Case Report

THYROID DYSFUNCTION AND CARDIOVASCULAR ABNORMALITIES IN A YOUNG PATIENT WITH TURNER SYNDROME

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Introduction

Turner's syndrome is a genetic syndrome that originates due to absence or structural anomaly of one of the X chromosomes in female and is characterized by short stature, gonadal dysgenesis, and physical stigmas[1,2]. Turner, in 1938, on studying a group of post-pubescent women, described the syndrome that carries his name. It is characterized by short stature, sexual immaturity, primary amenorrhea, webbed neck and cubitus valgus[2.] Ortiz et al pointed out that it was Ford who, in 1959, first described the karyotype 45,X. They also point out that there are other cytogenetic variants, among which important one is mosaicism XO or XX[3]. The association of this syndrome with inflammatory intestinal disease, rheumatoid arthritis, autoimmune thyroiditis and diabetes mellitus has been described[4]. At any age, Turner's syndrome may be difficult to recognize clinically because the characteristic facial features can be subtle. Key clinical features of Turner's syndrome are lack of breast development or amenorrhea, with elevated follicle-stimulating hormone levels by 14 years of age; and infertility in women. Other characteristics of Turner's syndrome include short stature, webbed neck, low posterior hairline, misshapen or rotated ears, narrow palate with crowded teeth, broad chest with widely spaced nipples, cubitus valgus, hyperconvex nails, multipigmented nevi, pubertal delay and cardiac malformation[5].

One third of patients with Turner's syndrome have a cardiac malformation; 75% of those having coarctation of aorta or bicuspid aortic valve[6]. Progressive aortic root dilatation or dissection can also occur, particularly in patients with a bicuspid valve, coarctation or untreated hypertension[7,8,9]. Patients with Turner 's syndrome often have an atherogenic cardiovascular risk factor profile[10].

Other potential complications of Turner's syndrome include strabismus, sensory neural hearing loss, recurrent otitis media, orthodontic anomalies, renal malformations (e.g., horseshoe kidney, duplicated or cleft renal pelvis), autoimmune thyroiditis, coeliac disease, congenital hip dysplasia, and scoliosis[9]. Girls with Turner's syndrome typically have normal intelligence (i.e. mean full scale IQ of 90); however, they may have difficulty with nonverbal, social, and psychomotor skills. If development is frankly delayed, an alternative explanation should be considered, along with prompt referral for early intervention[10,11].

Case Story

A 25 years old unmarried Muslim girl hailing from Fotulla, Narayangonj got admitted to Dhaka Medical College Hospital (DMCH) in Medicine Unit-5, on 8th July 2009 through outpatient department. According to the statement of the patient's mother-the patient was born as a full term baby through normal vaginal delivery at home. Her antenatal, intranatal and postnatal periods were uneventful except her milestone of development specially walking was slightly delayed. She started to go to school at 6 years of age and her school performance was average. As she grew older her family members noticed that her stature was short, had an abundant skin in her neck and a swelling over her throat. She was amenorrhoeic and her secondary sexual characteristics were poorly developed. With these problems, at her 16 years of age (in the year 2002) she got admitted into a hospital and was investigated. At that time her TSH was 13.75 μIU/ml, free triiodothyronine (FT_3) was 2.37 pg/ml and thyroxine/tetraiodothyronine (FT_4) was 1.65 ng/dl. Her karyotype showed 45,X and Barr body negative. She was diagnosed as a case of Turner's syndrome with Graves Disease (at hypothyroid state). She was prescribed tablet Thyroxine 0.25 μgm daily. In the year 2007, she developed episodic loose motion, heat intolerance, tremor, palpitation and exertional dyspnoea. She was investigated again and found thyroid stimulating hormone (TSH) 0.02 μIU/ml, FT_3 3.65 pg/ml and free FT_4 > 24 ng/dl. Now she was diagnosed as hyperthyroid state and was prescribed tablet Carbimazole 15 mg daily.

