

## Case Report

# 3C Syndrome (Cranio-Cerebello-Cardiac Dysplasia) or Ritscher-Schinzel Syndrome: A Rare Case Report with Review of Literature

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## ABSTRACT

A very rare case of 3C (cranio-cerebello-cardiac) syndrome is reported for the first time in an Arab infant from Kuwait. The diagnostic features and differential diagnosis is discussed. We support the autosomal recessive

inheritance of this condition due to consanguinity between the parents. Need of antenatal diagnosis and genetic counseling is highlighted for this prognostically poor condition.

KEYWORDS: autosomal recessive, consanguinity, 3C syndrome

## INTRODUCTION

Ritscher-Schinzel or cranio-cerebello-cardiac (3C) syndrome is a very rare condition and so far only 30 cases are reported all over the world, mostly from North America and Europe<sup>[1,2]</sup>. We are reporting a typical case for the first time from a Saudi family living in Kuwait.

## CASE REPORT

A baby girl was born to a 31-year-old para 5, Saudi mother at 37 weeks of gestation by normal delivery. The father was 40 years old and a distant cousin of mother. All four siblings (two brothers and two sisters) were healthy. Family history was not remarkable. The pregnancy was uneventful. Birth weight was 2.1 kg (10th centile); head circumference was 34 cm (90th centile) and length was 44 cm (3rd centile). Apgar scores were six and nine at one and five minutes.

Many dysmorphic features were noted after birth and they were as follows: cleft palate, low set abnormal ears, depressed nasal bridge, hypertelorism, prominent occiput, micrognathia, anteverted nostrils, long philtrum, overriding of fingers, rocker bottom feet, hypoplasia of the middle and distal phalanges of the 5<sup>th</sup> finger, large anterior fontanelle (4 x 4 cm) and anal atresia with recto-vaginal fistula (Figs. 1,2 and 3). The baby had respiratory distress and a significant cardiac murmur at birth, diagnosed as patent ductus arteriosus (PDA) with multiple ventricular septal defects (VSD's) by echocardiography. She was ventilated, given anti-failure treatment and subsequently operated by pulmonary artery banding for VSD and PDA ligation by midline

sternotomy (Fig. 1).

CT scan of the head showed Dandy Walker malformation, corpus callosum agenesis and large retro-cerebellar cyst (Fig. 4). Abdominal ultrasound revealed bilateral hydronephrosis with a normal sized bladder. Skeletal survey, eye examination, fundoscopy and karyotyping were normal. The baby is now three and a half month old with failure to thrive (Weight : 2.3 kg, Length : 46 cm, Head Circumference : 34 cm; all below the 3rd centile), severe psychomotor retardation and mild hypotonia. She is tube-fed and oxygen dependent for broncho-pulmonary dysplasia.

## DISCUSSION

Ritscher *et al* (1987) described two sisters with congenital heart malformation, cerebellar anomalies and craniofacial anomalies<sup>[3]</sup>. In 1989, Verloes *et al* reported a third case, a female with VSD, enlarged fourth ventricle and cisterna magna; and proposed the name Ritscher-Schinzel syndrome<sup>[4]</sup>.

Ritscher-Schinzel syndrome, also known as 3C (cranio-cerebello-cardiac) syndrome is a rare autosomal recessive syndrome characterized by craniofacial, cerebellar and cardiac anomalies. Cardiac anomalies include VSD, ASD, PDA, Tetralogy of Fallot, double outlet right ventricle; hypoplastic left heart syndrome, aortic stenosis, pulmonary stenosis and other valvular anomalies. Central nervous system anomalies include Dandy-Walker malformation, cerebellar hypoplasia, and enlargement of cisterna magna. Craniofacial abnormalities are cleft palate, ocular coloboma, prominent occiput, low set ears, hypertelorism,

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Fig. 1: Showing hypertelorism, anteverted nostril, overriding fingers and scar of cardiac surgery

down slanting palpebral fissures, depressed nasal bridge and micrognathia. These features may occur in isolation or as a part of many syndromes<sup>[5]</sup>. Other rare malformations noted in less than 10% of patients are absent ribs, adrenal hypoplasia, anal atresia, congenital glaucoma, cutis aplasia, hemangioma, hemi vertebrae, hypospadias, hypoplasia of nail, nipple or penis, inguinal hernia, malrotation of gut, polydactyly, renal malformation, single umbilical artery, growth hormone deficiency and immunodeficiency<sup>[6-13]</sup>. Recently, a case with heterochromia of iris has been reported<sup>[2]</sup>.

The proposed minimum criteria for diagnosis of this syndrome are the presence of cardiac malformation other than isolated patent ductus arteriosus, cerebellar malformation, and cleft palate or ocular coloboma or four of the following seven findings: prominent forehead, prominent occiput, hypertelorism, down-slanting palpebral fissures, low-set ears, depressed nasal bridge, and micrognathia<sup>[5]</sup>.

