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CASE REPORT

Proteus syndrome: presenting as a large ovarian cyst

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ABSTRACT

Abnormal huge progressive enlargement and fusion of digits with limitation of joint movements (macrodactyly, syndactyly, and arthrogryposis) are usually part of a syndromic manifestation. When associated with mosaic skeletal overgrowths, vascular malformations and internal organ cysts it could be a part of the very rare Proteus syndrome. Here we are presenting a case with macrodactyly, syndactyly, arthrogyrposis and bilateral ovarian cysts. When clinical criteria remain inconclusive the diagnosis of Proteus syndrome (PS) is established by identification of a heterozygous pathogenic variant in AKT1 gene, which here could not be done because of economical constraints.

Keywords: Macrodactyly, syndactyly, arthrogyrposis, ovarian cyst, proteus syndrome.

Macrodactyly is a rare congenital abnormality that involves thickening of both the soft tissues and bones of the affected digits [1]. It is more frequent in fingers than toes, and the condition is often progressive in both [2]. Etiology and pathogenesis are still unknown [3]. Such increased growth is also seen in neurofibromatosis, hemangiomatosis, arteriovenous malformations, congenital lymphedema, and syndromes such as Klippel–Trenaunay–Weber syndrome and Proteus syndrome [1]. Its location is 90% unilateral and in 70% of cases involves more than one digit [1].

Syndactyly is failure of separation of the developing digits during organogenesis. Being an explicit limb phenotype, it comes to immediate medical attention at child's birth, particularly when it appears in the upper limbs. The involvement of feet is more frequent than the involvement of hands, and males are affected twice as frequently as females [4]. It is one of the most common hereditary limb malformations depicting a prevalence of 3–10 in 10000 births, though higher estimates ranging from 10–40/10000 have also been reported [5].

Case Report

An18 year old unmarried girl belonging to a lower socioeconomic status presented to the Gynecological OPD with chief complains of abdominal distension and early satiety for the last 3 months. She also complained of associated weight loss. She had attained menarche at the age of 13 and her menstrual cycles were within normal limits.

On examination, she had syndactyly, macrodactyly and arthrogryposis of both the hands and left foot (Figure 1, 2). There was impairment of moments of inter-phalangeal and metacarpo-phalangeal joints of both hands. There were a few lipomas in the forearm and wrist

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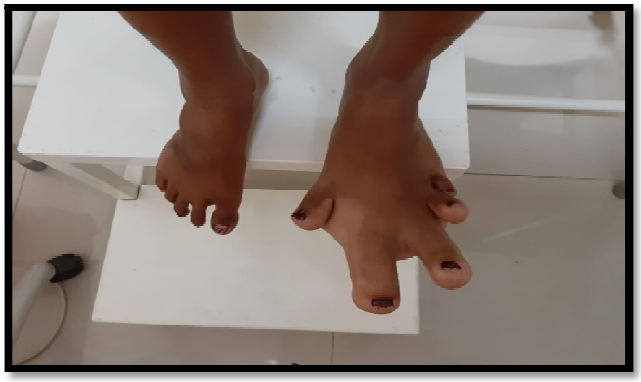

Figure 1: Foot of the patient

but the function of the wrist, elbow and shoulder were within normal limits. Both hands were grossly enlarged with excessive growth of the index, ring and middle fingers and syndactyly of middle and index finger of left hand.

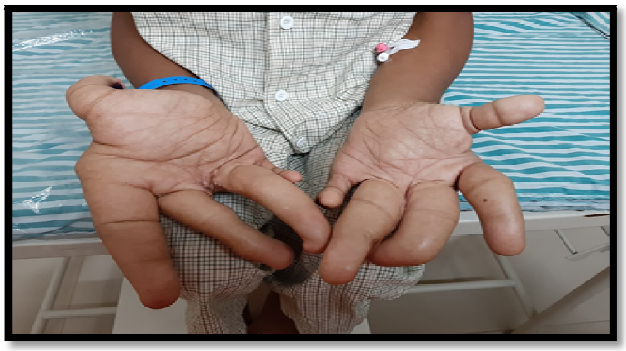

Figure 2: Hand of the patient

The enlargement was mainly composed of fibro

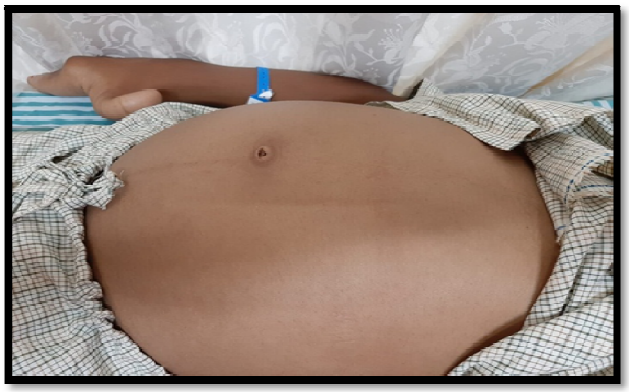

Figure 3: Lump occupying all quadrants of abdomen

fatty tissue without any hamartoma, angioma or discoloration of the skin. On examining the lower limb, the function of ankle joint was preserved with restricted movement of the metatarsophalangeal joints. On examination of the abdomen, there was a huge lump occupying all the quadrants of the abdomen with the upper border felt at the xiphisternum (Fig: 3). The lower border could not be felt. Fluid thrill was positive but there was no shifting dullness.

