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Original Contribution

Clinical and histopathologic characteristics of patients undergoing surgical excision with Essure coils: Longitudinal experience at a women's specialty hospital

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ABSTRACT

The introduction of the Essure (Bayer AG, Leverkusen, Germany) device made possible a less invasive approach for patients desiring sterilization. Following FDA approval in 2002, problems were reported in some patients with these devices including most commonly pain. Labeling changes were mandated in 2016, and as of late 2018, the devices are no longer being sold in the United States. A comprehensive description of Pathologic findings in patients with these devices has not been reported. This study characterizes pathologic findings in patients undergoing surgery who had Essure in place, regardless of the indication for surgery. 137 cases were found, 126 of which had submitted tissue, 121 of which had fallopian tube(s) submitted. Duration for coils being in place was available for 104/137 patients (mean 48 months; median 43 months, range 0–166 months). Cases ranged from 2009 to 19, with a peak in cases noted in 2016. A chief complaint relating to the phrase "pelvic pain" was the most common, noted in 72/137 cases. Obliteration, defined as loss of the fallopian tube epithelium with filling of the lumen with fibrotic material, was noted in 33/121 cases. Inflammation was noted in 59/126 cases, 31/59 showed with giant cells, chronic inflammation (lymphocytes and/or plasma cells) in 37/59 cases, and acute inflammation 19/59 cases, with 14/19 showing eosinophils. Acute inflammation was noted in those with a shorter duration of coil implantation, while chronic inflammation, including giant cells, were noted across the span. This study has expanded knowledge of patients with removal of Essure coil devices.

1. Introduction

The recent introduction of the Essure (Bayer AG, Leverkusen, Germany) device has made possible a less invasive, hysteroscopic approach for patients desiring sterilization [1,2]. The device, which gained FDA approval in 2002 [3], consists of a microinsert containing stainless steel, nitinol, and polyethylene terephthalate (PET) fibers [4]. The device is non-incisional, performed through hysteroscopically guided insertion of the microinsert into the interstitial portion of the fallopian tube [4]. The device is inserted in a wound-down form, and then expands, anchoring the device to the fallopian tube [4]. Consequently, the PET fibers stimulate a response in the fallopian tube which results in fibrous ingrowth causing tubal occlusion [4]. Tubal occlusion is confirmed 12 weeks post placement with a hysterosalpingogram [4]. However, problems have been reported in some patients with these devices, including most commonly: pain, heavier menses/menstrual irregularities, headache, fatigue, and weight fluctuations [3]. Also reported are device issues, including: nickel allergy, and problems related to device insertion [3].

Increasing numbers of patients have presented to treating clinicians for removal of their devices [5]. While limited discussions of the changes in patient tissues have been described [1,5,6], a thorough description of Pathologic findings has not been reported. This retrospective study aims to characterize findings including histologic changes in patients undergoing surgery who had Essure devices in place, regardless of the stated reason for surgery.

2. Materials and methods

The records of the Department of Pathology were searched from 2002 to the present for cases which included the word "Essure". Cases which included Essure coils as part of a resection specimen of any kind for any clinical indication were included in the study. In eligible cases, slides were pulled and examined. In fallopian tube sections with obliteration or suboptimal slide preservation (n = 63), an additional Hematoxylin and Eosin slide level was created. Patient records were

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searched for presenting symptoms, operative findings, and clinical parameters.

3. Results

There were 260 cases total, of which 137 met criteria for inclusion. The remaining cases were from patients in which Essure was mentioned in the clinical history in the context of device insertion or in which non-significant matches were found.

3.1. Clinical findings

The surgeries ranged from years 2009–2019, with a peak in cases noted in 2016. The average age of the patients included was 41-years-old, with a median of 42 (range 28–54). The average gravida was 3. The duration of the coils being in place was available for 104/137 patients, with an average of 48 months and a median of 43 months (range 0–166 months).

