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Study of mullerian duct anomalies using magnetic resonance imaging technique in a tertiary care hospital of Assam

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Abstract

Background: Mullerian duct anomalies (MDA) consist of a set of structural malformations resulting from abnormal development of the paramesonephric or Mullerian ducts. Mullerian duct is the embryonic structure that develops into the female reproductive tract, including the oviduct, uterus, cervix and upper vagina. The most widely accepted classification system of different mullerian anomalies was established by the American Fertility Society in 1988. This classification chart divides anomalies into seven classes: class I to class VII.

Aim: Magnetic Resonance Imaging (MRI) study of the mullerian duct anomalies with different age groups, religions, different classes established by American Fertility Society and associated other anomalies.

Materials and Methods: Patients with positive history coming to Radiology Department of Guwahati Medical College and Hospital, Guwahati were included in the study. After preliminary suspected ultrasonography (USG), MRI was done for all the cases.

Results: 31 cases of mullerian duct anomalies were included in the study and out of which 70.97% were of class I and 9.67% were of class II and IV mullerian duct anomalies. 48.39% of the cases of mullerian duct anomalies were in age group of 15 years to less than 20 years. 27.27% cases of class I mullerian duct anomaly were associated with other anomalies like renal agenesis, ectopic kidney and ectopic ovary.

Conclusion: Class I MDA is found to be most common variety; 15-20 years of age are commonly affected group and Renal anomalies are the commonly associated anomaly.

Keywords: Mullerian duct, Paramesonephric duct, Anomaly.

Introduction

Mullerian duct anomalies (MDA) consist of a set of structural malformations resulting from abnormal development of the paramesonephric or Müllerian ducts[1]. Mullerian duct (MD) is the embryonic structure that develops into the female reproductive tract, including the oviduct, uterus, cervix and upper vagina[2].

Initially, the reproductive tracts of males and females are identical, containing two pairs of fully formed wolffian ducts and mullerian ducts (MDs). In females, lack of anti-Mullerian hormone, testosterone, and insulin-like 3 (Insl3) permit differentiation of the MD into the female reproductive tract[3].

The prevalence of MDA ranges from 0.001 to 10% in the general population and from 8-10% in women with an adverse reproductive history[4,5].

Normal development of the Mullerian ducts depends on the completion of three phases: organogenesis, fusion and septal resorption. Organogenesis is characterised by the formation of both Mullerian ducts. Failure of this results in uterine agenesis/hypoplasia or a unicornuate uterus. Fusion is characterised by fusion of the ducts to form the uterus. Failure of this results in a bicornuate or didelphys uterus. Septal resorption involves subsequent resorption of the central septum once the ducts have fused. Defects in this stage result in a septate or arcuate uterus[6].

The most widely accepted classification system of different Mullerian anomalies was established by the American Fertility Society (AFS) in 1988. This classification chart divides anomalies into the following seven classes: (I) hypoplasia/agenesis, (II) unicornuate uterus, (III) uterine didelphys, (IV) bicornuate uterus, (V) septate uterus, (VI) arcuate uterus, and (VII) diethylstilbestrol-related[7].

Mullerian duct anomalies (MDAs) represent a wide spectrum of developmental abnormalities related to various gynecologic and obstetric complications, including primary amenorrhea, infertility, and endometriosis. The uses of diverse imaging modalities, in conjunction with clinical information, provide important clues to the diagnosis of MDAs[8]. Magnetic Resonance Imaging (MRI) has been gaining in popularity for use in evaluating MDAs, by virtue of its noninvasiveness, lack of ionizing radiation, and capability for multiplanar imaging and soft tissue characterization[8]. The study was carried out to increase knowledge about MDA cases of this part of North-East India.

Materials and Methods

The study is a retrospective study based on cases of MDA attending the Department of Radiology, Guwahati Medical College and Hospital, Guwahati, from June 2011 to June 2015 with positive history of gynecologic and obstetric complications like primary amenorrhea, infertility etc. In all cases MRI of the pelvis was done after preliminary suspected ultrasonography.

