

Decoding enigma: Turner syndrome with ring chromosome

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Abstract

Ring chromosome X is one of the rarest with some unique phenotypical features in Turner syndrome. A young female presented to us with anasarca developed over the past 2 months due to congestive cardiac failure along with jaundice and orthopnea. She had growth retardation, intellectual disability, primary amenorrhea, lack of secondary sexual character development and dysmorphic features like low posterior hairline, shield chest and cubitus valgus. She had dilated cardiomyopathy (DCM) with intracardiac thrombus on echocardiography. Skeletal survey revealed short fourth metacarpal/tarsal on limbs. Karyotyping showed a mosaic pattern, with 45, X,r(X)(p22.3q28), i.e. Turner syndrome karyotype with ring chromosome. Her heart failure with reduced ejection fraction was managed with vasopressor along with anticoagulant and given oral contraceptive pills for hormone replacement therapy. The ring chromosomal pattern of karyotype in this patient and DCM is a rare cardiological phenomenon that can be associated with Turner syndrome, making this case a unique one.

INTRODUCTION

Turner syndrome is the most common sex chromosomal abnormality in females and occurs in ~1 in 2000 to 1 in 2500 live female births [1]. It is caused by the loss of part or all of an X chromosome. Although many genotypes are associated with Turner syndrome, ring chromosome X is one of the rarest and it is associated with some unique phenotypical features.

This anomaly is functionally similar to a deletion of the distal part of the short arm (Xp deletion). If the X-inactivation site 'XIST' is also missing (usually with small rings), the risk for a significant developmental delay is substantially increased [1].

Turner syndrome is commonly associated with manifold cardiovascular issues but dilated cardiomyopathy (DCM) is a very rare association in a patient with Turner syndrome [2]. Our patient is one of a unique presentation of Turner syndrome with a genotype of ring chromosome.

CASE REPORT

A 17-year-old female presented to us with anasarca developed over the past 2 months, which started with bipedal edema gradually developing into anasarca for the last 15 days associated with intermittent fever for the same. Tracing backward this patient had a history of

progressive exertional breathlessness for the past 5 years and had a history of weakness of the right side of the body and facial deviation of angle of mouth to the left, which recovered spontaneously within 24 h, suggestive of transient ischemic attack (TIA), 1 month back. She also had developed jaundice throughout the last 2 weeks and orthopnea in the last 1 week.

Fever was associated with productive cough and expectoration. There was no history of rash, diarrhea, vomiting, joint pain, dysuria, hematemesis, melena, altered sensorium, renal failure or proteinuria. Her birth history was uneventful, developmental milestones were delayed along with poor scholastic performance and she didn't achieve her menarche yet.

On examination, she had sinus tachycardia, pallor, fever with 100.8°F, anasarca, suffering from cardiogenic shock with a blood pressure of 70/40 mm of Hg, raised Jugular Venous Pressure (JVP) and poor capillary filling. Cardiological auscultation revealed a systolic murmur of grade III over the left parasternal area with loud P2; chest auscultation revealed basal crepitations. She was malnourished with stunted growth. There was no organomegaly or clubbing or any abnormal fundoscopic picture. The patient was resuscitated, vasopressors added, blood cultures sent, empirical intravenous antibiotics started and urgent echocardiography planned

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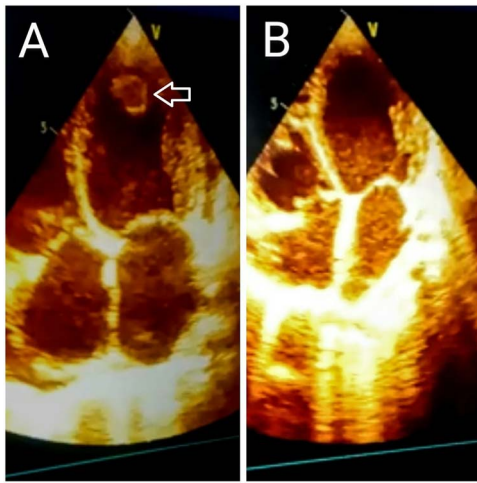


