VAGINAL AGENESIS (MAYER - ROKITANSKY - KÜSTER - HAUSER SYNDROME): RECENT ETIOPATHOGENETICAL AND ANATOMICAL VIEWS

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SUMMARY

Congenital absence of uterus and vagina is a picture known as Mayer-Rokitansky-Küster-Hauser syndrome. Six cases are reported and particular attention is devoted to the anatomical pictures, which can be found in typical or atypical form. Discussion on the etiopathogenetical problems, supporting Hauser's hypothesis of an inhibition of the müllerian ducts development by MIF production, allows to consider it as the slightest form of female pseudoermaphroditism. Moreover the terms used to delineate this condition, like "müllerian aplasia", "müllerian ducts aplasia", "müllerian ducts agenesis" and "utero-vaginal agenesis" may be misleading and the term of "müllerian dysgenesis syndrome" is proposed.

Congenital absence of the vagina is an anomaly of the genital system which can be found isolated or as characteristic finding in several malformative syndromes. In all these cases a cytogenetical differential diagnosis is necessary and an accurate phenotypical evaluation of the patient must be done as well [1].

In presence of a normal genotype, with normal secondary sex characteristics, vaginal agenesis can be found as isolated anomaly, with an overplaced functioning uterus, condition however very rare, but more often in association with uterine aplasia. As a matter of fact this latter is the more frequent syndrome presenting congenital absence of the vagina. This picture is known as Mayer-Rokitansky-Künster-Hauser syndrome (MRKHs), from some of the Authors who first described it Mayer (1829), Rokitansy (1838), Künster (1910) and finally Hauser, who recently clearly defined this anatomoclinical picture [2].

Many works on this topic are reported in literature. Nevertheless the problem has been discussed mainly from the clinical point of view and consequently a particular care has been put on the therapeutical problems of vaginal reconstruction [3-11]. Authors' attention has been therefore devoted principally to the vaginal agenesis and only few works deal with the anatomical aspects of this syndrome [12-15]. This probably is the reason why literature shows different views about the morphological aspects of it.

This communication deals with the anatomical and etiopathogenetical problems of the MRFHs, with report of 6 new cases.

MATERIAL AND METHODS

Clinical data, at the Department of Obstetrics and Gynecology of the University of Modena, were reviewed for all patients discharged between 1963 and 1979 with a diagnosis of utero-vaginal agenesis (MRKHs).

For this study were selected only patients where laparoscopic and urographic examinations

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were done. Of this group, patients without a genetic and/or hormonal evaluation done during the recovery were reexamined. Six patients were taken into consideration. Of these, 3 where reexamined with the following examinations: pedigree, phenotypic evaluation, karyotype on peripheral blood, FSH-LH RIA, gynecologic examination.

RESULTS

Results are summarized in table 1. At the second examination patient No. 1 showed a 6 cm deep vagina (neovagina e coitu) ([16]). Patient No. 2 did meanwhile a surgical vaginal reconstruction. Patient No. 4, seen only at the time of recovery for primary amenorrhea, had already regular sexual intercourses at that time, whereas patient No. 5, recovered for sterility and primary amenorrhea was already married and seen by a gynecologist for the first time. Both cases should be considered as "neovagina e coitu" ([16]). Only in 1 case associated anomalies were found. According to Hauser ([12-14]), the case No. 4 should be considered as typical MRKHs, whereas cases No. 1, 2, 3, 5 and 6 as atypical MRKHs.

DISCUSSION

The typical anatomical picture of the MRKHs is also defined as "uterus bipartitus solidus rudimentarius cum vagina solida". It is characterized by the absence of the vagina and the introitus ends in a small depression, 1-2 cm deep. The urethral orifice is usually placed lower than normal. The hymen is generally absent or vestigial. The uterus is replaced by two rudimentary comma-like horns, generally not canaliculated. They are placed near the ovaries, 3-4 cm long, running downwards lateromedially and joined one to the other, posteriorly to the bladder, by a müllerian ridge. The tubes are normal in appearance, although sometimes lengthened. The ovaries are normal, as well as the hormonal picture ([17, 18]). The somatic development and the secondary sex characteristics are normal female (case 1).

The syndrome may be pure or associated with further congenital defects, mainly urinary or skeletal (case 3) ([19, 20]). In addition to the classical one, it is possible to find two other pictures, combined in various degrees. In the first one, beside vaginal agenesis, no uterus or rudiment of it can be found and insted there is a sickle shaped cord (müllerian ridge), running the pelvic hollow from one side to the other (case 2).

The second one is characterized by a small uterine rudiment lodged medially in the pelvis (cases 3, 5, 6). In these "non classical pictures" frequent is the finding of morphostructural modifications of the ovaries (enlargement, polycistic degeneration etc.) and of the tubes (mono or bilateral rudiment).