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But she gradually developed enlargement of the neck gland, difficulty in deglutition, severe weight loss and stridor during sleep. In December, 2008 , her TSH level became <0.004 µIU/ml and she was prescribed tablet Carbimazole 20 mg and tablet Propranolol 120 mg daily. But failed to response and she was given Radioactive Iodine therapy. After this she developed severe palpitation and chest discomfort, for which the patient got admitted into medicine department. On general examination, she was short statured, her pulse- 128 beats /min, blood pressure- 140/100 mmHg, temperature- 98°F and respiratory rate 18/minute. She had webbed neck (Fig-1), low set ears and low hair lines. She had shield chest, infantile breast, widely spaced nipple and a wide carrying angle (Fig-2). Her axillary hair was absent and pubic hair sparse, lymphoedema, short small digits in finger and toes (Fig 3 and 4)

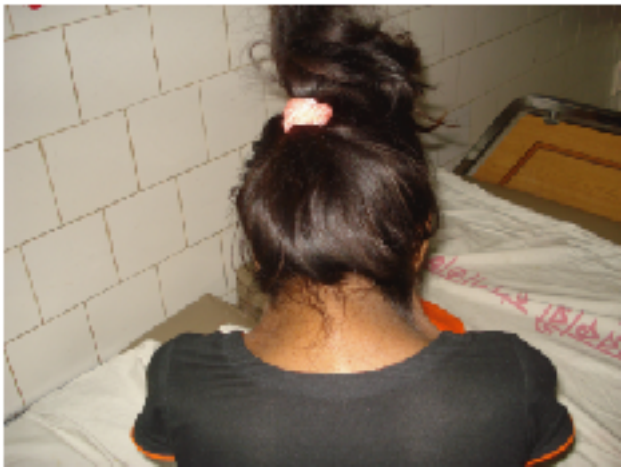

Fig 1: Web neck

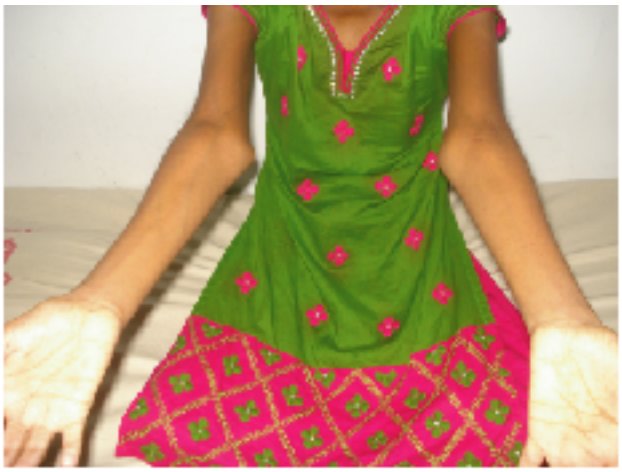

Fig 2: Wide carrying angle

Thyroid gland was enlarged about 8 cm × 6 cm in size. It was firm non-tender, surface was smooth and not fixed with overlying skin and underlying structures (Fig 5). Thyroid bruit was present. There was proptosis of the eyes.