Figure 1. apical four-chamber view of echocardiogram showing dilated chambers with a globular mass (white arrow) near LV apex (thrombus) (A) on admission; thrombus dissolved at the time of discharge with therapy (B).

in accordance with the infective endocarditis protocol. Electrocardiogram showed sinus tachycardia with features of biatrial enlargement. Echocardiogram revealed levocardia with situs solitus; a 1.8 cm × 1.8-cm sized mass suggestive of thrombus within the left ventricular (LV) cavity near apex was found with dilated all four cardiac chambers with no evidence of vegetation. Global hypokinesia of LV, right ventricular free wall with left ventricular ejection fraction of 21% associated with severe tricuspid regurgitation and severe pulmonary arterial hypertension were found. No abnormalities were found in the aortic valve cusp or aortic root. (Fig. 1).

Given the working diagnosis of heart failure due to DCM with intracardiac thrombus, we started the patient on anticoagulation with low molecular weight heparin 20 unit subcutaneously twice daily. After initial stabilization, we searched for the underlying etiology behind this early DCM and intracardiac thrombus. Anti-Nuclear Antibody (ANA)-Hep2 and anticardiolipin, antibeta-2glycoprotein antibody was negative along with normal protein C, S values, which ruled out some common causes of the thrombotic phenomenon.

On detailed anthropometric analysis, she had short stature (height 125 cm), underweight (17.5 kg), upper segment:lower segment of 0.87 and arm span being 110 cm. Other notable findings were short fourth toe in the bilateral lower limb and low intelligence [Intelligence Quotient (IQ) 72 (borderline) as per Wechsler Adult Intelligence Scale (WAIS-IV) classification] [3]. There was a history of amenorrhea, associated with scanty axillary and pubic hairs and breast development showed tanner stage 1 with widely spaced nipples. She had a low posterior hairline with micrognathia, a webbed neck and cubitus valgus (Fig. 2). Hormonal assay revealed normal levels of estradiol (129 pg/ml), follicle-stimulating hormone (6.21 mIU/ml), luteinizing hormone (0.56 mIU/ml) and low insulin-like growth factor-1 level (102 pg/ml).



Figure 2. patient's salient features: (A) dysmorphic face with webbed neck, cubitus valgus and shield chest of the patient; (B) low posterior hairline, micrognathia; (C) dysmorphic toe.

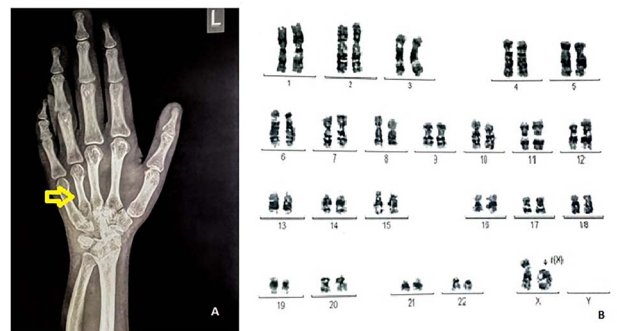


Figure 3. (A) showing short fourth metacarpal in left hand skiagram (yellow arrow); (B) karyotyping showing genotype suggestive of Turner syndrome with ring X chromosome (marked).

The skeletal survey revealed short fourth metacarpal and metatarsal in all four limbs. We had ruled out pseudohypoparathyroidism with normal serum calcium, phosphate and iPTH values along with the absence of other classical Albright's hereditary osteodystrophy phenotype morphology (early obesity, round face, heterotopic calcification) and sent sample for karyotyping from the blood that showed a mosaic pattern, with 45, X/46, X,r(X)(p22.3q28); i.e. Turner syndrome karyotype with a very rare variety that is ring chromosome [4] (Fig. 3).

