Psychiatr. Pol. 2017; 51(5): 937–952
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/10.12740/PP/67371

Vulvodynia and depression – a case study

Aneta Gerhant, Ewelina Soroka, Aneta Perzyńska-Starkiewicz, Magdalena Derewianka-Polak, Marcin Olajossy

2nd Department of Psychiatry and Psychiatric Rehabilitation,
Medical University of Lublin

Summary

The analysis of the case of vulvodynia coexisting with depression. Remission in terms of pain and affective symptoms was achieved simultaneously after including gabapentin in the treatment at a dose of 900 mg/d. Depressive disorders may constitute a risk factor for vulvodynia and occur as a secondary condition to pain. The frequency of other functional pain syndromes such as fibromyalgia and temporomandibular syndrome is much higher in patients with vulvodynia than in the overall female population. The risk of suicide in vulvodynia, similarly to other chronic pain syndromes, is relatively high, especially with coexisting depressive symptoms.

Key words: vulvodynia, mood disorders, depression.

Introduction

Pain is a subjective unpleasant, sensual and emotional experience resulting from stimuli damaging body tissues (nociceptive stimuli) or causing the risk of such damage. Acute pain is usually elicited by nociceptive stimuli and has an adaptive value as it makes it possible to locate the tissue damage and launches reactions that minimize the pain. Pain persisting for more than 3 months, when its duration is longer than the actual wound healing time, is called chronic pain [1]. In the biopsychosocial model, the suffering accompanying pain and the resulting disability are conditioned by a specific interaction of psychological, social, cultural, biological and genetic factors. The importance of social and psychological factors increases together with the chronification of pain [2]. Chronic pain is experienced by 12–30% of residents of Europe, negatively influencing the quality of their lives, impairing their daily functioning and hindering or making it impossible to carry out occupational duties [3].

The incidence of pain in individuals suffering from depression and that of depression in people experiencing chronic pain is significantly more frequent than each of

these conditions separately. Due to the frequent coexistence of depression and pain, the mutual induction of the two conditions, reaction to similar drugs and probably a common neurobiological basis, the literature on the subject has adopted an expression "the depression-pain dyad" or "the depression-pain syndrome" [3, 4]. A positive correlation was revealed between severity of depression and severity of pain, its duration, frequency and number of its locations [5, 6]. Table 1 contains the results of selected studies on the occurrence of depression in patients with chronic pain, and of chronic pain in people with depression.

Table 1. **Review of research on the coexistence of chronic pain and depression**

Occurrence of pain and depression	
Incidence of depressive disorders in people with chronic pain	Incidence of chronic pain in people with depressive disorders
Bair et al. [5] chronic pain in the course of somatic diseases 13% in gynecological clinics 27% in primary care 52% in pain clinics 56% in rheumatology and orthopedic clinics 85% in dental clinics Agüera et al. [8] people with chronic pain of unexplained etiology: 52% major depressive episode 17.8% minor depression or dysthymia	Bair et al. [5] an average of 65% of patients with major depression Ohayon et al. [7] 43.3% of patients with major depression vs. 16.1% in the control group

Pain contributes to a lower effectiveness and higher costs of treatment of depression [9].

There are 4 types of chronic pain:

1) neuropathic pain – caused and maintained by pathological lesions in the nervous system;
2) nociceptive pain – caused by tissue damage;
3) visceral pain – with internal organs being the source;
4) idiopathic pain – with an unknown or unclear etiology [10].

Idiopathic pain is also often called functional or psychosomatic and occurs in such disorders as fibromyalgia, temporomandibular joint pain syndrome, irritable bowel syndrome, and vulvodynia.

Vulvodynia is a type of vulvar pain, also described as itching, burning, hypersensitivity of the vagina opening, persisting for at least 3 months without a clear cause, with possible coexisting factors. Depending on its location, vulvodynia is divided into generalized, localized (clitorodynia, hemivulvodynia, vestibulodynia and other) or mixed. Pain can occur spontaneously or, in the case of provoked vulvodynia, can be caused by irritation or sexual contacts [11]. The score incidence of vulvodynia is

from 3.8% to 9% [12–15]. It was estimated that the disease may occur throughout the lives of 9% to 16% of women [12–14]. Vulvodynia is observed equally often in all decades of life of sexually active women. The incidence of the disease decreases in the case of women over 70 years of age, which is due to limited sexual activity [13, 15]. The first symptoms appear on average around the age of 30, although there are cases of the disease onset in childhood or adolescence [15]. The results of the longitudinal prospective population study by Reed et al. [16] demonstrate that a remission-free course of the disease is rather exceptional and concerns only approx. 10% of cases. The researchers considerably more often observed remission without relapse (50%) or periods of remissions and exacerbations after 6–30 pain-free months.