After taking a brief clinical history and performing a detailed clinical examination, the patient was put for MR Imaging in the MR Section. The machine used was SIEMENS TIM AVANTO 1.5 Tesla machine. Before the scans were performed, history of any metallic implant into the body was enquired from the patient or attendants; the procedure was explained to the patient so as to allay any apprehensions. The patient was asked to have nothing orally for at least 4 hours preceding the scan.

Altogether, 31 cases of MDA were included in the study and associated systemic anomalies (if any) were also considered. The cases were classified according to AFS classification into seven classes: class I to class VII. The study was approved by the Institutional Ethics Committee of Medical College and hospital.

Results and Observation

Among total number of 31 cases of MDA, class I MDA (Fig. 1) was the most common type with 70.968% followed by class II and class IV MDA (Fig. 3 and 5) with each of 9.677% (Table 1). 'IBM SPSS 21' (Statistical Package for the Social Sciences) software was used and descriptive statistical analysis has been carried out in the present study.

Table 1: Showing number and percentage of cases of mullerian duct anomalies according to AFS classification

AFS Classification of MDA	Number of cases of MDA	Percentage
Class I	22	70.968%
Class II	3	9.677%
Class III	1	3.226%
Class IV	3	9.677%
Class V	1	3.226%
Class VI	1	3.226%
Class VII	0	0
Total	31	100%
Mean	4.429	14.286
Standard Deviation	±7.829	±25.253
Standard Error of Mean	±2.959	±9.545

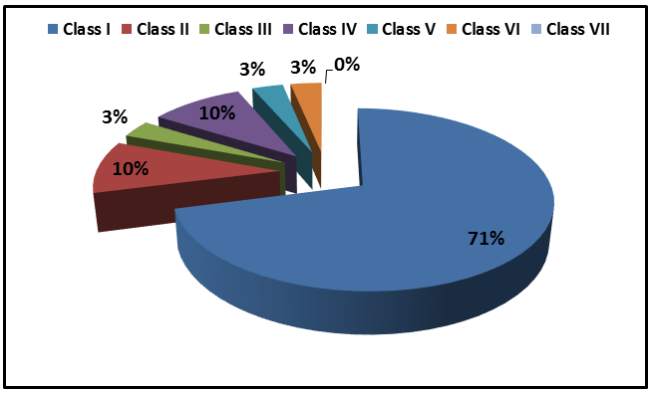

Fig. 1: Showing percentage of different classes of mullerian duct anomalies

Table 2: Number of cases of mullerian duct anomalies according to AFS classification with different age groups

Age groups	Number of cases of MDA according to AFS classification							Total
	Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII	
0 to <5 yrs	0	0	0	0	0	0	0	0
5 to <10 yrs	0	0	0	0	0	0	0	0
10 to <15 yrs	2	1	0	2	0	0	0	5
15 to <20 yrs	13	2	0	0	0	0	0	15
20 to <25 yrs	5	0	0	0	0	0	0	5
25 to <30 yrs	1	0	1	1	0	0	0	3
30 to <35 yrs	1	0	0	0	0	1	0	2
35 to <40 yrs	0	0	0	0	0	0	0	0
40 to <45 yrs	0	0	0	0	1	0	0	1
Total	22	3	1	3	1	1	0	31

Maximum numbers of cases of MDA were in the age group of 15 to less than 20 years and it can be noticed that 80.65% (25 out of 31 cases) were in the age between 10 to 25 years.

Table 3: Showing number of cases of mullerian duct anomalies with different religion

Religion	Number of cases of MDA according to AFS classification							Total
	Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII	
Hindu	13	3	1	3	1	1	0	22
Muslim	9	0	0	0	0	0	0	9
Total	22	3	1	3	1	1	0	31

Most of the cases of MDA were from hindu religion with 70.968% (22 out of 31 cases) and rest were from muslim religion. Two tailed p value between number of hindu and muslim MDA cases is 0.401 which is more than 0.05. Thus, there is no significance between number of hindu and muslim cases of MDA.