Hauser has studied in the last years the characteristics of these anatomical pictures, defining them as "atypical" ([12-15]). The term of "atypical MRKHs" defines therefore all the anatomical pictures different from the classical "uterus bipartitus solidus rudimentarius". But the world's literature do not show agreement about the terminology of this syndrome. Various definitions are used, like "müllerian ducts agenesis" ([21]), "müllerian ducts aplasia" ([22]), "müllerian aplasia" ([20]). These definitions are however misleading, as can be inferred from the analysis of the etiopathogenetical problems related to this syndrome.

The presence of a normal female karyotype permits to exclude a chromosomic defect ([1, 23, 24]). It is still uncertain whether the etiology is genic or epigenetic. The literature shows no agreement about it. On one hand rare cases of familial occurrence of the syndrome have been described ([25, 26]) and McKusick considers it as inherited autosomal recessive disorder ([27]). On the other hand the genetic hypothesis is questioned by Lischke and

Table 1. — *Anatomical and genetic findings in 6 patients with Mayer-Rokitansky-KüsterMauser syndrome.*

Case	Side	Ovary	Tube	Uterus	Vagina	Associated anomalies	FSH-LH	Phenotype	Karyotype	Familiarity
1	r.	policystic	rudiment	bilaterally	absent	—	normal	normal	46,XX	—
B.G.	l.	normal	normal	uterine horns	(6 cm at 2[a]			female		
2	r.	enlarged	normal	absent (mül-	exam. *)		normal	normal	46,XX	—
G.L.	l.	normal	normal	lerian ridge)	absent	—		female		
3	r.	normal	normal	median			normal	normal	46,XX	—
P.B.	l.	normal	normal	rudiment	absent	kyphoscoliosis		female		
4	r.	normal	normal	bilaterally		clinodactily	normal	normal	46,XX	—
C.W.	l.	normal	normal	uterine horns	5 cm *	—		female		
5	r.	normal	rudiment	median			normal	normal	46,XX	—
M.G.	l.	normal	rudiment	rudiment	6 cm *	—		female		
6	r.	enlarged	absent	median			normal	normal	46,XX	—
M.P.	l.	enlarged	absent	rudiment	absent	—		female		

* Neovagina e coitu.

Heidenreich's observations of cases of monozygotic twins, where only one twin was affected by the syndrome. These observations are strong evidence against the genic etiology, both mendelian and polygenic, of the syndrome ([28, 29]). Even Witkowski and Prokop do not take up a definite position for either of the two hypothesis ([30]). The epigenetic hypothesis is also supported by observations of atypical MRKHs due to thalidomide assumption by the mother during pregnancy ([31]).

But more important is the pathogenetical hypothesis recently proposed by Hauser ([12-15, 33]), as result of the observations about the anatomical modifications of the internal genitals in the cases of atypical MRKHs. Hauser considers this syndrome as the slightest form of female pseudoermaphroditism. The finding of different pictures, beeing anyway similar expression of the same syndrome, ranging from the complete müllerian aplasia (very rare, see case No. 6) to the classical picture, including all the possible degrees and the frequent ovarian modifications, as well as a lot of similarities between this and the testicular feminization syndrome ([33]), lead to believe in a gonadal inhibition of the müllerian ducts development.

In the male the regression of the müllerian ducts is a physiological event, occurring under the action of the "müllerian inhibiting factor" (MIF), produced in the medullary part of the undifferentiated gonad. Hauser believes that a limited medullary gonad differentiation with consequent MIF's production leads to a defective development of the müllerian ducts. Depending on the time of beginning of MIF's production the development of the müllerian ducts would stop at various stages. This could explain the morphogenesis of all the anatomical pictures found in the typical or atypical MRKHs. Hauser's hypothesis is also supported by the fact that gonadal differentiation and regression of the müllerian ducts occur at the same time. This hypothesis allows moreover to consider this syndrome as the slightest form of female pseudoermaphroditism and the various anatomical pictures found only as different expression of the same syndrome.

CONCLUSIONS

The above mentioned etiopathogenetical considerations make the current definitions of uterovaginal agenesis, müllerian aplasia ([20, 34]), müllerian ducts aplasia ([22]), müllerian duct agenesis ([21]) unacceptable. The complete aplasia of the müllerian ducts is almost never present and their development is nearly always normal cranially. Therefore the distal segment of the tubes is usually present. Hence it seems erroneous to speak of missed development of the müllerian ducts (aplasia), when there is only an altered development (dysgenesis).

For these reasons it would be more correct to use the term of müllerian dysgenesis syndrome, to indicate any case of typical or atypical MRKHs.

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