In practice, the diagnosis is based on eliminating other diseases which can induce vulvar pain: infectious, inflammatory, neoplastic or neurological ones [11]. However, it seems that the disease is rarely diagnosed and happens to be wrongly interpreted as estrogen deficiency, candidal infections, dermatological disorders or psychological problems. Therefore, in the event of the persistence of pain symptoms despite an adequate treatment of the mentioned diseases, vulvodynia should be considered as a possible diagnosis [6]. Women with vulvodynia are usually referred to 3 to 5 specialists, and in most cases leave without an adequate diagnosis [13, 17]. Nearly half of women suffering from vulvodynia do not attempt to seek diagnosis for their disease [13, 15].

The etiology of vulvodynia has not been sufficiently explained. Among the considered options are genetic predispositions, abnormal embryonic development, central and peripheral sensitization and increased muscular tension in the pelvic floor area. Generalized unprovoked vulvodynia is treated as a complex regional pain syndrome (CRPS), such as fibromyalgia and temporomandibular joint syndrome. There are assumptions that the CRPS is caused by central sensitization processes. The wind-up process may be of significance, causing increased neural activity in the posterior horns of the spinal cord as a reaction to a repeated stimulation of nociceptive primary group C nerve fibres. The mechanism is responsible for the chronicity of pain despite the lack of a stimulus causing it [18].

The case of vulvodynia coexisting with symptoms of a depressive syndrome described in the study calls for an analysis of correlations between chronic pain and depression. The patient gave her informed consent for publishing this case study.

Case study

A 45-year-old woman was referred to a psychiatry clinic due to the relapse of vulvar pain persisting for half a year and the coexisting symptoms of depression.

The patient was born postterm. Her early psychomotor development was normal. She was brought up in a full family together with her seven years younger sister. She had good results at school and did not cause any behavioral problems. She called herself “a timid child”. She completed a general secondary school. She did not take her final secondary school exams due to pregnancy. After getting married she started a business with her husband. She has been divorced for 10 years, now working occasionally as a carer of elderly people.

Her father completed higher education; he died due to a brain tumor at the age of 48. He abused his family physically and psychologically. At the time of her father's death the patient was 16 years old. Her mother is 67, with secondary education, and used to work as an accountant.

The patient got married when she was 18. Her husband was her first sexual partner. A year after marriage she gave birth to a daughter. Her marriage was a sort of "escape from her family home". Shortly after marriage the couple began to experience serious problems. The patient's husband was unfaithful to her and behaved in a crude and disrespectful way. The patient began to avoid intercourses with her husband ("I felt repugnance towards him"). Her husband never forced her into an intercourse. However, during sex he would ridicule the appearance of her genitals and say that she is sexually unattractive to him. Two years before the divorce the couple completely stopped having sexual relations. The marriage lasted 10 years. The patient was the one who filed for a divorce. She assesses her current relationship with her husband positively. Her daughter is 26 years old.

In her childhood she frequently experienced head trauma without the loss of consciousness (as she was beaten by her father). In her puberty she experienced loss of consciousness twice, without signs of seizures. For several years she has been treated for arterial hypertension. Her maternal grandmother was treated for depression, and her paternal grandmother committed suicide, and probably also suffered from depression.

The patient's first pain symptoms appeared during the divorce, when she was 28 years old; they started with aching teeth. A year later, when the patient went abroad for work, the pain was so intense that it prevented normal daily functioning. Therefore, the patient returned to Poland. The patient was diagnosed and treated in a dental clinic. At that time the pain was located in the temporal and mandibular area. The sanitation of oral cavity was performed, without a significant improvement. Trigeminal neuralgia was also ruled out. Carbamazepine and diazepam were administered, with no significant improvement. A year later the pain changed its location to the vulvar labia, the clitoris and the perianal area. Despite the change in location, the nature of the pain (its intensity and recurrence) was similar, described as an itching and burning sensation. The pain appeared spontaneously, was recurrent and its intensity increased in response to touch. Due to her symptoms the patient was referred to a dermatologist, a gynecologist and a neurologist while she stayed in a inpatient ward. On the basis of medical examinations (an MRI of the head and spine, vaginal swabs and an ultrasound of reproductive organs) other somatic causes of vulvar pain were ruled out. The gynecologist, suspecting vulvodynia, prescribed amitriptyline at a dose of 50 mg per day. After a few days the patient stopped taking the medicine due to poor tolerance (excessive sedation and vertigo). Clitoris cryotherapy did not bring the expected outcome either. The pain was so intense that it prevented the patient's normal daily functioning.