She was treated for heart failure with reduced ejection fraction as per standard protocol conservatively, with subsequent anticoagulation. The patient was cured of intracardiac thrombi and congestive cardiac failure and finally was discharged with oral contraceptive pills for secondary sexual character development, iron-folic acid supplementation therapy for iron deficiency anemia, was put on dabigatran for 3 months and regular follow-up is being done periodically.

DISCUSSION

This short adolescent presented to us with anasarca due to heart failure. Her presentation mimicked that

Table 1. Investigations

Complete hemogram		Liver function test		RFT	Others			USG abdomen	
Hb	8.9 g%	T.Bilirubin	6.4 mg/dl	Urea	26 mg/dl	PT	15.7	Liver	Normal
RBC	4.5 million	D.Bilirubin	3.6 mg/dl	Creat	0.4 mg/dl	aPTT	31.2	Rt & Lt ovary	Streak like
TLC	7600/cumm	SGOT	431	Blood C/S	neg.	INR	1.25	Uterus	Infantile
Neutrophil	66%	SGPT	124	Na+	115	D-Dimer	2.52	Kidney	Normal
Leukocyte	25%	ALP	92	K+	5.1	TSH	4.16		
Platelet count	4.4 lac	T. protein	7.6	Ca2+	9.2	CRP	82.6	HIV I,	NR
ESR	57	Albumin	3.2	Phosphate	4.1	iPTH	48.2	HIV II	NR
MCV	63.1	S. ferritin	356	s. iron	10	TIBC	512	HBsAg	NR
								AntiHCV	NR

Abbreviation: RBC red blood cells; TLC total leukocyte count; ESR erythrocyte sedimentation rate; MCV mean corpuscular volume; SGOT serum glutamate oxaloacetate transferase; SGPT serum glutamate pyruvate transferase; ALP alkaline phosphatase; C/S culture and sensitivity; PT prothrombin time; aPTT activated plasma thromboplastin time; INR international normalised ratio; TSH thyroid stimulating hormone; CRP C reactive protein; iPTH intact PTH; TIBC total iron binding capacity

of infective endocarditis that was ruled out subsequently by clinical examinations showing no evidence of classical immunological or vascular phenomenon; echocardiography and blood culture negativity. Since there was a history of exertional breathlessness without angina or cardiac syncope, aided by echocardiographic findings, we arrived at a diagnosis of idiopathic DCM.

The patient's DCM with an intracardiac thrombus explained the etiology of a previous episode of TIA suggestive of a probable embolic phenomenon. The risk of thrombus formation is increased even in the absence of functional or morphological cardiovascular substrates for cohorts with Turner syndrome [5]. In our patient, in the setting of a low flow state due to DCM, lead to blood stasis and intracardiac thrombus got arisen. Though transaminitis can be a part of the syndromic association of Turner syndrome, her conjugated hyperbilirubinemia and transaminitis (Table 1) were explained by a probable congestive hepatopathy that resolved following correction of the decompensated heart failure [6]. DCM is a very rare cardiological phenomenon that can be associated with Turner syndrome with a paucity of literature worldwide [7]. Along with the clinical presentation, the ring chromosomal pattern of karyotype analysis, which has shown mosaic patterned distribution in cells analyzed, is certainly a very rare genetic anomaly found in 2.9% Turner syndrome patients shown by Maiti and Chatterjee from eastern India [8]. More interestingly, classical Turner syndrome patients present with normal intelligence mostly and small X-ring chromosome is usually known to have intellectual disabilities due to failure of undergoing X-inactivation that was evident in our patient also [9]. Mondal et al. [10] from India in a cohort of Turner syndrome patients had a patient of ring chromosome who had extremely low-performance IQ as well as extremely low verbal IQ. Our patient represents an individual with a set of unique clinical abnormalities like DCM, intracardiac thrombi, intellectual disability in a Turner syndrome mosaic karyotype with ring chromosome.

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CONFLICT OF INTEREST STATEMENT

None declared.

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CONSENT

Written consent obtained.

GUARANTOR

Debarup Das is the guarantor of this article.

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