Case Report

A RARE CASE OF FEMORAL HYPOPLASIA (PROXIMAL FOCAL FEMORAL DEFICIENCY) WITH OVERLAPPING PHENOTYPE OF MULLERIAN DUCT SYNDROME (MAYER-ROKITANSKY-HAUSER SYNDROME)

Cheryl Melovitz-Vasan 1, Hiroshi Kitoh 2, Nagswami Vasan *3.

1 Assistant Professor, Department of Biomedical Sciences, Cooper Medical School of Rowan University, Camden, New Jersey, USA.
2 Associate Professor, Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan.
*3 Professor of Anatomy, Department of Biomedical Sciences, Cooper Medical School of Rowan University, Camden, New Jersey, USA.

ABSTRACT

Background: Congenital deformities of the femur vary from minimal hypoplasia to total absence with or without other skeletal or organ system involvement. The proximal focal femoral deficiency is a rare congenital deformity with various degrees of involvement.

Materials and Methods: During physical examination of a donated body (willed body program) we observed a donor with extreme hypoplasia of the left femur with other musculoskeletal anomalies. The donor was a 77-year old Caucasian female, who died of coronary artery and peripheral vascular disease.

Results and Observations: We report here a rare case of proximal focal femoral deficiency with overlapping phenotype of Müllerian duct anomaly typifying congenital absence of uterus, fallopian tube, uterine cervix and vagina (Mayer-Rokitansky-Kuster-Hauser (MKRH) syndrome). Dissection of the cadaver revealed unilateral hypoplasia of the left femur with an aplastic acetabulum, femoral head and patella. The left tibia and fibula were anatomically normal but shorter. The ovaries were small and atrophied. The external genital structure was normal with blind ending vagina. We also observed involvement of vascular structures.

Conclusion: The features we observed are described in the literature as that of proximal focal femoral deficiency with overlapping phenotype of Mayer-Rokitansky-Kuster-Hauser syndrome. This is first report of coexistence of a proximal focal femoral deficiency and congenital absence of uterus, Fallopian tubes, uterine cervix and vagina is a rare defect.

KEY WORDS: Proximal focal femoral deficiency, Mayer-Rokitansky-Kuster-Hauser syndrome, Al-Awadi-Raas-Rothschild syndrome, Fuhrmann syndrome, vascular defect, femoral hypoplasia, Müllerian duct anomaly.
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The proximal focal femoral deficiency (PFFD) is a rare congenital deformity with various degrees of involvement. Although the prevalence of PFFD is estimated to be 1 in 4500, females are more commonly affected than males [3] and left lower limb involvement seems to be more prevalent [4].

Aitken [5] described the congenital femoral deficit as ‘proximal focal femoral deficiency’ (PFFD) and distinguished four classes ranking A to D from the least severe form to the most severe form. In class A, a femoral head is present with a normal acetabulum and a short femoral shaft. In class B, there is more severe defect of proximal femur, dysplastic acetabulum, the femoral segment is short with proximal bony tuft and no osseous connection between the head and shaft. In class C, there is severely dysplastic acetabulum and femoral head, the proximal femoral shaft usually tapered and without defined trochanter. The class D is the most severe form with aplasia of the acetabulum and proximal femoral components, extremely short femur which often has only an irregular ossified tuft of bone proximal to the distal femoral epiphysis. There is a similarity in the musculoskeletal deformity between the class D phenotype of PFFD and those with Al-Awadi-Raas-Rothschild syndrome and Fuhrmann syndrome [6]. We report here a rare case of class D phenotype PFFD [5] with overlapping phenotype of Mayer-Rokitansky-Kuster-Hauser (MKRH) syndrome typifying congenital absence of uterus, fallopian tube, uterine cervix and vagina (Müllerian duct anomaly).

During the fifth and sixth weeks of human embryo, two pairs of genital ducts the mesonephric (Wolffian) ducts that is important in the development of the male reproductive system and the paramesonephric (Müllerian) ducts important in the development of the female reproductive system are present. In the female fetus, the paramesonephric duct differentiate into uterus, fallopian tube, uterine cervix and the upper part of vagina while the mesonephric duct degenerate [7].

MATERIALS AND METHODS

During examination of a donated body to our ‘Willed body program’ we observed a severely shortened left lower limb. Before a whole body dissection was performed on the 77-year old Caucasian female, who died of coronary artery and peripheral vascular disease, a complete physical examination was conducted and plain film x-rays of both lower limbs were obtained. Physical examination revealed the affected left side was bulkier and exhibited extremely short thigh, talipes valgus of the foot, and aplasia of the patella. The tibia and fibula were anatomically normal but shorter. The right lower extremity was unremarkable and no facial anomalies or other skeletal defects were observed. Further physical examination was unremarkable.

Radiographic assessment confirmed aplasia of the acetabulum and femoral head, and hypoplasia of the femur. We also observed a total right hip joint replacement with a titanium prosthesis (Figure 1). Dissection of the region revealed the hypoplastic femur was 14.5 cm long (Figure 2) and attached to the hipbone by the surrounding soft tissues. Aplasia of the acetabulum, patellar aplasia, the anatomically normal but shorter tibia and fibula, and deformed skeletal elements of the ankle and foot were also confirmed. Because of the thigh and the quadriceps muscles were rotated laterally and all hip and thigh muscles on the affected side were present but characterized by contracture and disuse atrophy.