Mood disorders appeared as secondary to the described pain symptoms. Her mood was low and her activity was limited; she reported attention disorders, a low self-esteem, anhedonia, a loss of interests, a prolonged sleep latency and a sense of guilt. She claimed that due to her disease she was a burden for her family. Furthermore, during pain-free periods, she waited in anxiety for another pain episode. The

patient herself associated her affective symptoms with the pain that she experienced. After around half a year from the onset of vulvar pain, the patient attempted suicide by swallowing 60 tablets of amitriptyline. Later on, when she was asked about the reasons for her suicide attempt, she said "the pain was unbearable, I no longer had any hope for improvement, and felt that I was a burden for my family". She was hospitalized at the Intensive Therapy Ward and a month later at the general psychiatric ward. The patient's hospital stay lasted 2 weeks. After introducing sulpiride to the treatment, the pain subsided only for a few days. The patient was treated on an outpatient basis for several months. When required, she took alprazolam, carbamazepine 400 mg/d, sertraline up to 150 mg/d, with no significant improvement.

She was again referred to a psychiatric hospital, this time to the neurotic disorders ward. At that time her vulvar pain had lasted a year. Her pharmacotherapy was modified; clomipramine at a dose of 225 mg/d and chlorprothixene up to 30 mg/d. She also underwent individual and group psychotherapy according to the psychodynamics theory. A gradual improvement in the patient's mood was observed, and her pain subsided. She was released home with a diagnosis of recurrent depressive disorder – moderate depressive episode.

For approx. 7 years the patient was taking clomipramine at a maintenance dose of 75 mg/d. Vulvar pain recurred during that time on average every half a year and quickly subsided after increasing the dose of clomipramine to 225 mg/d. The patient spent those years abroad and functioned quite well. The only episodes of low mood occurred when pain relapsed.

After that the patient was readmitted to the neurotic disorders ward due to pain in the left side of her face persisting for two months which did not stop after analgesics and high doses of clomipramine. After being admitted to the hospital, the patient's mood was low, she was weepy, reported night sleep disorders with waking up at around 2 a.m., experienced anxiety without a cause, which intensified in the morning, increased thirst, and a subjective sensation of rush of thoughts. It was decided to maintain clomipramine at a dose of 225 mg/d. The treatment was supplemented with valproate at a dose of 1,000 mg/d and chlorprothixene up to 45 mg/d. As in the fourth week of hospitalization the patient had urinary retention, clomipramine was discontinued and replaced with escitalopram, achieving a total subsiding of the pain and an improvement in the patient's mood. The patient was released home with diagnosed anxiety disorder with a somatic presentation and with a recommendation to take escitalopram at a dose of 30 mg/d, chlorprothixene at a dose of 45 mg/d and valproate at a dose of 1,000 mg/d.

For another 3 years, when the patient worked abroad, the symptoms did not recur. After that the patient again began to experience mandibular pain and anxiety, insomnia and intense suicidal thoughts. Due to her condition, the patient returned to Poland. After a few weeks the pain subsided, but her anxiety level was still high, accompanied with insomnia, low mood and suicidal thoughts and tendencies. The patient made a suicidal attempt by jumping from height, which, however, was foiled by her daughter. After that she was hospitalized at a psychiatric ward for the fourth time. She was released with a diagnosis of recurrent depressive disorders. Venlafaxine was included in her

treatment at a dose of 150 mg/d, with an improvement continuing for approximately a year, until her current hospitalization caused by recurring pain in the vulvar area.

The pain was described as itching, burning, a sense of pressure, occurring continuously during the day, with short pauses lasting a few hours at the maximum. The pain intensified with touch, during micturition and during irritation of the external urethral orifice by underwear or other factors. During intensified pain, the patient could not engage in sexual activity. In the pain-free periods, she experienced anxiety due to the possible return of the symptoms. The patient was not able to identify any factors that bring her relief. Her mood was low, she reported lack of energy, anhedonia, and she spoke with resignation about her condition, seeing no hope for improvement of her pain symptoms. The pain made it difficult to fall asleep and woke the patient up during the night. Within a few months before the hospitalization, the patient lost over a dozen kilograms, which was due to a slimming diet. No intensification of pain or depression at a particular time of the day was observed. The pain appeared unpredictably. The case history showed that depressive symptoms were secondary to pain. For approx. 2 months the patient has taken duloxetine at a dose of 60 mg/d and chlorprothixene at a dose of 45 mg/d, without any significant improvement.

