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# Postoperative evaluation of chronic pain in patients with Mayer – Rokitansky – Küster – Hauser (MRKH) syndrome and uterine horn remnant: Experience of a tertiary referring gynaecological department

Y. Dabi, V. Canel, D. Skalli, B.J. Paniel, B. Haddad, C. Touboul

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1 **Postoperative evaluation of chronic pain in patients with Mayer – Rokitansky –**  
2 **Küster – Hauser (MRKH) syndrome and uterine horn remnant: experience of a**  
3 **tertiary referring gynaecological department**

4  
5 **Short title:** Chronic pain in patients with MRKH

6  
7 DABI Y<sup>1\*</sup>, CANEL V<sup>1\*</sup>, SKALLI D<sup>1</sup>, PANIEL BJ<sup>1</sup>, HADDAD B<sup>1</sup>, TOUBOUL C<sup>1, 2</sup>

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9 \*These authors contributed equally to this work.

10  
11 *<sup>1</sup>Faculté de médecine de Créteil UPEC – Paris XII. Service de Gynécologie-Obstétrique et*  
12 *Médecine de la Reproduction. Centre Hospitalier Intercommunal de Créteil. 40 Avenue de*  
13 *Verdun, 94000 Créteil – France*

14 *<sup>2</sup>UMR INSERM U965 : Angiogenèse et Recherche translationnelle. Hôpital Lariboisière, 49*  
15 *bd de la chapelle 75010 Paris.*

16  
**Corresponding author:**

Cyril Touboul, M.D. Ph.D

Service de Gynécologie Obstétrique, Hôpital Intercommunal de Créteil

40 avenue de Verdun, 94000 Créteil, France.

Phone: +33.1. 45. 17. 50. 00

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19 Zeneca, AB Medica, Conmed and TBWA-Adelphi. The remaining authors have nothing to  
20 disclose.

21  
22

23 **Abstract**

24

25 **Introduction:** Patients with Mayer – Rokitansky – Küster – Hauser (MRKH) syndrome  
26 often experience chronic pelvic pain negatively impacting their life’s quality. Our  
27 understanding of the factors involved in this symptom remains poor. The aim of our  
28 study was to further investigate the different components of this pelvic pain in patients  
29 with MRKH undergoing pelvic surgery. Our second objective was to assess the evolution  
30 of this pain in patients undergoing surgical removal of their uterine horn remnant.

31 **Material and Methods:** We conducted a retrospective analysis of a cohort of patients  
32 treated in our tertiary referring gynaecological department. Patients included had a  
33 MRKH syndrome with at least one uterine horn remnant and all underwent at least one  
34 surgical procedure in our centre. Descriptive analysis of the main characteristics and of  
35 the management of these patients was conducted. Postoperative pain was evaluated  
36 using simple words and / or analgesic consumption evaluation.

37 **Results:** Between 1991 and 2013, twenty-one patients were included in our centre. Out  
38 of them, 20 (95%) had chronic pelvic pain, mostly cyclic pain lasting 2 to 3 days.  
39 Fourteen patients had surgical removal of their uterine horns remnant and only 3  
40 patients (21%) had persistent pain at their postoperative visit. Surgical findings  
41 included peritoneal endometriosis in 8 patients (38%) and other unexpected findings in  
42 6. At pathological analysis, secretary endometrium in the uterine horn remnant was  
43 found in 11 patients (79%).

44 **Conclusion:** The origin of chronic pain in MRKH is combining several factors such as  
45 endometriosis or secretary endometrium. Surgical removal of uterine horn remnant  
46 improved most of our patients’ pelvic chronic pain. Further studies should help improve  
47 our understanding of this specific entity.

48 **Keywords:**

49

50 Chronic pain ; Mayer – Rokitansky – Küster – Hauser (MRKH) syndrome ; uterine horn

51 remnant ; surgical management ; uterine malformation.