Dissection also showed the heart, lungs, gastrointestinal tract, kidneys and suprarenal glands were normal and the ureters entered the bladder normally. The uterus, uterine tubes, uterine cervix and vagina, however, were absent and the vagina ended blindly. A pair of small atrophied ovary was present. Since a surgical scar indicative of a hysterectomy was not detected, a congenital defect associated with the PFFD likely accounted for the observed visceral aplasia. The external genitalia, on the other hand, were normal and the urethra entered the anterior aspect of the vaginal vestibule. Compared to the right side, the left common iliac artery, left internal iliac artery, left external iliac artery, and left femoral artery were smaller in diameter (Figure 3) but the left superior hypogastric artery and left inferior hypogastric artery were slightly enlarged. From the information published in the obituary notice, the donor...
was gainfully employed in an international corporation indicating normal cognition and lived a normal life span of 77 years.

**Fig. 1**: Radiograph of the hip shows on the left side aplasia of the acetabulum and femoral head, hypoplasia of the femur and aplasia of the patella.

**RESULTS AND DISCUSSION**

Congenital defects of the long bones and the extent of the defects varied from total absence to minor differences [1,2]. Unilateral femoral dysplasia accounts for 85-90% of congenital skeletal defects [8] and the affected individuals are mostly female [9].

The clinical appearance of PFFD is not subtle and easily recognized. The femur is shortened, flexed, abducted, and externally rotated [5,10,11]. The bulbous proximal thigh quickly tapers to the knee and flexion of the hip and knee typically causes dysfunction of the joints [12]. Small or vestigial patellae were observed in affected children [11]. Accordingly, we observed patellar aplasia in the present adult case of PFFD. A substantial reduction in length and diameter of the ipsilateral external iliac, femoral, and deep femoral arteries was observed in PFFD patients [13]. Similarly, we identified smaller diameters of the ipsilateral common iliac, internal iliac, external iliac, and femoral arteries in the present case of PFFD (Fig 3).

Congenital PFFD in combination with other anomalies such as unusual facies syndrome [14], Al-Awadi-Raas-Rothschild syndrome [15,6] and Al-Awadi-Raas-Rothschild syndrome Fuhrmann syndrome [16] have been well documented. However, PFFD (class D [5]) with overlapping phenotype of MKRH syndrome typifying congenital absence of uterus, fallopian tube, uterine cervix and vagina (Müllerian duct anomaly) hitherto has not been reported. Additionally, MKRH syndrome in association with other conditions such as Klippel-Feil and VATER has been observed [17]. Taken together, what we have presented is unique in that in addition to Müllerian dysgenesis the musculoskeletal deformity is only restricted to lower limb. The upper limb, thoracic and head and neck musculoskeletal and facial features were unaffected and the condition did not affect normal intelligence. It has been described that “femoral hypoplasia- an unusual facies syndrome” in infants with diabetic mothers [18]. Since we found no evidence of facial abnormalities, maternal diabetes may not be relevant in the present case; however, the family history of the donor is unknown. Exposure of the donor (born in 1935)
to thalidomide, a drug closely linked with congenital skeletal defects was unlikely as thalidomide was not available until 1957.

Number of causes for PFFD has been postulated. One theory implies PFFD results from injury to neural crest cells that form the precursors to sensory neurons of the spinal ganglia at L4 and L5 [10]. Another theory suggested that PFFD might result from a defect in the proliferation and maturation of chondrocytes of the proximal growth plate [19]. Element of ilium and proximal femur develop from a common anlage, with subsequent formation of joint space [20].

Taken together the musculoskeletal aplasia and hypoplasia suggests an alteration of the ‘developmental field’ [21]. Possibilities of a defective Hox gene family have been implemented in hypoplasia of the skeletal elements [22,1,23].

The expression of Hox genes in the Müllerian duct determines differential developmental identity, leading to the distinct morphological and functional components of the adult female reproductive tract. Diethylstilbestrol and several environmental xenoestrogens disrupt the development of the female reproductive tract by altering HOX gene expression, leading to structural and functional defects [24].

In 1985 Al-Awadi [25] described a new syndrome with profound limb and other deficiency. Since then, a host of phenotypic patterns in limb malformations have been recognized and given specific names. Mutations in WNT7A caused a range of limb malformations, including Fuhrmann syndrome and Al-Awadi-Rass-Rothschild-Schinzel phocomelia syndrome [23]. In 2006, Guerrier [26] described the MKRH syndrome with congenital absence of uterus and vagina. In 2011 Garavelli [11] and more recently Matsushita et al [6] described Al-Awadi–Rass-Rothschild syndrome and without WNT7A mutations. Various forms of Müllerian duct anomaly that occurs 1 in 4500 women has been diagnosed [27].

As reported earlier [25] the donor in our case had normal intelligence as she was gainfully employed in an International corporation.

**CONCLUSION**

In conclusion, we have described an uncommon case of unilateral PFFD with overlapping phenotype of MKRH syndrome typifying congenital absence of uterus, Fallopian tube, uterine cervix and vagina (Müllerian duct anomaly). In addition, we also observed compared to the right side, the left common iliac, internal iliac, external iliac and femoral arteries were smaller in diameter.

**ABBREVIATIONS**

MKRH- Mayer-Rokitansky-Kuster-Hauser  
PFFD- Proximal focal femoral deficiency

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**Conflicts of Interests:** None

**REFERENCES**


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