In the first days of hospital stay the patient obtained 10 points on the Hamilton Depression Scale, which corresponded to mild depression. The results of psychological tests (the Graham-Kendall test for the memory of geometrical forms, the Bender test, the Mini–Mental State Examination and the Clock Drawing Test) were normal and did not show any organic lesions in the central nervous system. The patient's profile obtained within the MMPI-2 personality test showed an evident defensive tendency and the lack of inclination towards exaggerating symptoms. The results for most clinical scales, both content and supplementary scales, were within the interpretative silence. The tests showed that the patient is not an achievement-oriented person, but a pessimistic, introvert and restless one, weakly adapted in psychological terms, and having problems with coping with stress.

The laboratory test results: urinalysis, liver function tests and thyroid hormones were normal. The blood count revealed features of microcytic anemia due to iron deficiency.

The patient has menstruated regularly since the age of 15. During her periods, which last approx. 7 days, she experiences heavy bleeding. Her case history includes 1 pregnancy, 1 physiological delivery without peripartum complications, with episiotomy and normal wound healing. The gynecological examination results were as follows: normal vagina, cervix without any pathological lesions, uterus with a normal size, mobile and homogenous, and adnexa not palpable. The pelvic floor muscles were tense and tender. The periurethral area was also sensitive to pain. The intravaginal ultrasound revealed a fibroid in the posterior uterine wall, with a diameter of 2.5 cm, distorting the uterine cavity. The diagnosis included clitorodynia (vulvodynia) and a dysfunction of the pelvic floor muscles. The gynecologist recommended the supplementation of the treatment with gabapentin at a dose increasing from 900 mg/d to 1,800 mg/d if no improvement is observed. Introducing myofascial therapy was also suggested, but the patient was not interested in this type of treatment. Gabapentin was included

in her treatment at a dose of 1,200 mg/d. After 3 weeks a complete remission of pain and depressive symptoms was achieved. After 2 successful temporary releases, the patient was released from the hospital with the recommendation to continue treatment in outpatient settings.

Discussion

In the described case, the coexistence of a depressive disorder with vulvar pain was considered in the context of the following combinations of clinical diagnoses:

1) vulvodynia and a secondary depressive reaction;
2) recurrent depressive disorder coexisting with vulvodynia.

The results of longitudinal studies demonstrate that depression may be a predictor of chronic pain, and chronic pain is associated with a higher risk of depression [19, 20]. Fishbain et al. [6] suggested a few hypotheses explaining the coincidence of these conditions. According to the first, depression precedes pain and is a predisposing factor for its occurrence. Based on another hypothesis, depression is secondary to pain and is its natural consequence. The third hypothesis, referred to as the scar hypothesis, assumes that depression occurring before the onset of pain is a predisposing factor of depression after the pain starts. Pain functions as a kind of stressor which induces relapses of depression in individuals with genetic predispositions. This hypothesis is supported by Magni et al. [21], who state that from 37.8% to 69% of individuals with chronic pain have at least one first-degree relative who suffers from a disorder within the depression spectrum. According to the fourth hypothesis, the correlation between pain and depression is mediated by psychological variables. In the study by Masheb et al. [22] on patients with vulvodynia actively seeking treatment, 17% of women met the criteria for a major depressive disorder, and 45% confirmed having depression episodes in the past. In as many as 62.5% of them the first episode of depression preceded the first vulvodynia symptoms, and in the remaining cases it was secondary to the symptoms.

The results of the population study show that women who experienced mood disorders in the past (major depression, dysthymia) are at three times higher risk of vulvodynia in comparison to the control group. However, the risk of the first depressive episode or its relapse in women with vulvodynia is 1.7 times higher than in the reference group [23]. In the case described in the present study a depressive episode developed secondary to pain, and the symptoms might be a psychological reaction to pain or to a lengthy diagnostic and treatment process or the lack of expected outcomes. Further relapses of depression were also preceded by pain in the vulvar or mandibular area. During the fourth hospitalization depressive symptoms continued despite the relapse of pain, and their intensity was so high that the patient made a suicide attempt.

