

# Vulvar Endometriosis Mimicking as Primary Vulvodynia in a Young Nulliparous Woman: Algorithm of Care Following a Rapid Literature Review

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## Abstract

Endometriosis occurs in 10% of women aged 19 - 45 years. There is a rare incidence of spontaneous vulvar endometriosis, a possible subset of cutaneous endometriosis. Few cases of vulvar endometriosis have been reported in literature and are often related to large lesions. The occult cases of vulvar endometriosis have been identified mistakenly following response to hormone use after being misdiagnosed as intractable primary vulvodynia. With this mis- or delayed diagnosis comes increased psychological distress adding to the burden of disease. This management algorithm following a rapid literature review of cases using recognized databases such as PubMed, Medline, SCOPUS, CINAHL and EMBASE addresses the needs of this group of vulvar endometriosis. Vulvar endometriosis is rare and can present as primary vulvodynia in the young woman. It may mimic vulvodynia or other chronic pelvic pain disorders such as interstitial cystitis leading to conflicting management. However, a strong correlation of vulvar pain or discomfort to her menstrual cycle activity with or without a visible lesion should raise the likelihood of this condition.

**Keywords:** Vulvar endometriosis; Primary vulvodynia; Dyspareunia; Young woman; Cutaneous endometriosis

## A Case Description

A 21-year-old nulliparous woman had been seen with a history of increasing cyclical dull achy vulval pain with associated discharge described as an intermittent red-brown loss. There was intermittent superficial dyspareunia with mild pain with orgasms. She reported no associated deep pelvic pain or features suggestive of pelvic endometriosis, dermatoses, preceding vulval infections nor gastrointestinal symptoms. Menarche was at age 15 years. There was a strong family history

of endometriosis. Mother had endometriosis of her episiotomy scar whilst her older sister had deeply infiltrating pelvic endometriosis. She had been treated unsuccessfully as a case of primary vulvodynia by three previous physicians. Pelvic examination, despite no identifiable pathology on two pelvic ultrasound scans, towards the middle of her menstrual cycle, had shown a normal vulva architecture with no skin lesions nor fissures. A small tender reddish-blue endometriotic spot, 1 - 2 cm away from the introital ring, deep within the anterior wall of a slightly hypertonic vagina, the site of her pain, was seen and palpable. Other pelvic examination was normal.

She declined to have biopsies due to the lesion's proximity to her G-spot and possible worsening effect on her ability to orgasm. A laparoscopy to identify for pelvic endometriosis was also declined and she preferred to continue with her medical management - progestogen-only pill (POP) - which she found was helping with her pain and contraceptive needs. Psychosexual advice had been given. Follow-up with possible biopsy has been arranged in a few months.

## Prevalence and Pathophysiology

Endometriosis is a common gynecologic disorder characterized by the presence of endometrial tissue outside the uterine cavity, affecting up to 10-15% of women in reproductive age, with a 0.1% annual incidence in women in the age range of 15 - 49 years [1, 2]. It affects over 10% of women worldwide and has a significant burden on the woman, her family and the society. Though endometriosis is largely in the pelvis, the prevalence of extra-pelvic endometriosis is also recognized, with increasing reports of spontaneous cutaneous endometriosis, a subgroup [3].

Vulvar endometriosis, an uncommon subset of cutaneous endometriosis can sometimes present as primary vulvodynia in the young nulliparous woman. Only a few cases have been reported in the last half-century. It may present as an ulcer or a small lesion - old blood clots or blue in color with cyclical changes in size or pain and sometimes might mimic a vulvar varicosity [4]. The difference is in the color and lack of reducibility or change in size upon gentle pressure. However, it may not have the above physical stigmata, presenting insidiously at first with increasing pain the further from menarche the young woman gets.

Though it is presumed to be rare, this may not be the case

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but could be simply under-diagnosed as is found with pelvic endometriosis, which is beleaguered by problems with identification and confirmation. It has been reported that 33-50% of diagnostic laparoscopies will be negative for pelvic endometriosis with much of the identified pathology not necessarily the cause of pain [5]. In addition, despite progress made in endometriosis diagnosis, adjunct histological confirmation of excised presumed lesions at diagnostic laparoscopy is confirmatory, 60-80% of the time, particularly in mild disease depending on site [6, 7].