52 **Introduction**

53

54 Mayer – Rokitansky – Küster – Hauser (MRKH) syndrome is the second most common  
55 cause of primary amenorrhea and occurs in around 1 of 4500 female lives birth [1]. It  
56 results from interrupted embryonic development of the paramesonephronic (müllerian)  
57 ducts and associates both uterus and the upper two-thirds of the vagina aplasia. Two  
58 distinct forms of this syndrome have been described: 1) Type 1 (or simple) with isolated  
59 utero – vaginal aplasia 2) Type 2 (or complex), more frequent, with other malformations  
60 associated, mostly of the urinary tract.

61 The diagnostic is usually performed in patients with primary amenorrhea or following  
62 first sexual intercourse failure [2–4]. Patients with MRKH syndrome often have a  
63 reduced quality of life due to chronic pelvic pain and current understanding of the origin  
64 of this pain remains poor [1]. This pain could result from a secretory endometrium in  
65 the uterine remnant leading to painful hematometra [5,6] but this hypothesis has never  
66 been proved completely. As MRKH is a rare disease, scientific literature is mainly  
67 composed of either case reports or limited – sized cohort always limiting the extent of  
68 the conclusions reached.

69 The aim of our study was to further investigate the different components of this pelvic  
70 pain in patients with MRKH undergoing pelvic surgery. Our second objective was to  
71 assess the evolution of this pain in patients undergoing surgical removal of their uterine  
72 horn remnant.

73

74 **Material and Methods**

75 We conducted a retrospective study within a tertiary referring gynaecologic department  
76 in the Centre Hospitalier Intercommunal de Creteil, in France. Between 1991 and 2013,  
77 all patients treated with an MRKH syndrome and with at least one uterine horn remnant  
78 were included. Patients with total utero – vaginal aplasia (no uterine remnant) were  
79 excluded. Formal written consent of the patients was not required nor asked  
80 considering our study design. The research protocol was approved by the Institutional  
81 Review Board (IRB) of the French College of Obstetrics and Gynaecology (CEROG 2019-  
82 GYN-0301).

83 All the patients included had their diagnostic confirmed by a clinical examination and an  
84 imaging exam, pelvic ultrasonography and / or magnetic resonance imaging (MRI).

85 All relevant data were extracted from their charts, which included general demographic  
86 characteristics, disease history and treatments received, pain description and analgesic  
87 consumption. As some patients were referred from other centres, some have had genital  
88 surgery before and this information was recorded as well.

89 Decision to proceed to surgery was taken in multidisciplinary committee. The first step  
90 of any surgery performed within our centre consisted in pelvic and abdominal  
91 exploration and confirmation of the diagnostic if needed. All additional findings during  
92 this exploratory step were recorded, which included other pelvic lesions, peritoneal  
93 endometriosis or any other specificity. The gestures performed were based on both pre-  
94 surgical and per-operative data, at surgeon discretion. Surgical horn removal decision  
95 was taken in cases its aspect was dilated on pre operative workup and the symptoms  
96 (and especially the pain) were compatible with the pain. All specimen removed were  
97 addressed for pathological analysis. The presence on the uterus remnant of a secretary  
98 endometrium was specified.

99 All patients had a postoperative visit 4 weeks following surgery, which included a  
100 clinical examination. Postoperative pain was evaluated at this time in all patients and  
101 was assessed using simple words (“better” / “worse”) and / or analgesic consumption  
102 evaluation.

103 The database was managed using Excel (Microsoft Corporation, Redmond, WA, USA).

104 Considering the size of the cohort, no comparative statistics were performed as they  
105 would be meaningless. Descriptive statistics were performed using R software ((3.3.1  
106 version, available online).

107

108 **Results**

109 Between 1991 and 2013, 21 patients fitted our inclusion criteria and were included in  
110 our tertiary referring department. The main characteristics of the patients are  
111 presented in table 1. All patients had female phenotype with normal secondary sexual  
112 characteristics. Three patients (14%) had a family history of genital malformation  
113 (bicornuate or septate uterus, but no MRKH syndrome). Four patients (19%) also had  
114 urinary tract malformation and one of them had a polymalformative syndrome.  
115 Before surgery, 20 patients (95%) declared having chronic pelvic pain and in 16 among  
116 them (76%), this pain occurred cyclically every month and lasted 2 or 3 days. Thirteen  
117 patients (62%) had regular analgesic consumption for this pain and one of them even  
118 required opioids on a regular basis. Nine patients (42%) had hormonal therapy for this  
119 indication and pain relief was obtained in 6 of them.

