

**Original contribution**

Postablation neuroma of the myometrium— a report of 5 cases^{☆☆}



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Summary When hysterectomy is performed for chronic pelvic pain, routine pathology examination often provides no explanation. However, analysis of small uterine nerves using immunostains may help to address this deficiency. Small uterine nerves tend to be sparse or absent in wide areas of normal myometrium. Some studies of uterine nerves have suggested that endometriosis, adenomyosis, and fibroids are not inherently painful, with increased small nerves in the inner uterine wall associated with the history of pelvic pain. Although such areas may appear normal on hematoxylin and eosin (H&E), we have found a subtle inner wall lesion termed inner myometrial elastosis, best detected with trichrome or elastic stains, which may be a reaction to microscopic tears of inner myometrium. Such tears may induce increased inner wall innervation via the generation of nerve growth factor in granulation tissue. In the course of studying uterine nerves with immunostains, we found 5 cases with florid nerve proliferation, after deep endometrial ablation for abnormal uterine bleeding led to increased pelvic pain. We suggest that immunostains for postablation neuromas should be done in hysterectomies when pelvic pain increases after endometrial ablation. This may offer gynecologists and their patients an objective finding with a rational, scientific explanation for the pelvic pain.

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1. Introduction

Chronic pelvic pain is common, and may lead to hysterectomy. Reasons for chronic pelvic pain include endometriosis, adenomyosis, fibroids, pelvic adhesions, pelvic inflammatory disease, ovarian cysts, and polycystic ovaries, but oftentimes an explanation is lacking [1–4]. Recent studies have suggested

that an increase in innervation of the inner myometrium and endometrium may play a role in the pathogenesis of chronic pelvic pain [2,3,5]. This led us to evaluate our own experience, and to consider whether pathologists should routinely evaluate for uterine nerves in hysterectomies for pelvic pain.

In 2005, Atwal et al demonstrated an increased number of nerve fibers in the inner wall in women with advanced endometriosis [2]. They also found increased nerve fibers in women with chronic pelvic pain but without endometriosis. Since their control group was uteri removed for painless conditions, this suggested that the endometriosis itself was not the cause of pain. In 2010, Zhang et al found increased nerves in the endometrium and inner myometrium in women with painful adenomyosis and painful fibroids [3]. Again, the increased nerves were not in the lesions themselves, but in adjacent tissues.

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Large areas of normal myometrium can lack demonstrable nerve fibers [5]. Normal uterine nerves in nulliparous women are mainly in three distributions: the subserosa, in sparse neurovascular bundles coursing through the myometrium, and at the endomyometrial junction [5]. Based on prior literature [2,3,5] and our personal experience, we classify 5 or more nerve fibers/field at 200 $\times$ magnification as abnormally increased (Fig. 1A).

It has been reported that 30% of multiparous uteri had foci of abnormal clusters of small nerves, called microneuromas, whose clinical significance is not established [5]. Microneuromatous clusters may have 10 or more nerve fibers. In our experience (unpublished), microneuromas are associated with naturally occurring outer wall scars (fibrosis uteri) (Fig. 1B and C). Fibrosis uteri generally has a component of elastosis, and it was a matter of common knowledge 40 years ago that this was a marker for parity; but many recent texts have failed to cite the references to naturally occurring myometrial scars that date back more than a century [6,7].

Since starting to evaluate hysterectomies for pain with immunostains for nerves, we encountered 5 cases in a single year with a striking pattern of uncountable small nerve proliferation (dozens or hundreds) in the myometrium. All 5 had previously undergone ablation for abnormal uterine bleeding; and all 5 ablations had gone quite deep, focally ablating the inner third of the uterine wall (Fig. 2). The purpose of this article is to describe 5 cases of postablation neuromas as the likely cause of pelvic pain, leading to hysterectomy.