She also gave history of reconstructive surgery for the syndactyly and macrodactyly at the age of 2, both of

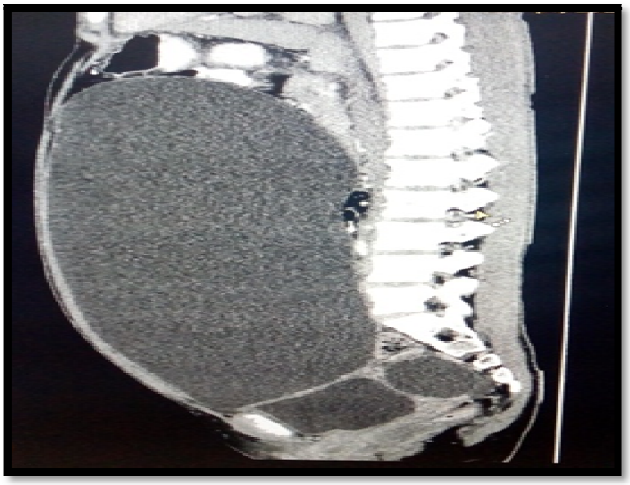

Figure 4: CT Scan showing large, cystic space occupying lesion arising from adnexa

which subsequently recurred. There were no other structural or functional anomalies. None of her other siblings (2 sisters) had any of the above issues. On enquiry her mother gave history of intake of indigenous unknown substance for treatment of infertility for a period of one month prior to conceiving.

Systemic examination was within normal limits and neurological examination did not reveal any deficit. Her ultrasound reported a huge cyst originating from the pelvis with a likely diagnosis of a mesenteric cyst or an adnexal cyst. Her CT scan (Figure 4) reported a large, cystic space occupying lesion arising from the right adnexa, covering almost the entire abdominal cavity and displacing other organs and structures. Another smaller cystic lesion was noted in the left adnexa. Ovarian tumor markers CA-125, inhibin, beta-HCG and alpha feto proteins were within normal limits.

On exploratory laparotomy there was large cyst (25x 18cm^2) originating from the right ovary [Figure 5] and another small cyst (5x5 cm^2) was also present on the left

ovary. Both cysts were removed and both ovaries were

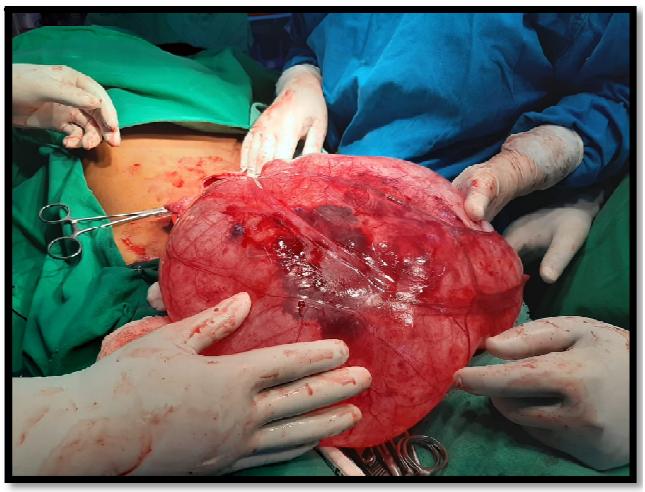

Figure 5: Large cyst originating from ovary

conserved. Histopathology showed both cysts to be simple serous cystadenomas.

Discussion

Our case had macrodactyly of both the hands and the left foot with syndactyly of middle and index fingesr of the left hand. There was also associated arthrogryposis of the interphalangeal and metacarpo-phalangeal joints of the hands which could be attributed to restriction of active movements of the joints [7]. The mother does not give any history of any infections in the antenatal period but does give a history of some indigenous root intake throughout the first trimester of pregnancy Fetal contractures can also occur in maternal diseases such as toxoplasmosis, rubella, varicella, coxsackie viruses, and enteroviruses; toxins and drugs (alcohol, d-tubocurarine, methocarbamol, misoprostol, phenytoin, and cocaine); pyrexia or overheating (hot baths, hot spa), and serious abdominal trauma [1, 8, 9].

Proteus syndrome is a rare condition characterized by progressive segmental or patchy overgrowth, most commonly affecting the skeleton, skin, adipose, and central nervous systems. It is a complex disorder with multisystem involvement with great clinical variability.

For the purpose of diagnosis the Proteus syndrome has been assigned certain general and certain specific features.

The three general characteristics are as follows -

1. Only some areas of the body are affected by the overgrowth whereas other areas are absolutely normal. This is termed as mosaic distribution.

2. Since it is a mutation no one else in the family is affected. This is termed as sporadic occurrence:

3. The overgrowth has noticeably altered the appearance of the affected body parts over time or those new areas of overgrowth have appeared over time. This is termed as a progressive course.

Besides these three general characteristics there are some specific characteristics that the case should have and based on this there are three categories A, B and C. For clinicians to consider the case as that of a Proteus syndrome it should have all the three general characteristics and either one feature from Category A, or two features from category B or three features from Category C [10]. Our case had all the three general characteristics and two features of the category B namely asymmetric, disproportionate growth of limbs and bilateral ovarian cystadenoma.

Establishing the diagnosis involves identification of a mosaic, somatic, heterozygous pathogenic variant in AKT1 gene by molecular genetic testing. In our case the general criteria as well as category B specific criteria were satisfied however due to economical constraints genetic studies were not done [10].

Conclusion

Proteus syndrome is a varied and complex disease, and its diagnosis is challenging. Although AKT1 mutations have been identified as a cause of Proteus syndrome, the precise pathogenesis and etiology of this syndrome require further investigation. Interestingly due to the varied manifestations of this syndrome it can present to any specialty and also requires a multidisciplinary approach for holistic management. The psychological issues related to disfigurement and the accompanying social stigmas are also important aspects of the management.

Conflict of interest: None. **Disclaimer:** Nil.

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