120 Data regarding the surgical findings is presented in table 2. Twenty patients (95%) had  
121 bilateral uterine horn remnants. In 13 patients (62%), per-operative additional findings  
122 were reported, mostly peritoneal endometriosis (8 patients). Fourteen patients (67%)  
123 had surgical removal of uterine horn remnant and 6 patients (29%) had other surgical  
124 gestures. One patient had surgical removal of a subserous myoma developed from the  
125 uterine horn remnant. Another one had a strong desire of pregnancy and have  
126 undergone unification of her two uterine horn remnant as well as an uterine – vaginal  
127 anastomosis. She successfully got pregnant after multiple attempts of in vitro  
128 fertilisation but had uterine rupture at 18 weeks of amenorrhea.

129 Mean length of hospitalization was  $2.3 \pm 1.8$  days (Table 3). One patient (5%) had  
130 postoperative complication: a short - term recurrence of a recto – vaginal fistula after  
131 surgical treatment.

132



133 Pathological analysis retrieved secretory endometrium in 11 patients and confirmed  
134 peritoneal endometriosis in 5 patients. Only 3 patients (21%) had persistent residual  
135 pain following surgery (Table 3).

136

137 **Discussion**

138           Twenty-one patients with MRKH syndrome and uterine horn remnant underwent  
139 surgery in our tertiary referring centre and almost all of them (95%) described chronic  
140 pelvic pain, on a cyclic basis for 2 to 3 days. Only 3 patients (21%) that underwent  
141 surgical removal of uterine horns remnant had residual pain after surgery.

142           This cyclic pain alters those patients quality of life and so far, despite some  
143 hypotheses from small cohorts, no consensus has been reached to explain their origin.  
144 The hypothesis of a secretary endometrium mimicking regular periods is plausible and  
145 if valid, continuous hormonal therapy should improve the pain by preventing  
146 endometrial decidualization. Elliott et al. reported a case of a MRKH patient successfully  
147 improved with low dose monophasic oral contraceptive [5]. However, in our experience,  
148 only 66% of patients felt improved by such treatment. There is two ways to interpret  
149 failure of hormonal therapy in some patients: either a secretary endometrium is not  
150 responsible (alone) for the pain or there is a residual bleeding in atrophic endometrium.  
151 Furthermore, if secretary endometrium was the only factor responsible for cyclic pelvic  
152 pain, patients undergoing surgical removal of uterine horns remnant should fully  
153 recover. This was not the experience we had in our centre with only half patients with  
154 no residual pain following surgery. Those arguments supports the idea secretary  
155 endometrium is not the sole responsible factor for chronic pelvic pain in those patients  
156 but might be part of it.

157           Another factor probably implicated is the presence of peritoneal endometriosis  
158 [5]. Peritoneal endometriosis could provoke cyclic chronic pain by itself and it has been  
159 described in patients with müllerian abnormalities more than 30 years ago [7]. In our  
160 cohort, peritoneal endometriosis was discovered during surgery in 8 patients (38%).  
161 Continuous hormonal therapy should improve those patients too. A more radical

162 treatment is the surgical removal of the uterine horns remnant, easily feasible by  
163 laparoscopy with a low rate of complications [8]. In our cohort, 14 patients had such  
164 surgery and none experienced postoperative complications. Besides, patients with  
165 MRKH are often operated multiple times and postoperative adhesions could partly be  
166 responsible for their pain.

167 Finally, peritoneal irritation following ovulation or organic lesions such as  
168 ovarian cyst and uterine myoma could induce pelvic pain in those patients [7]. Those  
169 findings were not anecdotic in our cohort (29%). In our experience, pelvic MRI had a  
170 higher sensitivity than ultrasonography for the diagnostic of the MRKH syndrome. Some  
171 of those lesions could be diagnosed prior to surgery and this highlights the importance  
172 of a meticulous preoperative workup.