In 20 patients, there were abnormal findings related to the coils noted in the operative report. In seven cases, the coil migrated outside uterus, defined as no longer within the uterine cavity or fallopian tube. Of these cases, 2 noted the coil within the omentum, 2 within the bowel/epiploica, 2 outside the ovary or tube, and 1 noted only as "intraabdominal." In 14 cases, at least one coil had migrated within the uterus, but was still within the myometrial wall/fallopian tube. There were 6 cases with the coil embedded within the uterine wall, 4 cases with perforation of the fallopian tube, 2 cases with perforation of the uterine wall, and 1 case with unspecified "perforation." In one case, it was noted that at least one coil was partially expelled from the fallopian tube, and in one case one coil was described as "adherent" to the fallopian tube. The duration of the coils between implantation and surgery for this group of patients was available in 17/20 patients, with an average of 36 months.

A chief complaint in the operative report relating to the phrase "pelvic pain" was the most common, noted in 72/137 cases, with a distribution which followed the overall case distribution (Fig. 1). The duration of the coils between implantation and surgery for this group of patients was available in 48 patients, with an average of 45 months.

In 45 cases, some form of excessive or abnormal uterine bleeding was noted. Urinary incontinence or prolapse was noted in 6 patients. A total of 5 patients were noted to have a potential allergy to the implanted devices within the clinical history. Non-specific autoimmune/systemic symptoms post device implantation were noted in additional 3 patients. Endometriosis was noted in the history of five patients, and fibroid uterus in 10 patients. One patient was noted to be pregnant at the time of device removal. For further details on presenting symptoms, see Table 1.

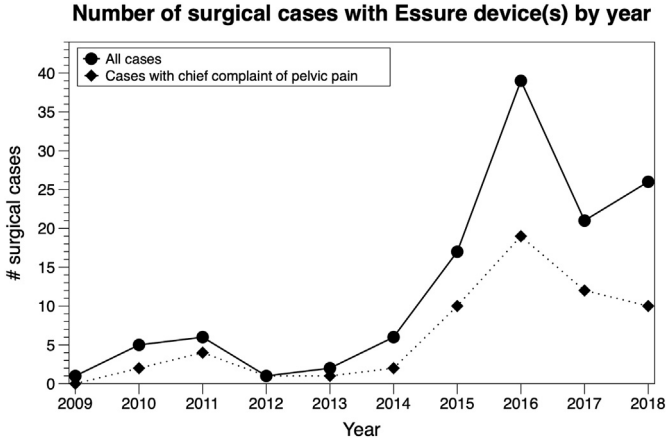

Fig. 1. Cases included over time with Essure coils, both in total and those with "pelvic pain" listed as the chief operative complaint.

Table 1
Chief complaint, as noted per operative report.

Chief complaint, operative report	n
Pelvic pain	72
Excessive/abnormal uterine bleeding	54
Undesired fertility	14
Fibroid uterus/adenomyosis	10
Urinary incontinence/prolapse	6
Endometriosis	5
Potential allergy to device	5
Autoimmune symptoms	3
Dysparaneuria	3
Family history of breast/ovarian cancer	3
Endometrial polyp	2
Ovarian cyst/hydrosalpinx	2
Pregnancy/Fertility treatment	2
Headache	1
Endometrial hyperplasia	1
Cervical dysplasia	1

3.2. Gross findings

Of the 137 cases included in the study, 11 cases consisted of only the Essure coils. The remaining 126 cases had tissue submitted. Five cases had only peri-coil soft tissue submitted. Fallopian tube was submitted in 121 cases. Bilateral salpingectomies without hysterectomy were submitted in 61 cases, 5 of which also had endometrial biopsies, 2 of which had ovarian cystectomies, and 2 of which also had bilateral oophrectomies. Unilateral salpingectomy was performed in 7 patients. A total of 53 patients had hysterectomy with bilateral salpingectomy. Gross photos were taken in selected cases, both in situ in the uterine cornu and after removing from salpingectomy specimens (Fig. 2).

Five sections per fallopian tube were sampled on average, with sampling of the fimbria and non-fimbriated portion in each case. Precise orientation of the non-fimbriated sections was not available, though on some sections surrounding myometrium localized selected sections to the uterine cornu. The coils were grossly noted within the tubal lumen with the exception of the cases noted in Section 3.1. Representative sections were submitted in 118/121 cases. In three cases, the tube was entirely submitted. Two of these patients were undergoing prophylactic bilateral salpingoophrectomy due to a history of breast cancer.