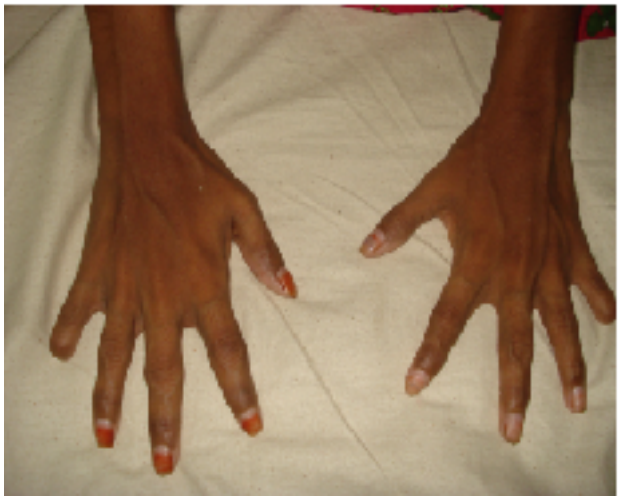

Fig 3: Small little fingers

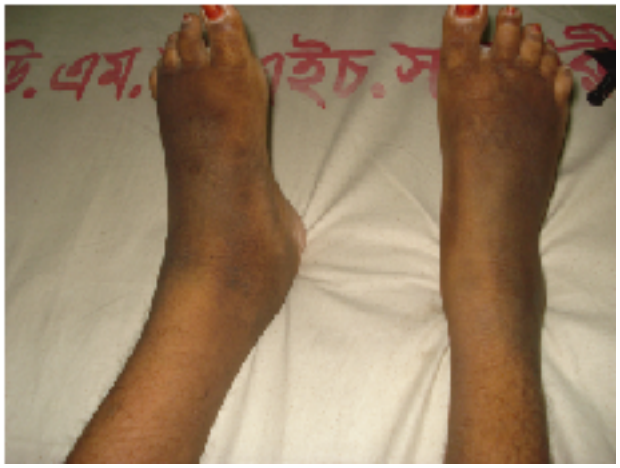

Fig 4: Small toes and lymphoedema

Lid lag and lid retraction were present (Fig 6). There were no ophthalmoplegia and no disturbance in visual acuity. There was non-pitting oedema over the both feet and lower part of the both legs. There were multiple furrows over the swollen feet and some blackish spots over them. Cardiovascular system examination showed- pulse was 128 beats/min and regular in right radial artery but it was non-palpable in left radial and left axillary artery. Pulses of lower limbs were palpable but there was significant radiofemoral delay. Blood pressure was 140/100 mmHg, jugular venous pressure (JVP) was not raised. Apex beat was in left 5th intercostals space, 8 cm from midline. First and second heart sounds were audible in all four cardiac areas and there were no added sound. For her thyroid problem- Radio iodine uptake test was done, which showed 50% uptake in 2 hours and 53% uptake in 24 hours (High RAI uptake), TSH level 0.08 µIU/ml, FT3 level 6.74 pmol/L and FT4 level 32.65 pmol/L (Hyperthyroid state). Thyroid scanning showed- thyroid gland mildly enlarged in size, radioactivity was increased in both lobes with no background activity.

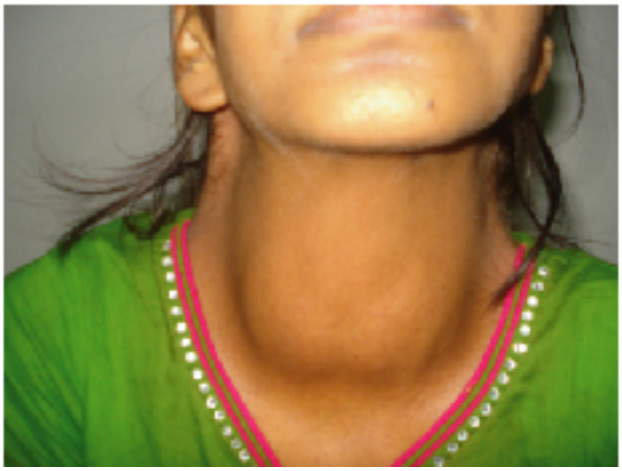

Fig 5: Thyromegaly with webbed neck

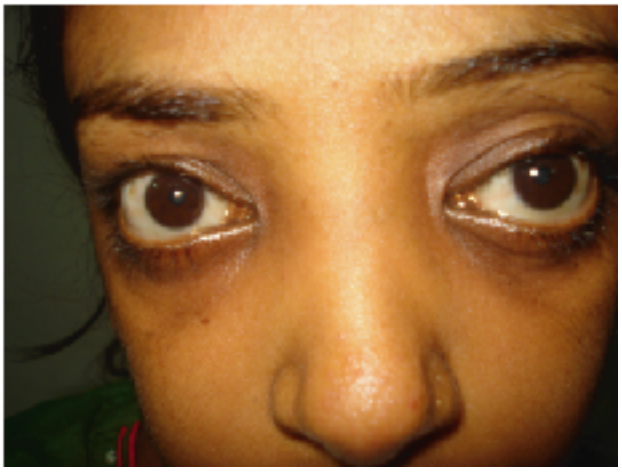

Fig 6: Lid lag and Proptosis

For this problem she was consulted with Endocrinology Department Dhaka Medical College (DMC) Hospital and was given Tablet Carbimazole (5mg, daily dose=2+1+1) and Tablet Propranolol (40mg, daily done=1+1+1). The doses of these drugs were gradually adjusted according to the clinical response and serum TSH, FT_3 and FT_4 levels. Ultrasonogram of lower abdomen was done which showed infantile uterus, non-visualized ovaries and crossed ectopic left kidney. Serum FSH level was 83.80 mIU/ml and serum Oestrogen level was 7.94 pg/ml. For the gynaecological problems of the patient, we consulted with Department of Gynaecology and Obstetrics, Dhaka Medical College Hospital. They diagnosed the patient as a case of primary amenorrhoea with absent secondary sexual characteristics and the suggested to give Oral Contraceptive Pills (OCP) for this problem. Consultation with Department of Cardiology, DMCH for her cardiovascular problems were done. Echocardiography showed no abnormality with LV Ejection Fraction of 62%. Color Doppler finding showed - Coarction of Aorta. Cardiac catheterization was done which showed - Coarction of Aorta and persistent left Superior Vena Cava (fig 7 and 8). Duplex flow examination of both lower limbs revealed arterio-venous malformation present in both lower limbs, specially, in both feet. But no stenosis or occlusion was observed.