There are no studies on incidence and prevalence. The syndrome seems to be pan ethnic: 18 cases were Caucasian, two African-American, three Canadian



Fig. 2: Showing prominent occiput, low set abnormal ears and anteverted nostril



Fig. 3: Showing anal atresia and rectovaginal fistula

Native Americans, three Pakistanis and four of unspecified race and ethnicity. The gender ratio of 10 males to 18 females is not significantly different from expected 1:1 for an autosomal recessive inheritance, which is supported by reports of four sets of affected siblings born to unaffected parents and of affected children born to consanguineous parents<sup>[15]</sup>. Our case is from an Arab family and this was not reported earlier. We also support autosomal recessive etiology as both parents are related<sup>[1]</sup>. Karyotyping was normal in all reported cases, as also in our case.

Several syndromes should be considered in the differential diagnosis of patients with suspected 3C syndrome<sup>[5]</sup>. Joubert syndrome involves cerebellar vermis hypoplasia, ataxia, hyperpnoea, abnormal eye movements and occasionally cleft lip and palate. Patients with Joubert syndrome may have heart malformation. Ellis-Van Crevald syndrome can involve alveolar ridge anomalies, heart defects and occasionally Dandy-Walker malformation. Dandy-Walker malformation has been described along with craniofacial and congenital heart defects in the Brachmann-de Lange syndrome. The latter two syndromes however, have other distinctive extra cranial anomalies, which distinguish them from the Ritscher-Schinzel syndrome<sup>[5]</sup>.

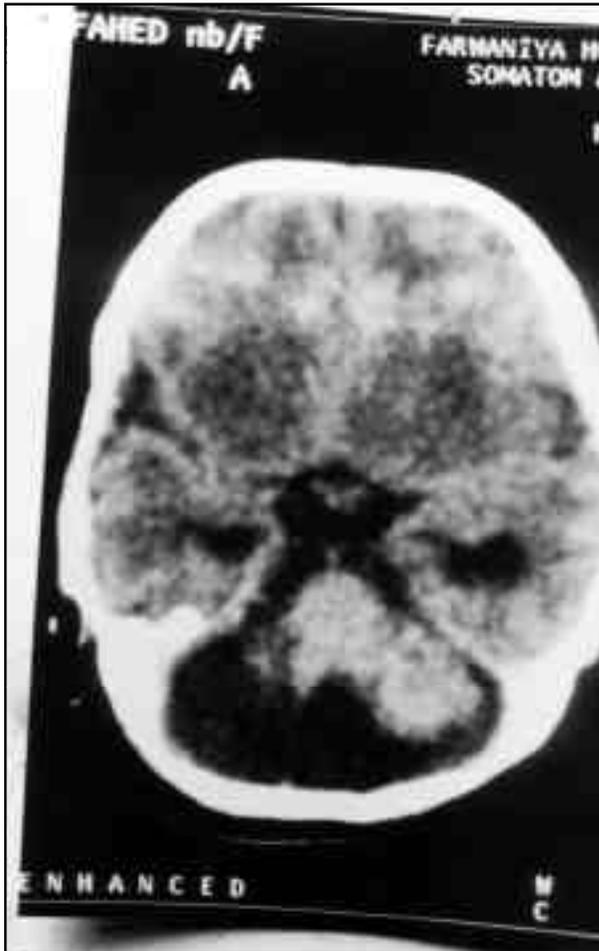


Fig. 4: CT scan of brain showing Dandy Walker malformation and retrocerebellar cyst

Most of the cases die before the age of six years, but one case is reported to have survived upto the age of 21 years. All cases were invariably retarded physically and mentally<sup>[14]</sup>.

Because the diagnosis of an autosomal recessive syndrome implies a 25% risk of recurrence of Ritscher-Schinzel syndrome in siblings of affected children, an accurate diagnosis is important for genetic counselling. Use of the proposed diagnostic criteria will enable more accurate diagnosis and more reliable counselling of affected families<sup>[5]</sup>. A prenatal sonogram done in second trimester can easily diagnose the cardinal features of 3C syndrome viz., Dandy-Walker malformation or its variants like posterior cranial fossa cyst or aplasia / hypoplasia of cerebellar vermis, congenital heart disease and intrauterine growth retardation<sup>[5]</sup>. If these features are found in association with

consanguinity in parents with or without positive family history, the antenatal diagnosis of 3C syndrome is very likely; and the option of therapeutic abortion may be discussed with parents in view of the poor prognosis of this condition. We therefore advocate an early antenatal diagnosis of the 3C syndrome.

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