3.3. Microscopic findings

3.3.1. Obliteration

Obliteration, defined as loss of the fallopian tube epithelium with filling or near filling of the lumen with fibrotic material, was noted in 33/121 cases. The obliteration was noted in non-fimbriated sections, and in all of these cases, findings were confirmed on examined levels. In some cases, the obliteration was accompanied by foreign material, with focal adjacent tissue reaction. In 1/5 patients with a noted history of potential allergy, obliteration was present. In 1/3 patients with autoimmune symptoms, obliteration was present. In the patients who presented with a clinical symptom of pelvic pain who had Fallopian Tubes submitted, (n = 65), 16 showed obliteration.

3.3.2. Glandular proliferation

In 9/121 cases, a proliferation of glands was noted in a concentric pattern around the fallopian tube lumen, occasionally accompanied by endometrial stroma, reminiscent of salpingitis isthmica nodosa with features of endometriosis. In 2/9 of these cases, the changes were seen proximal to a tubal lumen which was occluded. In the remaining cases, dilatation of the fallopian tube lumen was noted. The changes were all noted in non-fimbriated sections which could not be more precisely

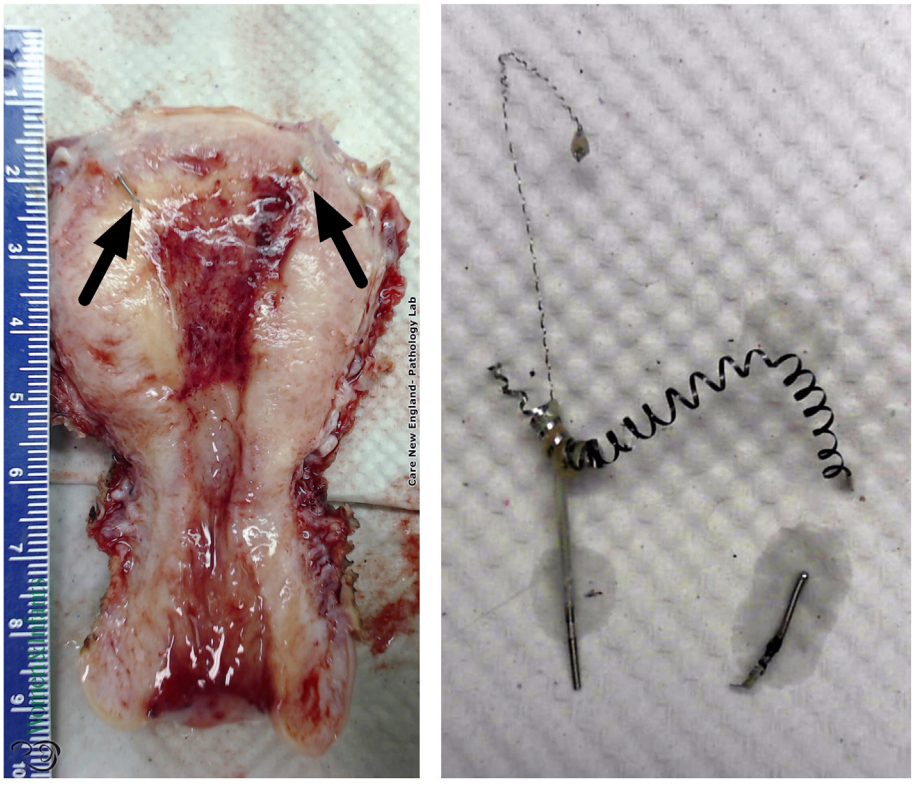

Fig. 2. Photos taken at the time of gross examination. A. Uterine specimen with clips located in situ, seen here protruding from cornu (arrows), and (B) a coil after removing from a salpingectomy specimen, which is pictured in fragmented form, including the component parts (small silver tube shaped fragment at lower right corner) from the contralateral tube. Note: images A and B not to scale, no concurrent scale available for (B).

oriented.

