Specific Symptoms Flag Endometriosis Diagnosis

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — The constellation of symptoms characterizing endometriosis may be more specific than currently thought, Karen D. Ballard, Ph.D., said at the annual meeting of the AAGL.

There is often a long delay in the diagnosis of endometriosis, in large part because the symptoms—primarily pelvic pain and dysmenorrhea—are nonspecific and can overlap with other conditions. But now, a case-control study from a primary care database in the United Kingdom suggests that women with a combination of gynecologic, urologic, and bowel symptoms are likely to have the condition.

"Specific, unremitting symptoms should raise a high suspicion of endometriosis," said Dr. Ballard of the University of Surrey, Guildford, England.

Data were collected from the General Practice Research Database, the largest computerized database in the world containing longitudinal medical records from primary care. It currently comprises more than 3 million active patients from about 450 primary care practices, the setting in which all nonemergency patients in the United Kingdom are first seen.

During 1992-2002, 5,540 cases of endometriosis were identified from a total of 1,276,100 women aged 15-55 years. The average age at diagnosis was 35 years. The incidence of diagnosed endometriosis was 0.97 per 1,000 women-years, and the prevalence—calculated from the incidence rate and the average disease duration—was 1.5%. This proportion is lower than what has been reported in the literature, probably because it comes from general medical practice rather than a gynecology-based setting, Dr. Ballard noted.

There were 21,239 matched controls. The women with endometriosis were significantly thinner, with 49.3% having a body mass index less than 25 kg/m^2, compared with 42.1% of the controls. They were also 20% less likely than were the controls to have had a previous pregnancy.

As expected, the women with endometriosis had high rates of pelvic pain (15.6%) and dysmenorrhea (24.6%). But somewhat surprising was how low those rates were in the controls—1.5% and 3.4%, respectively—suggesting that "these symptoms are actually more specific than previously acknowledged," Dr. Ballard said.

Other menstrual/pain symptoms reported significantly more often by the endometriosis patients than the controls were dyspareunia (9% vs. 1%, respectively), abdominal pain (45% vs. 13%), menorrhagia (23% vs. 6%) and menstrual problems (27% vs. 13%).

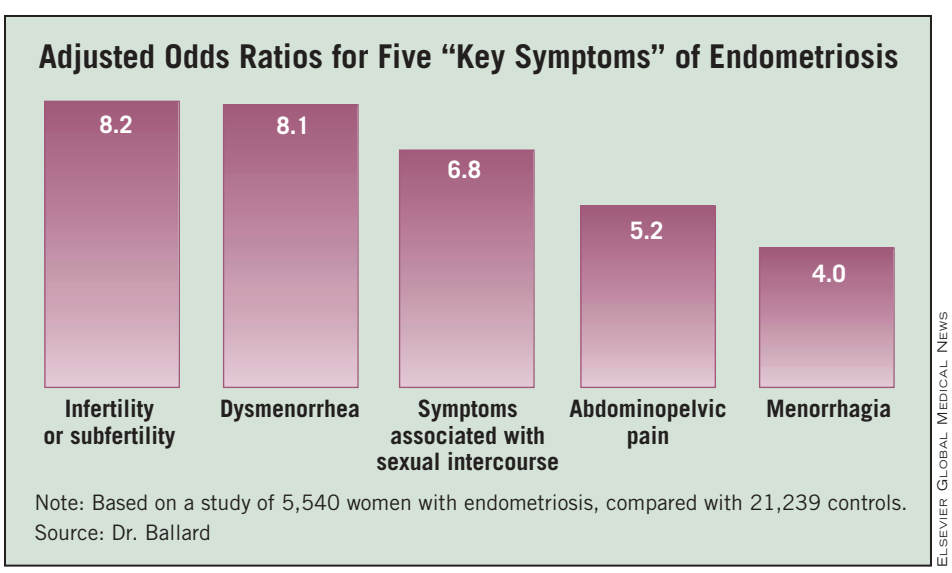
Gastrointestinal symptoms were also more common in the endometriosis group than in the control group, including constipation (9.2% vs. 4.4%) and rectal bleeding (2.0% vs. 1.1%), as were the urologic symptoms cystitis (8.8% vs. 5.3%) and dysuria (6.1% vs. 2.7%). Postcoital bleeding was reported by 2.9% vs. 0.7% and backache by 16.4% vs. 11.0%. All of these differences were statistically significant.

Women with endometriosis were also significantly more likely than were controls to have been diagnosed with subfertility (9.6% vs. 1.8%). But less expected was an association with the diagnosis of irritable bowel syndrome: 10.6% vs. 3.3%. Other diagnoses reported significantly more often among the women with endometriosis were urinary tract infection (18.5% vs. 9.8%), pelvic inflammatory disease (10.3% vs. 1.8%), and ovarian cysts (6.8% vs. 0.6%).

Stepwise regression analysis showed that the five "key symptoms" most strongly associated with endometriosis were infertility or subfertility (adjusted odds ratio 8.2), dysmenorrhea (8.1), symptoms associated with sexual intercourse (6.8), abdominopelvic pain (5.2), and menorrhagia (4.0).