2. Case reports

2.1. Case

A 47-year-old woman had an endometrial ablation in 2007. She also had progressively worsening chronic pelvic pain since

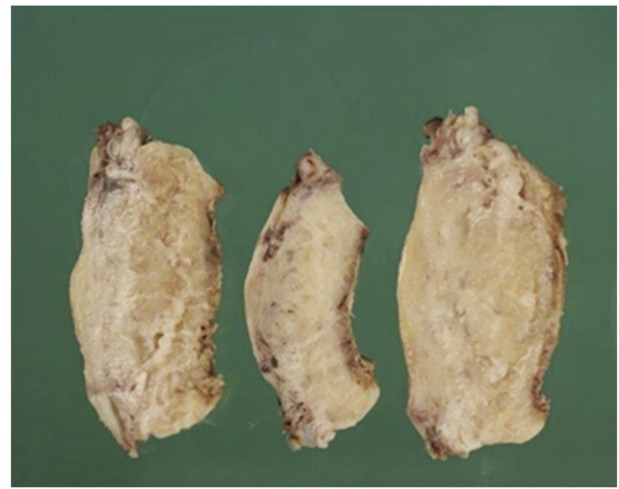


Fig. 2 These 3 slices are all from the same uterus. Deep ablation has focally destroyed the inner third of the uterine wall in the middle (thin) slice. Intact inner third is seen on the right side of the slice on the left (from the anterior wall), and the slice on the right (from the posterior wall). Note the outward bulge of the middle slice with the deep ablation, which is relatively pale due to postablation scar.

2004, which increased after the ablation, leading to a hysterectomy in 2012. The 40-g uterus was symmetrical with a 1.4 cm myometrium with no gross lesions or masses. Microscopically, there was no residual endometrium (Fig. 3A). Large vessels, markers for the junction of middle and outer third of the wall, were seen close to the surface scar; indicating that this had been a deep ablation. She had myometrial hyperplasia (MMH) [8,9], a large postablation scar with marked globular elastosis [10], and separate foci of inner myometrial elastosis (Fig. 3B and C) as described previously in hysterectomies for pelvic pain [11]. S100 immunostains showed innumerable small nerve fibers in the scar tissue on the surface (Fig. 3D), far exceeding what is seen in “microneuromas,” and consistent with postablation neuroma.

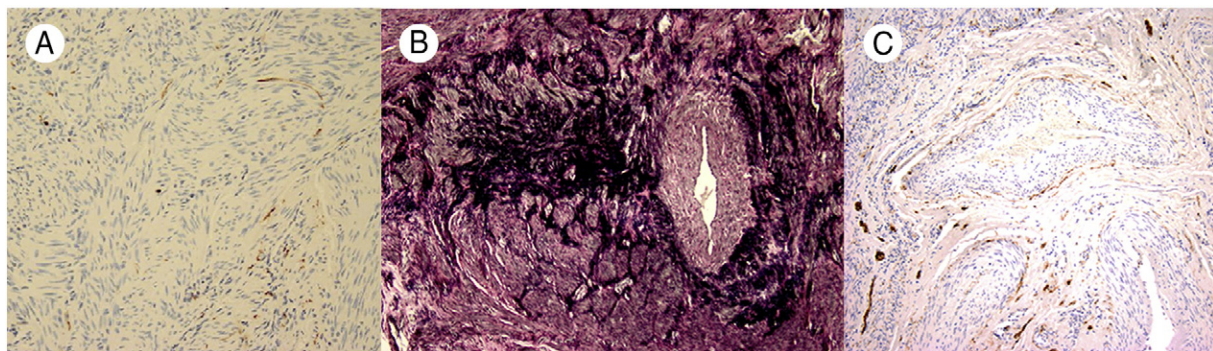


Fig. 1 A, S100 stain shows increased nerves in inner myometrium, in a routine hysterectomy for otherwise unexplained pelvic pain $\times 200$. About a dozen small nerves were seen in this field. They comprise only a tiny fraction of the field, the rest of which serves as an internal negative control; reflecting that large areas of myometrium are routinely completely negative for small nerves, both in our experience and as reported in the literature [5]. B, Elastic van Gieson stain of outer wall scar (fibrosis uteri [6]) shows marked globular elastosis (black). The upper left corner and lower left corner are negative for elastic fibers, serving as an internal negative control. Both in the literature, and in our experience, uterine elastic fibers are generally too small to be seen on EVG stains, even when they can be seen on electron microscopy [26]. C, S100 stain of microneuroma associated with outer wall scar.

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