3.3.3. Inflammation

Inflammation was noted in 59 of the 126 cases with tissue submitted. Of these, 31/59 showed at least some component of giant cells. Chronic inflammation, in the form of lymphocytes and plasma cells, were noted in 37/59 cases. Acute inflammation was noted in 19/59 cases, with 14/19 showing at least focal eosinophils. None of the cases with eosinophils had a noted history of allergies or autoimmune findings in the clinical history. An overall trend was noted, favoring relatively shorter range for duration of implantation for cases with acute inflammation, versus a longer range for those with chronic inflammation (Fig. 3). Foreign, polarizable material was noted in 29 cases within the fallopian tube sections. Selected microscopic findings are presented in Fig. 4.

Paratubal adhesions were noted in 6 patients. Paratubal cysts were noted in 41 patients. In the five cases with only soft tissue from the removed coil submitted, 4/5 showed inflammation, with 3/5 cases showing chronic inflammation consisting of lymphocytes, and 3/5 showing giant cells.

Other pathologic findings in the concurrent, non-fallopian tube specimens include adhesions in seventeen patients. In 16/17, adhesions were noted on the uterine serosa, in 2/17 on the ovarian surface, and in 1/17 in an additionally submitted epiploica. In the 53 patients with hysterectomy specimens, uterine adenomyosis was noted in 24, endosalpingiosis of the uterine serosa in 2, uterine leiomyoma in 20, endometrial polyp in 4, and a myometrial adenomatoid tumor in 1.

Of the five patients with a history of potential allergy, one patient showed giant cell inflammation and obliteration of tubal lumen. One patient had only the coils submitted for examination. The remaining patients showed no other abnormal findings. In the three patients with autoimmune symptoms, one showed mild tubal lymphocytic inflammation and adhesions of the uterine serosa. Another showed giant cell inflammation and obliteration of the tubes. The remaining patient showed no abnormal findings. In the patients who presented with a clinical symptom of pelvic pain who had tissue submitted, (n = 71), 30 had inflammation in associated tubal specimens, the most common being chronic inflammation (18), with giant cells noted in 15, and acute inflammation noted in 5, and eosinophils in 3.

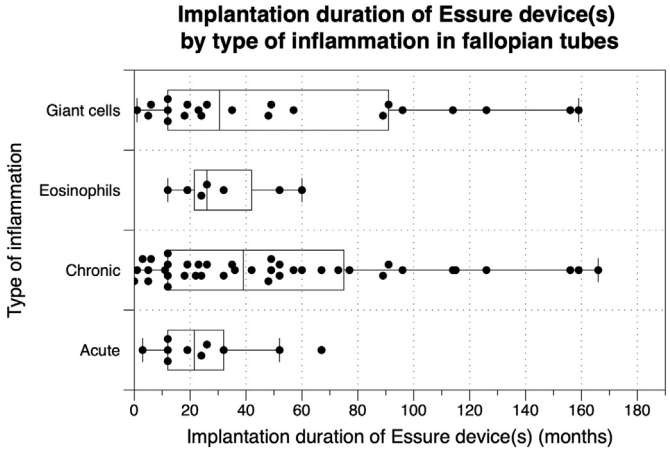

Fig. 3. Data distribution for inflammation type noted in fallopian tube by duration of implantation of the Essure device by months. Categories of inflammation are giant cells, eosinophils, chronic (plasma cells and lymphocytes), and acute (neutrophils). The vertical line in the middle of each box indicates the median, the left and right edges of the box mark the 25th and 75th percentiles, the whiskers to the left and right of the box represent the 10th and 90th percentiles, and the point beyond the whisker is an outlier beyond the 90th percentiles.

4. Discussion

The aim of this retrospective study was to further characterize histologic findings in patients who had surgery which resulted in excised specimens containing Essure coils at a specialized Women's hospital.

