A 53-year-old, gravida 2, para 2, perimenopausal, white woman presented to her gynecologist with persistent, worsening urinary incontinence and pelvic pain. History of abnormal vaginal bleeding was unknown. On physical examination, it was noted that she had a grade I cystocele, grade II rectocele, and an enlarged, irregular uterus, approximately 16-week size. Pelvic ultrasound showed the uterus to be displaced by an 11 × 12 × 12-cm complex mass that resembled a fibroid. She underwent exploratory laparotomy and elective total abdominal hysterectomy and bilateral salpingo-oophorectomy.

On gross examination, the uterus weighed 910 g and was distorted and displaced to one side by a 10.5 × 10 × 10-cm, variegated, rubbery mass. The cut surface of the mass showed multiple varying-sized, white-yellow, whorled areas with scattered, interspersed areas of hemorrhage and cystic degeneration at the periphery. Histologic examination confirmed the mass to be a leiomyoma with mucinous degeneration and areas of necrosis. No increase in mitoses was seen.

More interestingly, within the endometrial cavity of the distorted uterus, a well-circumscribed, 3 × 2 × 1.5-cm polypoid mass was noted on gross examination (Figure 1, arrow). This polypoid mass had a gray-white solid cut surface and appeared to be confined to the endometrium. On histologic examination, the mass was composed of numerous closely spaced glands lined by slightly atypical cells infiltrating among the fibromuscular stroma (Figure 2). Extensive squamous metaplasia was seen within many of the glands, and in several areas there was central necrosis of the metaplastic epithelium (Figure 3). Mitoses were found within the glands. In some areas the glands were back to back, whereas in other areas smooth muscle was present among the glands (Figure 4). The lesion did not invade the myometrium, and there was an abrupt transition between the lesion and the underlying myometrium.

What is your diagnosis?
Pathologic Diagnosis: Atypical Polypoid Adenomyoma of the Endometrium

The term atypical polypoid adenomyoma (APA) was first adopted by Mazur in 1981 when he reported 5 cases of unusual endometrial polypoid lesions occurring in premenopausal women. The histologic pattern of irregular atypical glands with squamous metaplasia and a smooth muscle stroma mimicked infiltrating adenocarcinoma, but the polyps had a benign clinical behavior.

Atypical polypoid adenomyoma is an uncommon endometrial tumor that typically occurs in women of reproductive age. Average age of occurrence is 39 years, but ages have ranged from 21 to 73 years. Rarely, affected patients are postmenopausal. Of the nearly 100 cases reported to date, APA has been found in only 6 postmenopausal women. In addition, APA has been seen in at least 3 patients with Turner syndrome, possibly representing a complication of long-term estrogen therapy in these patients.

Most patients present with abnormal uterine bleeding. Less frequently, vaginal discharge, pelvic pain, or postcoital spotting may be seen. An associated clinical history of infertility is not uncommon. Pelvic examination is usually unremarkable, unless the patient has a concomitant pathologic condition, such as leiomyomata. Rarely, the lesion may be seen extruding from the endocervical canal. Most lesions are detected on endometrial biopsy specimens or dilation and curettage specimens obtained for workup of the abnormal bleeding. However, APAs have been discovered incidentally during routine hysteroscopy and biopsy for infertility or, as in our patient, when the uterus is removed for other reasons, such as leiomyomata.

Grossly, APA resembles an endometrial polyp, presenting as a single, well-circumscribed, polypoid mass. It frequently occurs in the lower uterine segment and may be either sessile or pedunculated. Also, APA has been reported to involve the uterine fundus and endocervical canal. Typically, the mass averages 2.0 cm, but reported maximum dimensions have ranged from 0.1 to 6 cm. The cut surface of the tumor is often gray-tan, lobulated or bosselated, and firm to rubbery. Grossly, most lesions remain confined to the endometrium and have a pushing margin.

Microscopically, APA is a biphasic tumor, consisting of atypical endometrial glands separated by intersecting fascicles of smooth muscle and fibrous stroma. The endometrial glands may vary from simply branched, widely spaced glands to closely packed, markedly complex, branching glands. Architecturally complex glands with back-to-back pattern are typically not seen, but when present the architectural complexity may be indistinguishable from well-differentiated endometrial adenocarcinoma. The glands are lined by cuboidal to low columnar to pseudostratified columnar epithelium with varying degrees of cytologic atypia and mitoses.

