene affect foetus at around 5th or 6th week of gestational age up till that lower limbs are not differentiated. Many clinical and genetic studies have shown that almost all cases of HOS had upper extremity involvement. Females have more severe anomalies.

This feature matches with our case. In cardiac abnormalities atrial or ventricular septal defects are most common. These defects may be isolated or may be associated with other cardiac anomalies like tetralogy of Fallot, endocardial cushion defects, total anomalous pulmonary venous return, pulmonary stenosis and mitral valve prolapse [4]. Different types of heart blocks and AV conduction defects up to variable extent may be found in electrocardiogram. Our case had sinus bradycardia and first degree AV block. The degree of upper limb defects does not correlate with the severity of cardiac defects. Holt Oram syndrome must be differentiated from TAR syndrome, Fanconi anaemia and thalidomide embryopathy where genetic studies may be helpful in the diagnostic. Unfortunately, in our case we were unable to make up genetic study of patient.

CONCLUSION

Holt Oram syndrome is a very rare clinical entity, but management can be difficult if not recognized timely, especially in emergency. Clinicians should have high index of suspicion of cardiovascular defect related emergency in a patient who has associated congenital musculoskeletal defects.

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