Table 4: Showing number of cases of mullerian duct anomalies with associated other systemic anomalies

Associated Anomalies		Number of cases of MDA according to AFS classification							Total
		Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII	
Renal agenesis	Right kidney	0	1	0	0	0	0	0	1
	Left kidney	2	0	0	0	0	0	0	2
Ectopic kidney	Right kidney	1	1	0	0	0	1	0	3
	Left kidney	2	0	0	0	0	0	0	2
Ectopic Ovary	Right Ovary	1	0	0	0	0	0	0	1
	Left Ovary	0	0	0	0	0	0	0	0
Anal canal stenosis		0	2	0	0	0	0	0	2
Total		6	4	0	0	0	1	0	11

Out of 22 cases of Class I MDA (Fig. 1), six (27.27%) cases were associated with other systemic anomalies like renal agenesis, ectopic kidney and ectopic ovary. 66.67% (2 out of 3 cases) Class II MDA (Fig. 3) cases were associated with anal canal stenosis. One case of class II MDA having left sided non-communicating rudimentary horn was associated with contralateral renal agenesis. On the other hand, another case of class II MDA having right sided non communicating rudimentary horn was associated with ipsilateral renal agenesis. 22.73% (5 out of 22) cases of class I MDA were associated with renal anomalies.

Two tailed p value between number of class I and class II MDA cases with associated other systemic anomalies is 0.539 which is more than 0.05 (>0.05). Thus, there is no significance between number of class I and class II MDA cases with associated other systemic anomalies.

Table 5: number of cases of mullerian duct anomalies with associated complications

Associated complications	Number of cases of MDA according to AFS classification							Total
	Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII	
Hematometra	3	1	0	0	0	0	0	4
Hematosalpinx	2	2	0	0	0	0	0	4
Hydrosalpinx	2	0	0	0	0	0	0	2
Blood in the horn	0	1	0	2	0	0	0	3
Pelvic Ascites	4	0	0	0	0	0	0	4
Ovarian Cyst	5	0	0	0	0	1	0	6
Multiple Uterine Fibroid/ Myoma	1	0	1	0	1	0	0	3
Total	17	4	1	2	1	1	0	26

Two tailed p value between number of class I and class II MDA cases with associated complications is 0.030 which is less than 0.05 (<0.05). Thus, there is significance between number of class I and class II MDA cases with associated complications.

Discussion

Class I MDA (Fig. 1) includes vaginal and uterine agenesis and hypoplasia result from variable degrees of early failure of the paramesonephric ducts to develop prior to fusion and compose approximately 5%–10% of müllerian duct anomalies. Mayer-Rokitansky-Kuster-Hauser syndrome is the most common manifestation: It results in complete vaginal agenesis, with 90% of cases associated with uterine agenesis. The ovaries are normal in the majority of cases[9]. **Class II: Unicornuate Uterus** (Fig. 3) results due to failure of one müllerian duct to elongate while the other develops normally results in the unicornuate uterus and accounts for approximately 20% of mullerian duct anomalies[9]. **Class III includes uterus didelphys** (Fig. 4), which constitutes approximately 5% of MDA, is the result of nearly complete failure of fusion of the müllerian ducts. Each müllerian duct develops its own hemiuterus and cervix and demonstrates normal zonal anatomy with a minor degree of fusion at the level of the cervices[9]. **Class IV: bicornuate uterus** (Fig. 5) results from incomplete fusion of the uterovaginal horns at the level of the fundus and accounts for approximately 10% of müllerian duct anomalies[9]. **Class V: septate uterus** (Fig. 6) is the most common müllerian duct anomaly. This anomaly composes approximately 55% of müllerian duct anomalies[10]. **Class VI: arcuate uterus** (Fig. 7) is characterized by a mild indentation of the endometrium at the uterine fundus as a result of near complete resorption of the uterovaginal septum[9]. **Class VII: diethylstilbestrol exposed Uterus** in which diethylstilbestrol is a synthetic estrogen that was introduced in 1948 and prescribed for women experiencing recurrent spontaneous abortions, premature deliveries, and other pregnancy complications. Structural anomalies of the uterine corpus, cervix, and vagina were subsequently described and shown to affect reproductive potential[11].