The stromal component, however, typically appears benign and predominantly consists of interlacing bundles of smooth muscle. The stroma of APA differs from normal myometrium by exhibiting increased cellularity, short interlacing fascicles rather than elongated muscle bundles, and a minor component of fibrous tissue. In nearly all of the cases reported by Longacre et al, trichrome stain confirmed an admixture of spindled smooth muscle cells and collagen, reflecting their preference for the term atypical polypoid adenomyofibroma. Occasionally, mild-to-moderate nuclear atypia is seen, but mitoses are rare and do not exceed 2 per 10 high-power fields. Both immunohistochemical and electron microscopy studies have confirmed the smooth muscle differentiation of the stromal cells.

Squamous metaplasia is found in more than 90% of the cases and is often extensive. Thereby, it can be a useful marker for this lesion. Centrally within the larger foci of squamous metaplasia, necrosis may be seen. However, cytologic atypia of the squamous epithelium is unusual. The uninvolved endometrium is typically benign, most often with a normal proliferative pattern. Rarely, the adjacent endometrium may be secretory or hyperplastic. Adenomyosis but more commonly one or more leiomyomata may also be present in the uteri removed for APA.

Most APAs do not invade the myometrium, and on microscopic examination, a well-defined pushing margin with the adjacent endometrium, myometrium, or both is seen in most cases. Despite the atypical glandular features of APA, the lesion does not display aggressive behavior. No APA has been reported to spread beyond the uterus. Also, Ki-67 immunohistochemical studies have shown the proliferative activity of the glands in APA to be fairly low when compared with glands of usual endometrial adenocarcinoma.

Focally, the lesion may show a cribriform glandular pattern and severe cytologic atypia, raising the possibility of associated endometrial adenocarcinoma. Longacre et al have proposed that if the APA contains markedly complex glands indistinguishable from carcinoma and these constitute 30% or more of the polypoid glandular proliferation (ie, high architectural index), the lesion should be designated as APA of low malignant potential. Superficial myometrial invasion was seen in 2 of their cases, and both had high architectural indexes. Also, in their series, the incidence of recurrence or persistence after local excision was higher in the lesions with high architectural indexes compared with those with lower architectural complexity.

In rare cases, the APAs are contiguous with or appear to be the site of origin for well-differentiated adenocarcinoma. In only 5 cases to date has invasive endometrial adenocarcinoma most likely arisen from APA. More interestingly, 4 of these 5 cases have been in postmenopausal women.

The most important differential diagnosis is adenocarcinoma invading the myometrium. Although APA architecturally may resemble endometrial adenocarcinoma, it lacks stromal desmoplasia. Also, adenocarcinoma, in general, occurs in older women and may grossly demonstrate invasive margins, large size, and areas of hemorrhage and necrosis. In endometrial carcinoma, the glands are overtly malignant with more marked atypia and frequent cribriform pattern.

Other tumors in the differential diagnosis of APA include the related mixed Mullerian neoplasms, in particular, adenofibroma, adenosarcoma, and malignant mixed Mullerian tumor (MMMT). The young age of the patient with APA, typically 35 to 45 years, should be a clue. Adenofibroma, adenosarcoma, and MMMT all typically occur in postmenopausal women. The uncommon adenofibroma differs from APA in that its stromal component lacks smooth muscle and it typically has large papillary epithelial fronds with cystic glands. The small, solid, well-
circumscribed polypoid gross appearance of APA also differs from the large exophytic masses seen in most adenomas and MMMTs. Additional features favoring adenosarcoma would be a more atypical stromal component lacking smooth muscle, cuffed periglandular stromal condensation, and glands that are predominantly cystic and less atypical than those of APA. In MMMTs, both the glandular and stromal components show frankly malignant features. Increased mitoses and diffuse nuclear atypia of the stroma is absent in APA, but virtually always present in MMMTs.1,2

Treatment may vary depending on the patient’s age, her desire to preserve fertility, and the severity of her symptoms. Since many APAs have an indolent behavior and are seen in young, nulliparous women during workup for infertility, conservative polypectomy and curettage with close follow-up are appropriate and may be curative. In the cases reported by Longacre et al,3 persistent or recurrent lesions were seen in 13 of 29 patients managed with polypectomy or complete curettage, but in no case where a subsequent hysterectomy was performed was there evidence of infiltration into the myometrium. Also, 5 patients with persistent or recurrent APAs subsequently became pregnant and delivered healthy, full-term infants. Because of the severe degree of glandular atypia in some cases of APA, rare association of endometrial adenocarcinoma, and the potential for recurrence after local excision, simple hysterectomy may be preferred in perimenopausal or postmenopausal women for complete removal of the lesion.

References