In all, 84% of those with endometriosis had at least one of those symptoms, compared with 23% of those without, Dr. Ballard said.

The data also suggest there is opportunity for intervention: Nearly all (98%) of the women who were ultimately diagnosed with endometriosis had made at least one visit to a physician in the year before the diagnosis, compared with 81% of the controls. In fact, 62% had visited the physician at least six times in that year, compared with 27% of those not diagnosed with endometriosis, she reported. ■



Diagnose and Treat Interstitial Cystitis, Painful Bladder Early

BY NANCY WALSH
New York Bureau

MINNEAPOLIS — Early recognition of interstitial cystitis/painful bladder syndrome by the primary care physician can prevent this common and debilitating condition from becoming refractory, Dr. Robert Moldwin said at the annual meeting of the Association of Reproductive Health Professionals.

This is an invisible condition, and there often is a lag time of 5-7 years between symptom onset and diagnosis, with patients being given multiple diagnoses, improper treatments such as antibiotics, and referrals to psychiatrists, he said.

IC/PBS is an invisible condition, often with a delay of 5-7 years from onset of symptoms to diagnosis. It's key to identify it early, while symptoms are intermittent.

The hallmarks of interstitial cystitis/painful bladder syndrome (IC/PBS) are pelvic pain, pressure, or discomfort, typically associated with a persistent urge to void or urinary frequency. Frequent nocturnal voiding is typical, and symptoms do not relate to infection or other pathology.

Although the precise etiology of IC/PBS remains unknown, it is now considered to be a hypersensitivity condition of the bladder wall, and increased understanding of the changes seen in the bladder urothelium are beginning to permit targeted therapies, explained Dr. Moldwin of the urology department at Albert Einstein College of Medicine, New York, and director of the Pelvic Pain Center at Long Island Jewish Medical Center, New Hyde Park, N.Y.

The normal bladder surface is coated with impermeable mucin; in patients with IC/PBS this layer is disrupted, permitting noxious substances such as potassium in urine access to nerves and muscles in the bladder. This sets off an inflammatory response with mast cell activation and the release of histamine, substance P, and other mediators, which results in neurogenic upregulation and a pain response.

In early stages of IC/PBS the symptoms tend to be intermittent, but with increasing duration the pain can become centralized and once that happens, even if the bladder is removed, the pain may remain. This is similar to phantom limb pain, Dr. Moldwin said. "The key is identifying these patients when they still have intermittent symptoms."

The differential diagnosis includes overactive bladder, endometriosis, and bladder cancer. IC/PBS can be differentiated from overactive bladder by the pattern of urinary urge, with overactive bladder characterized by sudden sporadic urges, whereas IC/PBS is characterized by a steadily and sometimes exponentially increasing sense of discomfort that eases with voiding, he said.

"Of course you don't want to miss bladder cancer, but a 30-year-old nonsmoker is unlikely to have bladder cancer. If there's any hematuria or you are especially concerned you can send off a urine specimen for cytology," he said.

Otherwise, the diagnosis is empiric, and diagnostic tests such as hydrodistention under anesthesia are not routinely done. In a patient for whom infection has been ruled out, and particularly with pronounced nocturia, it's reasonable to begin empiric therapy, Dr. Moldwin said.

Management encompasses both nonpharmacologic and pharmacologic strategies. Dietary changes often help, and many patients benefit from avoidance of carbonated and caffeinated beverages, alcohol, and citrus fruits. Behavior modification, with gentle exercise, stress reduction, and muscle relaxation, also can help, he added. "I'm a big believer in having patients become empowered, taking control of their own care."

Oral medications used for IC/PBS include pentosan polysulfate sodium, amitriptyline, and hydroxyzine. Pentosan polysulfate, the only Food and Drug Administration–approved oral medication for this condition in doses of 100 mg three times per day, coats the bladder wall and decreases sensitivity. The drug can take several months to work, and is effective in up to 60% of patients.

The tricyclic antidepressant amitriptyline is useful in helping patients troubled with nocturia sleep at night, and it also has pain reduction properties, probably through inhibition of norepinephrine reuptake in the central and peripheral nervous systems, he said. Amitriptyline can be given in low doses of 10-50 mg per day, preferably at 7 p.m. to avoid a morning hangover effect, he said.

The H_1 histamine antagonist hydroxyzine inhibits the mast cell degranulation and histamine release characteristic of the hypersensitive inflammatory response in the bladder wall. The drug is usually given at night, beginning in doses of 25 mg, but response can take a couple of months.

Intravesical agents that are used include dimethylsulfoxide, which is FDA-approved, and unapproved agents such as lidocaine and heparin.

Increased recognition of the importance of IC/PBS, which afflicts 1.2 million women and 82,000 men in the United States, along with an improved understanding of the associated pathologic events, is allowing the development of many new treatments, including antiproliferative factor, liposomes, and intravesical botulinum toxin type A.

Patients often experience comorbid conditions such as allergies, sensitive skin, irritable bowel syndrome, fibromyalgia, and pelvic floor dysfunction. "There are a lot of comorbidities with IC/PBS, but there probably is a common thread running through these patients. When we find that, we should have some better therapies," he said. ■