Table 6: showing comparison of studies regarding percentage of occurrence of different mullerian duct anomaly cases

AFS Classification of MDA	Percentage of MDA cases in present study	Percentage of MDA cases in Chandrayan P et al.[12] (2016) study	Percentage of MDA cases in Rani H et al.[13](2009) study	Percentage of MDA cases in Patel SN et al.[14] (2015) study	Percentage of MDA cases in Nath J et al.[15] (2015) study
Class I	70.968%	61.5%	48.15% (13/27)	14.7%	18.7%
Class II	9.677%	30.7%	11.11% (3/27)	14.7%	25%
Class III	3.226%	7.6%	11.11% (3/27)	2.9%	6.25%
Class IV	9.677%	-	3.7% (1/27)	17.7%	18.7%
Class V	3.226%	-	7.4% (2/27)	20.6%	6.25%
Class VI	3.226%	-	3.7% (1/27)	5.9%	6.25%
Class VII	0	-	-	0	0

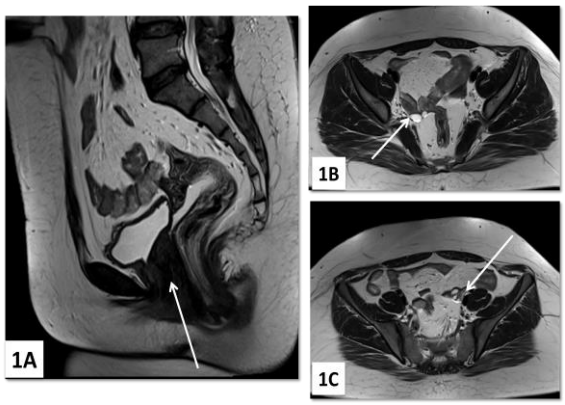

Fig. 1: Class I mullerian duct anomaly. A. T2WI Sagittal image showing absence of uterus and vagina (arrow). B & C. Axial images showing bilateral normal ovaries

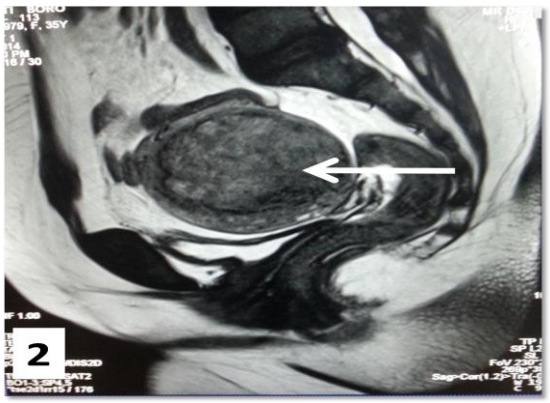

Fig. 2: T2WI sagittal image showing an uterine fibroid replacing the uterine tissue present. There is absence of the cervix and vagina

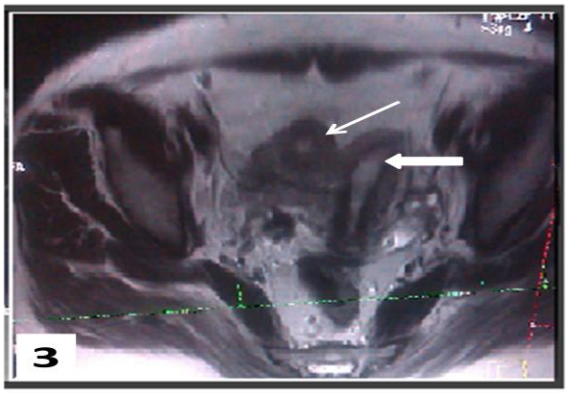

Fig. 3: T2WI coronal images showing an abnormal shaped uterus tilted to one side with a single cornu. The endometrium and zonal anatomy of the uterus is normal (thick arrow). A rudimentary horn is noted on the right side (thin arrow). Unicornuate uterus with rudimentary non communicating horn (thin arrow), class II mullerian duct anomaly