It could also be misdiagnosed as primary or secondary vulvodynia or simply as a referred pain of other causes of chronic pelvic pain such as deeply infiltrating pelvic endometriosis.

Vulvodynia, as defined by the International Society for the Study of Vulvovaginal Disease (ISSVD), refers to medically unexplained vulvar discomfort and pain of greater than a 3-month duration. It can be localized, generalized or mixed. It can be primary or secondary [8]. Vulvodynia affects women of all ages, reproductive stages, and ethnicities. The lifetime prevalence of this condition has been estimated at 8%, and this prevalence remains constant across all decades up to the age of 70 years [9].

Vulvodynia or vulvar pain syndrome is a multifactorial clinical syndrome of vulvar pain, sexual dysfunction, and psychological distress. It is estimated that 10-18% of American women have the disease with an economic burden of \$31-72 billion dollars a year [10-12].

The underlying problem in vulvodynia appears to be inflammation caused by trauma of the vestibular mucosa, which leads to peripheral and central sensitization [10].

The etiological factor most widely described and most frequently found is a history of previous infections. This has been identified as the causal factor in 36.3% of cases in one study [13]. It identified that a history of vaginal candidiasis was commonly reported by women with vulvodynia, although rates of colonization by *Candida* in these women were not higher than those found in control groups. It seems that sensitization occurred due to contact with yeast allergens [13]. A theory has been supported by many animal studies.

It has also been suggested that vulvodynia could be a psychological disorder, and specific psychological states, such as anxiety, fear of pain, hypervigilance, catastrophizing, and depression, are more frequently reported by these women [14]. Whether this is etiological in nature or a sequela may be dependent on other disease associations.

In addition to the etiological factors mentioned above, many others have been proposed. Recently, research has been conducted regarding the role of hormones and hormonal changes in women with vulvodynia. Results are conflicting: whilst some studies report an association between provoked vestibulitis (PVD) and oral contraceptives [15], others have found no such relationship [16].

Other pathophysiological theories proposed include abnormalities of embryologic development, infection, inflammation, genetic/immune factors, and nerve pathways. Though the condition is frequently complicated by psychological morbidity, there is no evidence for a primarily psychological cause for pain [17].

In summary, the exact etiology of vulvodynia is unknown.

Most likely, there is not one single etiology but a set of overlapping etiologies, more so as the disease progresses.

## Associations

Endometriosis has a recognized association with dyspareunia: largely deep dyspareunia due to involvement of the uterosacral ligaments, ovarian fossa, bladder base and pouch of Douglas. There is recognition of an increasing association with secondary vulvodynia, which may sometimes present as superficial dyspareunia, and is supported by the following schools of thought.

The primary theory of secondary vulvodynia associated with endometriosis in the absence of overt endometriosis deposits could be that of pain elicitation through neural pathways: a replication of the peripheral sensitization pathway of pelvic endometriosis resulting in activation of sensory nerve endings which abound in the vulva by pro-inflammatory mediators which could include prostaglandin E2 (PGE2), interleukins, tumor necrosis factor and nerve growth factor.

The second theory focuses on the recognized role of referred inflammatory pain from a low-lying rectovaginal endometriotic nodule or other deeply infiltrating endometriosis [18].

Superficial dyspareunia and vulvodynia are often used interchangeably leading to diagnostic confusion. Superficial dyspareunia which is pain upon penetration, in the vestibular area and the lower vagina, is distinctly different to unprovoked largely persistent pain/ache or discomfort in the vulva and vaginal introitus [19]. Either condition could also coexist with endometriosis, interstitial cystitis, pelvic floor myalgias and vulvar dermatoses creating more confusion as to etiology and appropriate treatment regimes [19].

Theories which may underpin vulvar endometriosis include the actual physical insemination of endometrial cells in areas of trauma in the vulva. These cells with high aromatase enzyme levels lead to estradiol biosynthesis becoming self-sustaining and proliferate further. This could be the underlying pathophysiology in cyclical secondary vulvodynia in women who have a history of vulval surgery or trauma, i.e., episiotomy or Bartholin's cyst marsupialization or failed recurrent marsupialization. The distinctive factor is the connection of her pain or increasing vulvar lesion with her menstrual cycles which may be insidious in onset.