Prior descriptions of histologic changes in this setting are somewhat limited. The largest study, performed on patients in the Netherlands

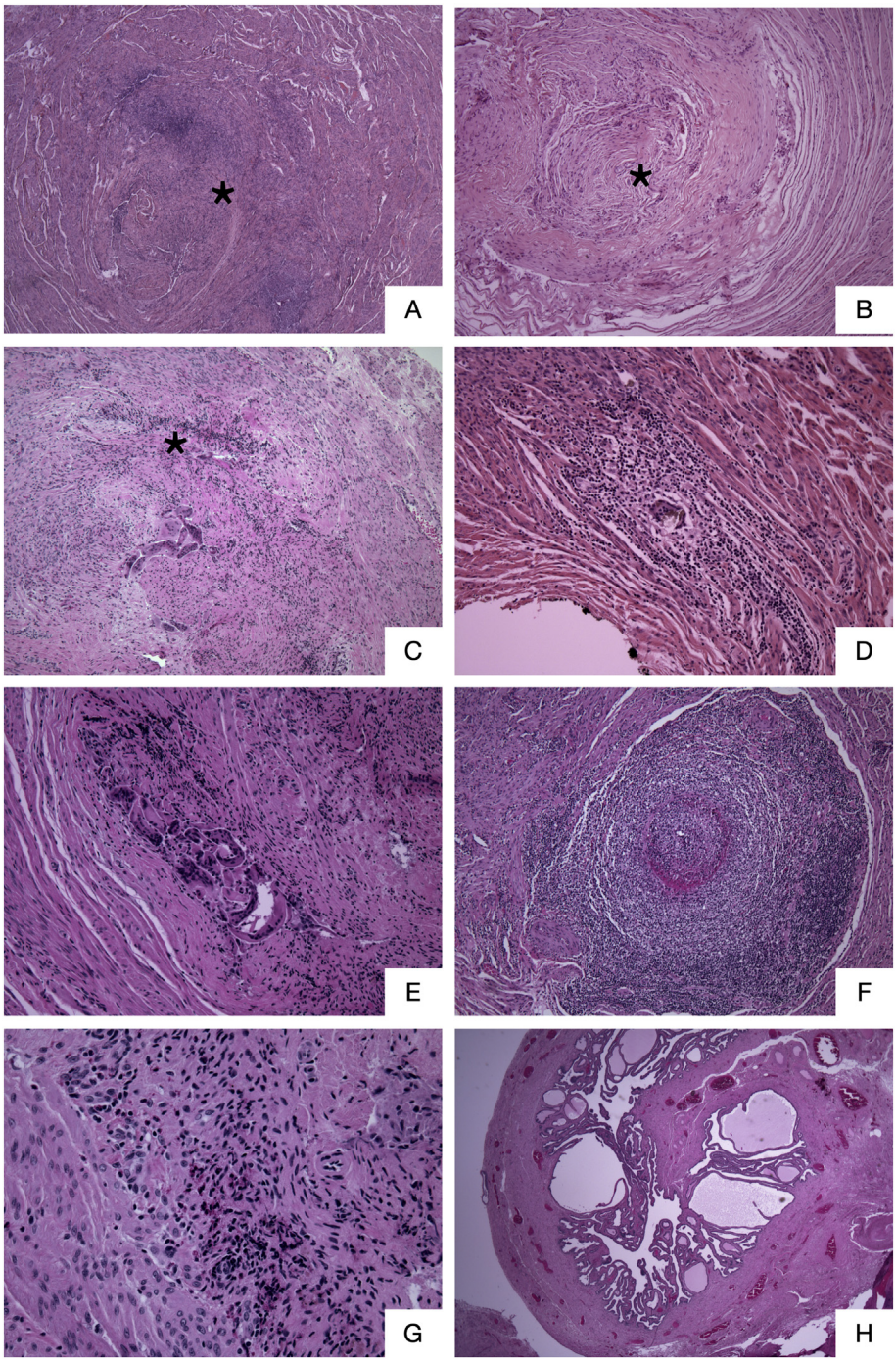

Fig. 4. Obliteration of the tube, shown at 20× (A) and 40× (B), characterized by loss of the tubal lumen (designated with *) with fibrous ingrowth of bland, spindled cells. In selected cases (C), obliteration of the tubal lumen (*) was accompanied by foreign-body type giant cells (40×). In some cases (D), foreign, polarizable material was noted within the giant cells, while in others (E), they were arranged adjacent to the obliterated tubal lumen (both 100×). Chronic inflammation of lymphocytes and plasma cells was marked in some cases (F, 40×), while in others (G), eosinophilic inflammation was prominent (200×). Changes reminiscent of salpingitis isthmica nodosa (H) were noted in selected cases (20×).