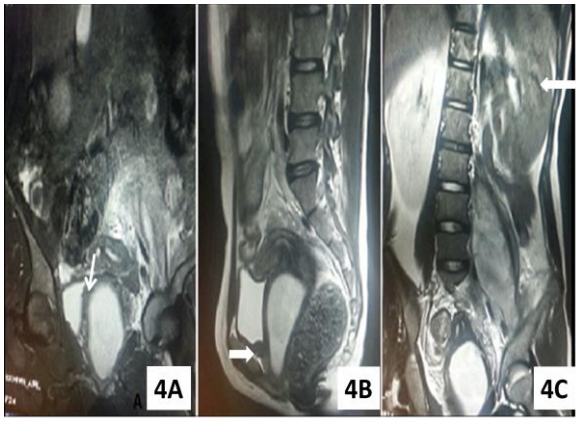

Fig. 4:A. T2-weighted coronal MR images showing complete duplication of uterine horns (thin arrow). Class III mullerian duct anomaly. B. Saggittal T2 weighted MR images showing dilated hemivagina showing hypointense signal within a background of hyperintensity (T2 shading), suggestive of blood products within (hematocolpus), a finding that corresponds to the obstructed right hemivagina (thick arrow). Mild dilatation of the right endometrial cavity and a non-distended left endometrial cavity are also seen. C. Coronal T2-weighted MR image shows a solitary left kidney (thick arrow)

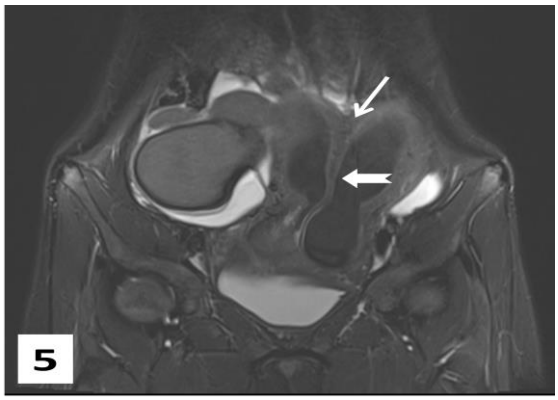

Fig. 5: T2WI FS coronal image showing two uterine cavities. The external fundal contour is concave (thin arrow). A myometrial signal intensity septum is noted separating the two uterine cavities and the cervix (thick arrow). Class IV mullerian duct anomaly. The uterine cavities and the cervices are distended with T2 hypointense and T1 hyper intense fluid suggesting blood. The patient had hematosalpinx also on the right side (*)

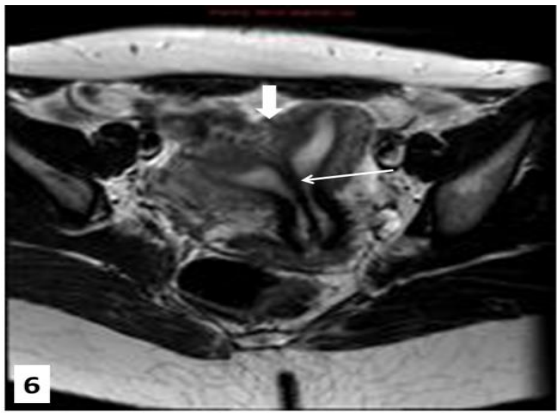

Fig. 6: T2WI Axial image showing thin T2 hypointense septa (thin arrow) separating the two uterine cavities. The external uterine contour (thick arrow) is flat. Class V mullerian duct anomaly

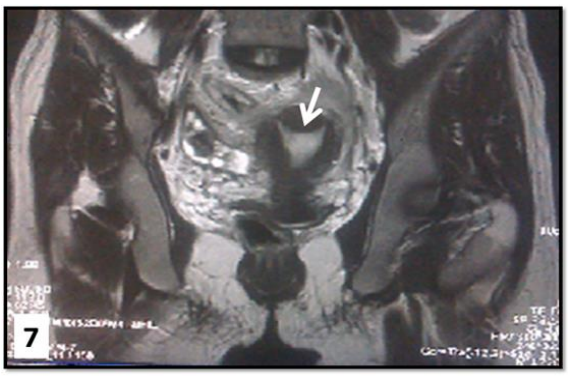

Fig. 7: Transverse fast spin-echo T2-weighted MR image showing smooth and broad myometrial fundal indentation (arrow). Normal external uterine

contour is maintained. Class VI mullerian duct anomaly

Chan et al. reported an MDA prevalence of 5.5% in the general population; they also found that arcuate uterus was most common in the general population, affecting 3.9% of women, followed by bicornuate uterus (0.4%). Among women who experienced challenges conceiving (e.g., infertility or miscarriage), septate uterus was a frequent finding, affecting 15.4% of women[16]. In the present study, most common MDA was the uterine agenesis and hypoplasia (Table1, 6 and Fig. 1) and this is similar to the findings of Chandrayan P et al.[12], Rani H et al.[13] studies (Table 6).