173 It is far more likely all the parameters aforementioned are somehow combined in  
174 pelvic pain. The aim of our study was to further investigate the origins of those patients'  
175 pain and we recognize some limits to our analysis. Firstly, when studying a rare disease,  
176 prospective design is not feasible and some biases are unavoidable. While we report one  
177 of the largest cohorts ever, the number of patients included remains low; all the more  
178 we restricted inclusion to patients with MRKH syndrome and at least one uterine horn  
179 remnant. Our results are strictly descriptive. Since the literature is mainly composed of  
180 case – reports and limited cohorts, a meta – analysis would be of great interest to take  
181 fully advantage of the work of different teams worldwide. Secondly, we were not able to  
182 report long – term evaluation of those patients pain following surgery and our analysis  
183 is limited to postoperative evaluation. This is all the more unfortunate that it would be  
184 of great interest to evaluate pain reduction following surgery over more than one cycle,  
185 and this could bias our results. As a tertiary referring centre for this disease, we often  
186 manage patients from many different centres across France and a long term follow up is

187 delicate. Eventually, pain evaluation was not systematically assessed using a  
188 reproductive validated scale, neither was recorded the analgesic consumption at the  
189 time of the postoperative visit, which limits the precision of the analysis of the surgical  
190 impact.

191

## 192 **Conclusion**

193 We report a cohort of 21 patients with MRKH syndrome and at least one uterine horn  
194 remnant. Only 3 of them (21%) had residual disease following surgical removal of their  
195 uterine horn remnant. Management of those patients in relative high – volume centres is  
196 of paramount importance to keep improving our understanding of their symptoms and  
197 decide the proper management.

198

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**Table 1: Initial characteristics of the patients included**

	<b>N = 21</b>
<b>Age at diagnosis (years)</b>	18.9 ± 4.8
<b>Height (cm)</b>	160.8 ± 4.8
<b>Weight (kg)</b>	55.0 ± 8.1
<b>IMC (kg/M2) (mean (±SD))</b>	21.1 ± 3.4
<b>Family history of genital malformation</b>	3 (14)
<b>Cyclic pelvic pain</b>	20 (95)
<b>Cyclic pain</b>	16 (76)
<b>Regular analgesic use</b>	13 (62)
<b>Hormonal therapy</b>	9 (42)
<b>Sexual intercourses</b>	
<i>Spontaneous</i>	9 (42)
<i>After surgical procedure</i>	6 (29)
<b>Initial assessment of the syndrome</b>	
<i>Pelvic ultrasonography</i>	19 (90)
<i>Pelvic MRI</i>	13 (62)
<b>Urinary malformation associated</b>	4 (19)
<b>Multiple congenital malformation</b>	1 (5)

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Data are given as mean ± standard deviation or n (%)

232 **Table 2: Surgical findings in the patients included**

233

<b>N = 21</b>	
<b>Number of laparoscopies</b>	1.9 ± 0,9
<b>Uterine remnants</b>	
<i>Unilateral uterine horn remnant</i>	1 (5)
<i>Bilateral uterine horn remnant</i>	20 (95)
<i>Maximal size (cm)</i>	4.6 ± 1.4
<b>Additional findings</b>	
<i>Total</i>	13 (62)
<i>Ovarian Cyst</i>	2 (10)
<i>Uterine myoma</i>	4 (19)
<i>Peritoneal endometriosis</i>	8 (38)
<b>Surgery performed</b>	
<i>Removal of uterine horn remnant</i>	14 (67)
<i>Myomectomy, Cystectomy or Peritoneal resection</i>	6 (29)

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235 Data are given as mean ± standard deviation or n (%)

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239 **Table 3: Postoperative data and pathological findings in the patients included**

240

	<b>N = 21</b>
<b>Postoperative data</b>	
<i>No complication</i>	20 (95)
<i>Any complication</i>	1 (5)
<i>Length of hospitalization (days)</i>	2.3 ± 1.8
<b>Pathological findings*</b>	
<i>Secretory endometrium</i>	11 (79)
<i>Endometriosis</i>	5 (29)
<b>Postoperative pain evolution in patients with uterine remnant removal</b>	
<i>No residual pain</i>	7 (50)
<i>None modification</i>	3 (21)
<i>Missing information</i>	4 (29)

241

242 Data are given as mean ± standard deviation or n (%)

243 Pathological report was available for 17 patients

244