The other theory of lymphatic spread of the endometrial cells could explain the neurogenic pain component: vulvar pain from nerve ischemia from surrounding inflammation/edema +/- chronic pelvic floor muscle hypertonicity resulting from endometriosis deposits or plaques amongst pudendal vessels. The lack of pain radiation from deep in the pelvis may help to differentiate from deeply infiltrating endometriosis. The specific rather than diffuse generalized nature is a distinctive factor.

The coelomic metaplasia transfer theory where coelomic epithelium develops into the peritoneum, pleura and ovarian surface, as proposed by Sampson, is not well understood and may be of little application, in vulvar endometriosis development [20].

However, any lesion that evolves in response to the men-

strual cycle should be considered endometriosis [21]. Early identification of a possible vulvar endometriosis helps in getting the therapy right at first visit and hopefully reduces the burden of disease. As it is recognized that these women will get a diagnosis only after several physician reviews [20], the potential psychological trauma of this disabling condition is immense alongside burden of disease. This is increasingly being recognized.

## Rapid Review

A rapid review of literature was performed via a retrospective review covering the last few decades of database in English language literatures using “vulvar endometriosis”, “vulvar pain”, “cutaneous endometriosis”, “vulvodynia” as keywords, once appropriate ethical approval had been sought.

The PRISMA model was used to identify papers across different databases which include Medline, PubMed, Cochrane library, CINAHL and SCOPUS.

The streamlined overview was then analyzed via an Excel spreadsheet.

Results identify 15 papers on vulvovaginal endometriosis in English literature. Most were case reports and described initial presenting symptoms of pain with associated cyclical increase in vulvar lesions or in one case, an ulcer. Many of these lesions were over the vulva, some sub-urethral and a few were vaginal lumps. A few of the cases presenting with recurrent lesions had developed extra-uterine endometrial stromal sarcoma. The optimum management as determined by primary outcomes of symptom resolution and non-recurrence was deemed surgical excision if possible.

This rapid review has helped inform management of this cohort of women which has been described down below.

## Clinical Management

A good history-taking session will identify any factors leading to vulvodynia such as previous infections, Crohn’s disease, presence of dermatoses, vulvar trauma, surgery and previous sexual assault and/or coitus with poor vaginal lubrication. In a young woman who presents without the above but reports a cyclical pattern to her vulvar pain, vulvar endometriosis should be considered. The use of validated self-report questionnaires such as female sexual function index has been reported as a better objective assessment of her pain than her self-reported assessment on a Likert scale of 1 - 10.

Physical examination should be systematic and may identify lesions ranging from swellings to bleeding old ulcers. The insidious vulvar cyst such as Bartholin’s or an inclusion cyst filled with old blood or chocolate-colored heterogeneous fluid which is tender on palpation, is pathognomonic. These obvious signs may not be present at time of presentation.

Gentle thorough systematic examination of the vulva, vagina and perineal area which includes a one-digit internal vaginal examination prior to identifying specific areas of tenderness with the use of the Q-tip cotton ball alongside a gen-

tle clear speculum examination of the vagina identifying for trauma, dermatoses, infection, atrophy, fissure or erythema or swellings, should be performed in a sensitive interactive manner. Identifying pelvic floor muscle hypertonicity is a must as is often exaggerated with vulvodynia or superficial dyspareunia but cyclical in vulvar endometriosis. Careful check of previous vulvar or perineal scars for endometriosis deposits whilst eliciting for pain should be done. Assessment of pain with or without accompanying pelvic floor tonicity with active distraction should be made afterwards.

In occult vulvar endometriosis, differentiating the disease from allodynia (painful response to non-painful stimuli) or hyperalgesia (exaggerated painful response to painful stimuli), both of whom may represent a neuropathy can be difficult. The menstrual pattern association of pain presence or exacerbation may help point towards the diagnosis.

Investigating deep seated cysts or no visible cysts with a definitive history of a growing sensation by the woman - as is sometimes experienced with Gartner’s duct cyst or other mesonephric remnants, suggests a role for imaging, preferably pelvic magnetic resonance imaging (MRI) or computed tomography (CT) scan [22]. This helps not only in identification but also to help map out strategy for surgical excision, which remains gold standard treatment. This is best performed during the first half of the menstrual cycle with or without pre-operative hormonal agents. Skene gland cysts have also been described as known associations. Histological analysis of all excised vulvar cyst wall should be encouraged as it may identify atypical endometriosis or worse still cancer - extra-uterine endometrial stroma sarcoma or clear cell cancer metastasis which have been described in literature [23, 24].