Table 7: Showing comparison of studies regarding the commonly affected age groups of mullerian duct anomaly

Various studies of MDA	Most Common Age group with MDA and its percentage	Second most common age group with MDA and its percentage
Chandrayan P et al.[12] study	16-18 years, 47%	19-21 years, 38%
Roy D[17] study	12-20 years, 61.11%	21-30 years, 37.33%
Banerjee I et al.[18] study	15-17 years, 52.6%	18-20 years, 26.4%
Patel SN et al.[14] study	21-25 years, 52.9%	10-15 and 16-20, 14.7%
Nath J et al.[15] study	15-17 years, 66%	18-20 years, 20 %
Present study	15 to <20 years, 48.39%	10 to <15 years and 20 to <25 years, 16.13%

Most common age group affected with MDA in the present study was between 15 years to less than 20 years (Table 2 and 7) and this is close to the findings reported by Chandrayan P et al[12], Banerjee I et al.[18], Nath J et al.[15] studies (Table 7).

Roy D et al.[17] in her study reported that 72.23% MDA patients were hindu and 27.77% were muslims by religion. This data is almost similar to the present study in which 70.97% were hindu and rests were muslims (Table 3).

Renal anomaly was associated with all Class II mullerian anomaly whereas Class I had 75% association with renal anomaly as reported by Chandrayan P et al.[12]. In Nath J et al.[15] study, out of 16 MDA cases, only one (6.25%) case, which is class II MDA, having unilateral renal agenesis. Banerjee et al. found 21% renal, 10% cardiac and 5% gastrointestinal anomalies associated with MDA cases. In the present study, out of 31 cases, 25.81% (eight cases) having renal anomalies, 3.23% (one case) having ectopic ovary and 6.45% (two cases) having anal canal stenosis associated with MDA (Table 4). El Ameen NFE et al.[19] reported 21% cases of MDA associated with renal anomalies in their study. Allen JW et al.[20] concluded that the incidence of incomplete ovarian descent is increased in women with mullerian duct abnormalities. The association was highest in patients with fusion abnormalities such as bicornuate and didelphys uterus or various forms of uterine agenesis.

13% and 2% cases of MDA associated with ovarian cyst and hematometra respectively as reported by El Ameen NF et al.[19] whereas in the present study 19.35% cases (6 out of 31 cases) and 12.9% cases (4 out of 31 cases) of MDA associated with ovarian cyst and hematometra respectively (Table 5).

Out of 31 cases, three cases, one each of class I, class III and class V were associated with multiple uterine fibroid (Table 5) (Fig. 2). Valecha SM et al.[21] reported a case of Mayer-Rokitansky-Küster-Hauser associated with multiple fibroids and similarly a case of uterus didelphys with multiple fibroids was reported by Ali MK et al.[22]

According to a new study, the investigation of women with mullerian disorders should be thorough, and array comparative genomic hybridization (CGH) should be considered, given the potential highly significant familial implications of a chromosomal abnormality[23]. A recent study indicated that mutation (p.V362M) of DACT1 protein (Dapper antagonist of catenin-1) may be an underlying cause of MDA[24].

MRI is currently considered the best imaging modality for MDA. It lacks radiation and provides clear delineation of both the internal and the external uterine anatomy. MRI has been shown to have excellent agreement with the clinical diagnosis of the subtypes of MDA[25].

Operative hysteroscopy is the gold standard in the treatment of most of those anomalies amenable to surgical correction. The evidence to date shows an ongoing increase in the release of recommendations in favour of operative hysteroscopic treatment, in concert with the progressive refinement of hysteroscopic technologies and techniques[26].

Conclusion

Based on the results we conclude that Class I MDA i.e. vaginal and uterine agenesis or hypoplasia, is the most common type of MDA. Patients between 15 years to 20 years of age are commonly affected with MDA. Renal anomalies are the commonly associated anomaly. Study of MDA cases in this part of the country is not frequent and this study will definitely be informative to the physicians and radiologists. Though the sample size is not large enough, the study can be further extended with inclusion of more and more cases in near future.

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