Haemophilia A in a Female Patient with Turner Syndrome

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Abstract

A 28-year-old female presented with occasional swelling of knees and prolonged bleeding after trauma. She also complained of gum bleeding in few occasions. She also gave history of primary amenorrhoea and failure of development of secondary sexual character. There was negative family history of bleeding tendency in both maternal and paternal family. Her investigation profile showed prolonged Partial Thromboplastin Time and reduced factor VIII activity (2.5%). Karyotyping showed (45 XO) Turner syndrome. This is the reported first case of association of Turner syndrome with moderate Haemophilia A in Bangladesh.

Key words: Haemophilia, Turner syndrome, female haemophilia.

Introduction

Haemophilia A is a sex-linked recessive disorder that is expressed in males who inherit the haemophilic gene from their mothers and because of which produces reduced amount of factor VIII. Haemophilia A is the most common coagulation factor deficiency around the world.¹ It affects all ethnic population and its prevalence varies among different countries but estimated at a rate of 3-20 cases per 1,00,000 population.^{2,3} Being an X-linked recessive disorder, females are generally not affected, although they can be carriers of this disorder. A classical female haemophilia is possible only when a carrier female marries a haemophilic male, of which there are only few reports in the literature.⁴⁻⁶ In India, as consanguineous marriages are very common in certain communities (up to 30%), the likelihood of encountering female haemophilia is higher, although one case is found out of 1600 haemophilia families.⁷ In certain conditions, it can affect females too: X-chromosome lyonization, inactivation of normal X chromosome in a carrier and Turner's syndrome.^{1,8,9} Haemophilia is classified clinically on presence of clotting factor activity into - severe when <1% of normal, moderate when 1-5% of normal and mild 5-40% of normal.

Turner syndrome was first reported as a clinical syndrome prior to availability of karyotyping in 1938 by Henri Turner, an Oklahoma physician.¹⁰ It is the most common sex abnormalities in female occurs in approximately 1 in 2000 to 1 in 2500 live female birth based on epidemiological and newborn genetic screening data from Europe, Japan and the United States.¹¹ Turner syndrome occurs with more or less the same prevalence in all ethnic groups and in different

countries. Its number is declining in some countries due to termination of pregnancy. On the other hand, most gestations (likely more than 99%) affected by X chromosome monosomy (45, XO) do not survive to birth and 45 XO genotype is found in at least 10 percent of spontaneous abortion.^{12,13}

Figure 1: USG of abdomen and pelvis showing absence of uterus and ovaries

Case Report

A 28-year-old female presented with occasional swelling of knees and prolonged bleeding after trauma. She also complained of gum bleeding in few occasion. She needed transfusion 6-10 times for severe bleeding due to trauma. She also gave history of primary amenorrhoea and failure of development of secondary sexual character. There was negative family history of bleeding tendency in both maternal and paternal sides. On examination she was found to be of short stature. Her facial appearance included low nasal bridge, short nose, smooth philtrum and thin upper lip. She also had webbing of neck. Secondary sexual character was absent. The investigation results were as follows. Bleeding time: 3 minutes; prothrombin time (PT):13 seconds (control 12 seconds); activated partial

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Case Report

thromboplastin time (APTT): 116.1 seconds (control 28 seconds); APTT mixing study: 38.3 seconds (immediate) & 40.6 seconds (2 hours after incubation); factor VIII: 2.6% (normal: 60-150%); Von Willebrand Ag (vWF:Ag): 88% (normal: 50-160%); haemoglobin: 10 gm/dl; Total WBC: $9.08 \times 10^9/L$; Platelet: $255 \times 10^9/L$. Ultrasonography report shows absence of uterus and ovaries. Chromosomal analysis (Karyotype) shows abnormal female chromosome monosomy X, 45XO, consistent with Turner syndrome.

Figure 2: Karyotype showing 45XO (Turner Syndrome)

Discussion

The expression of a recessive X-linked disorder such as haemophilia A and B is rare in females. The incidence of haemophilia is about 1:7500 live male birth and 1:25,000,000 live female birth.¹⁴ Although Turner syndrome incidence is 1:2000 to 1:2500, very few number of haemophilia with concomitant Turner syndrome have been reported.^{9,12,15-22} This is the first reported case of Turner syndrome with haemophilia in Bangladesh. Our patient, as she has moderate haemophilia and had primary amenorrhoea, her symptoms were mainly when becomes injured, therefore, she presented lately. She lives in a remote place and had no facilities for diagnosis.

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