Medical management can include hormonal interventions such as oral contraceptive pills, progestogens, gonadotrophin-releasing hormone agonists (GnRHa) with regular imaging surveillance, particularly if there are no distinct large lesions on imaging or if the surgical risks greatly outweigh the benefits. There is no current consensus on mode of management for these women with occult or small vulvar endometriosis lesions.

Following surgical excision, particularly in those that have disease overlap, there is still a role for medical treatments which have been described in literature. Some of them include topical lidocaine use, tricyclic antidepressants, botulinum toxin A perineal infiltration, the use of injectable anti-inflammatory agents such as corticosteroids, interferon and mast cell stabilizers, pelvic floor physical therapy, cognitive behavioral therapy alongside a vulvar care regime which include the use of 100% cotton undergarments, regular use of alcohol - free emollients and hypo-allergenic oil-based lubricants during intercourse whilst avoiding irritants, douching and the use of harsh soaps [25-29].

A tabular representation of the discussion above is shown in Table 1.

## Impact on Quality of Life

It is important to note that many women “suffer in silence” and

**Table 1.** Differences Among Vulvar Endometriosis, Superficial Dyspareunia and 1ry Vulvodynia

	Vulvodynia (1ry)	Superficial dyspareunia	Vulvar endometriosis
Duration of symptoms	Usually chronic	Varied, but could be of short duration	Chronic with cyclical variation
Site	Introitus lower vagina	Vestibule	Specific areas over the vulva, lower vagina
Age of woman	Variable	Variable	Usually younger if no preceding vaginal trauma
Trigger factor	Present: candidiasis is a common agent	Present: tampon use, negative sexual/relationship history	None, menstrual cycle predisposition
Coexisting/aggravating factors			
Swellings	None	Maybe present	Small or tiny deposits/bluish nodules or chocolate fluid-filled cysts
Dermatoses	None	Maybe present	None
Ulcers	None	Maybe present	Has been described
Infections	None	Maybe present	None
Pelvic floor muscles	Very hypertonic	Some hypertonic	Hypertonia during menstruation
Treatment			
Medical treatment	Benefit +/++	Benefit ++	Benefit
Physical therapies	Benefit +/++	Benefit +/++	No benefit
Psychological therapies	Benefit +/++	Benefit ++	Of no benefit
Vulval care regime	Benefit +/++	Benefit +/++	Of no benefit
Hormone use	May be beneficial	May be beneficial	Estrogen exacerbates: POP/GnRHa may help
Surgical intervention	Benefit + vestibulectomy	Benefit depending on etiology	Benefit +++ Excision of small area/cyst as cancer risk in recurrent cases

+: some benefit; ++: more benefit; +++: great benefit. GnRHa: gonadotrophin-releasing hormone agonists; POP: progestagen-only pill.

do not seek medical help.

If left alone, this small cohort of women are tagged as vulvodynia, and as a result, are poorly managed, leading to increasing psychological trauma. The incorrect diagnosis and chronicity of the problem can lead to feelings of frustration, anxiety, chronic stress and depression, and has been described in literature. They are left in the bandwagon of chronic pelvic pain or even worse thought to have psychosomatic symptoms.

This cohort do not readily seek for help, as less than half of women who met screening criteria for vulvodynia, sought for medical help, in a telephone survey. This further worsens the chronicity of their symptoms, increasing their trauma [19]. This results in a significant negative impact on a woman's psychosexual health and overall quality of life alongside an increase in disease burden. This only emphasizes the need to identify this small subgroup of women at presentation and get their diagnosis and subsequent treatment right, first time.

## Conclusions

Vulvar endometriosis is rare and can present as primary vulvodynia in the young woman. It may also mimic other causes of chronic pelvic pain such as interstitial cystitis leading to conflicting management. However, a strong correlation of progressively increasing vulvar pain or discomfort to her men-

strual cycle activity with or without a visible lesion should raise the likelihood of this condition. There may or may not be features of concurrent pelvic endometriosis with a familial association. More research is needed to aid early and prompt diagnosis.

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## Conflict of Interest

None to declare.

## Author Contributions

Both authors researched and contributed to the article after TA designed the study.



## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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