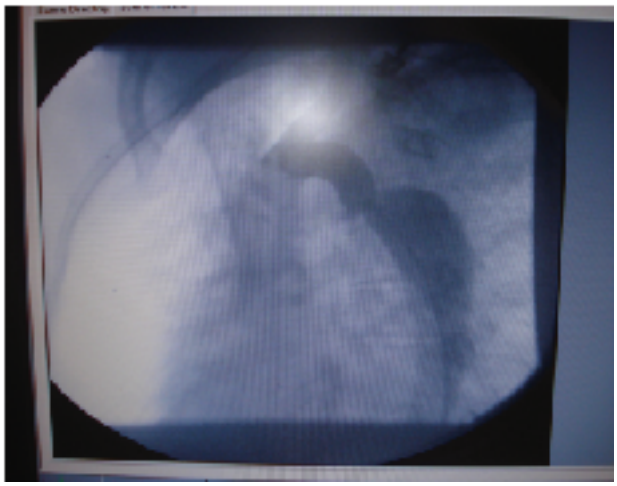

Fig 7: Catheterasation showing coarctation

The patient was finally diagnosed as a case of Turner's syndrome with Graves' Disease (now at hyperthyroid state) with Primary Amenorrhoea with Hypertension with Coarctation of Aorta with Persistent left Superior Vena Cava and Arterio-venous malformation of both lower limbs.

Discussion

Turner's syndrome (TS) is due to the absence of a sex chromosome or the presence of a structurally abnormal sex chromosome in a phenotypic female. Congenital malformations such as coarctation of the aorta and horseshoe kidneys are overrepresented[12,13]. Hypothyroidism or subclinical hypothyroidism, i.e. free T_4 within the normal range but elevated TSH, is thought to increase the risk of coronary artery disease[14]. The association has since been confirmed in TS and in gonadal failure with a high incidence of Hashimoto's disease and elevated thyroid antibodies[15-19]. Hypothyroidism is related to monosomy (the 45,X karyotype). This has been seen in congenital heart disease and hearing loss, but not in osteoporosis and fractures, in the present TS women[20-22]. However, elevated thyroid peroxidase (TPO) concentrations were evenly distributed between the different karyotype variants. The risk of developing hypothyroidism therefore appears to be high for all TS women, independent of karyotype. In this case, it was observed that initially the patient was hypothyroid and she also had hypertension, coarctation of aorta, arterio-venous malformation and left sided superior vena cava which all increases cardiovascular risk. High blood pressure (HBP) is found in these patients more commonly than in the general population. Hypothyroidism and variations in ovarian hormone supplementation may also play a role in the risk for HBP and hyperlipidemia.

Although coarctation of aorta is a common cardiovascular abnormality followed by HBP and bicuspid aortic valve (BAV), a host of other structural alterations were also found[23,24]. In reported case, BAV was absent but left sided superior vena cava was an unusual finding in cardiac catheterisation. Chance of dissection of aorta is no less than other patient without turner syndrome. Cardiac magnetic resonance imaging (MRI) rarely fails to visualize the aortic valve and is clearly superior to echocardiography in detecting abnormalities of the aorta, which is clearly visualized in both ascending and descending aspects. The risk for aortic dissection in TS appears to be almost entirely a consequence of structural cardiac malformations and haemodynamic risk factors, rather than a reflection of an inherent abnormality in connective tissue. In those individuals with structural changes known to predispose to dissection and it is not known whether dissection is an acute process or the result of slow, progressive dilatation.

HBP is found in these patients more commonly than in the general population. Hypothyroidism and variations in ovarian hormone supplementation may also play a role in the risk for HBP and hyperlipidemia. In reported case the patient was also having hypertension for prolonged which may be secondary to coarctation of aorta or partly may be due to thyroid hormone supplementation.

Conclusion

The index case is now on regular follow up. She is well tolerated with antithyroid drugs and is in euthyroid condition. Her blood pressure is well controlled with antihypertensive. On regular echocardiography and Doppler study, no new change of coarctation is seen and no episode of dissection is seen. She is on oral contraceptive regularly. A comprehensive care with coordination of medicine specialist, cardiologist, endocrinologist and Gynaecologist is essential for TS to have a decent life.

Refernces

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