who presented to their providers for removal of their Essure devices, has a limited description of histologic changes in 93 patients [5]. Normal findings are reported in majority of cases, with abnormal findings described generally as “chronic inflammatory infiltrate” and “reactive tissue changes” in 13 and 6 patients, respectively [5]. In an early study, Valle et al., described devices which were implanted into 33 women (47 fallopian tubes) who required a hysterectomy for unrelated reasons in order to assess efficacy of the devices and tissue responses [6]. The devices were worn for 1 to 30 weeks, and the entire fallopian tubes were subsequently examined histologically. The authors report a fibrotic response consistent with occlusion in a majority of patient specimens (39/47), defined as at least 80% occlusion histologically [6]. This rate of noted tubal occlusion is higher than the current study. However, the tubes were much more extensively sectioned for the express purpose of confirming tissue changes. The current retrospective study is limited, and it is likely that if the entire tubes had been examined, the occlusion rate would have been higher. Additionally, a trend toward acute inflammation in patients with shorter device duration and chronic inflammation in patients with longer duration was reported, which was replicated in this study (Fig. 3).

Eosinophils have been reported in a variety of clinical scenarios involving the uterus, including post-instrumentation [7,8], within and surrounding squamous cell carcinoma of the cervix [9], within uterine leiomyoma [10], and in association with parasitic infection [11]. Specific findings related implanted devices and a resulting infiltrate with eosinophils have not been characterized. It is possible that in some patients the eosinophils were a result of a response to the Essure device. None of the patients with eosinophils had a reported history of allergy

to the device or autoimmune-like symptoms. Further study is warranted to clarify this issue.

Polyethylene terephthalate (PET) fibers were chosen for the device, as they are known to cause tissue ingrowth of medical devices [4]. The accompanying inflammatory infiltrate caused by the fibers has been described as a mix of macrophages, foreign-body giant cells, and plasma cells [6], and has been characterized as peaking at 2–3 weeks post-implantation, with resolution by 10 weeks [12]. Though the mix of inflammatory infiltrate is similar in the current study, the duration of inflammation in this study ranged to 156 months for foreign-body type giants cells, and 166 months for lymphocytic inflammation, which exceeds this characterized limit.

Clinical parameters in this patient population must be approached with caution, as this cohort is not representative of the general population, those with Essure coil devices, nor is there a control population available for comparison. Nonetheless, in a population of patients who presented for removal of their devices for assorted symptoms [5], similar common symptoms of pain and increased or abnormal uterine bleeding were noted. However, this was conducted by clinicians with access to patients with the specific aim of symptom characterization, which was outside the scope of the current study. Of note, the duration of coil implantation for these two studies are similar, 0–125 months [5], compared to 0–166 (current study). Though the current study cannot be faithfully extrapolated to reflect the general public, the overall pattern of complaints with the device registered with the FDA are similar to those noted in patients in this study [Table 1] [3]. Of note, an increase in patients presenting with self-reported pelvic pain was noted in the same time period of 2015–2016 [Fig. 1] in which the FDA lodged a citizen petition and subsequently issued labeling changes to the device [3].

The study is limited by the availability and depth of clinical information and follow-up. Available records were consulted when possible. However, pertinent information such as the number of patients who underwent the mandatory confirmatory hysteroscopic salipingogram (HSG) were unavailable. As patients continue to present for removal of these devices in the setting of increased awareness, additional investigation by clinical teams will expand the findings in their appropriate context.

Seeing as Pathologists in routine practice continue to encounter these specimens, this study will prove useful due to expansion of knowledge of tissue findings in patients with Essure coil devices.

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Declaration of competing interest

The author declares no conflict of interest.

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