Although the patient denied having depressive episodes before the onset of pain in the mandibular and vulvar area she is at a higher risk of recurring depressive disorder due to the presence of depression in her family history. It seems that in this patient's case vulvodynia could theoretically coexist with recurring depressive disorder, but the

hypothesis can only be confirmed if in the future there is a depressive episode occurring independently of pain in the vulvar or facial area.

The review of studies conducted by Tang et al. [24] shows that the risk of suicide death in individuals suffering from chronic pain is twice as high than in the control group. From 5% to 14% of persons experiencing chronic pain attempt suicide, and approx. 20% have suicidal thoughts. The suicide risk factors applicable to individuals suffering from chronic pain are: being female, a high intensity of pain, the coexistence of depression, suicide in the family, past suicidal attempts and pain-related sleep disorders. In this case suicidal behavior is associated with catastrophism related to pain. It is a set of negative cognitive and emotional processes related to pain such as exaggerating the symptoms, ruminations on pain, the sense of helplessness with regard to pain and a pessimistic approach to the future course of the disease and treatment outcomes. Its intensity positively correlates with pain intensity, the level of pain-related disability, the treatment outcomes of the primary disease and the intensity of depression. Individuals with such an attitude more often apply non-adaptive strategies of coping with pain and less frequently show pro-health behavior. They may perceive their pain as more intense as they selectively and intensely focus their attention on the pain stimuli and wait for their recurrence with anxiety. Despite the fact that this type of behavior may result in receiving more support from the environment, the result can also be the opposite [25].

Vulvodynia is associated with a considerably higher level of catastrophism related to pain symptoms in the vulvar area as compared to other areas of the body [26]. Catastrophism is a phenomenon independent of depression and other negative affective states and positively correlates with pain intensity. Pain-related catastrophism is associated with a higher risk of chronification of acute pain [27]. The risk of suicide in the described case was increased due to suicide in the family and the coexisting depression. The first suicide attempt was due to a high level of pain-related catastrophism. The second suicide attempt made during the pain-free period was a consequence of a lowered self-esteem due to depression, the sense of being a burden to the family and the assumption that despite the temporary improvement the pain will recur.

In the discussed case pain in the vulvar area was preceded by pain in the mandibular and temporal area. A growing number of reports shows that vulvodynia is a complex pain disorder similar to other idiopathic musculoskeletal pain syndromes such as fibromyalgia and temporomandibular joint syndrome. In patients with unprovoked vulvodynia a higher sensitivity to pain was also found in areas other than genitals [28]. Nguyen et al. [17] carried out a study the results of which demonstrate that 45% of patients with vulvodynia also suffer from at least one other pain syndrome, most often the irritable bowel syndrome (25.3%), fibromyalgia (12.6%) or interstitial cystitis (17.5%). In the total population of women, the incidence of the irritable bowel syndrome is 14% [29], of fibromyalgia – 4.2% [30] and of interstitial cystitis/painful bladder syndrome – 0.5% [31].

Special attention should be drawn to the frequent coexistence of vulvodynia and painful bladder syndrome. Both these conditions are often accompanied by a dysfunction of pelvic floor muscles with hypertonia. The symptoms include spasticity,

myofascial pain and micturition disorders. So far it has not been determined whether the pelvic floor muscles dysfunction precipitates the symptoms of vulvodynia or the painful bladder syndrome, or it is a reaction to pain. However, it is known that these conditions induce each other [32]. Perhaps due to hypertonia of pelvic floor muscles, the described patient was particularly susceptible to urinary retention after clomipramine and duloxetine. Chronic idiopathic orthofacial pain was found in as many as 78% of patients with localized vulvodynia. Most often it took the form of a temporomandibular joint syndrome, which in the general population occurs with a frequency of 7–15%. Women in whom vulvodynia co-occurs with orthofacial pain are characterized with a higher level of anxiety, somatization and psychological distress [28].

A number of depressive disorder symptoms, such as sleep, attention and appetite disorders, catastrophic thinking, may be a natural reaction to pain. Including them in a psychiatric diagnosis may result in overdiagnosing depression in individuals with chronic pain. This can be supported by the results of the study by Wilson et al. [33], in which the incidence of major depression diagnosed on the basis of the DSM-IV criteria dropped from 37.5 to 19.4% after excluding from diagnostic criteria the symptoms which are a natural consequence of pain. A large group of patients covered by the study was convinced that depressive symptoms that they experienced would disappear together with pain. As shown in the studies performed with the use of the Beck Depression Inventory II, the profile of the symptoms of "plain" depression and depression accompanied by pain is quite different. In depression coexisting with pain, symptoms associated with self-depreciation are less frequent, with more emphasis on such symptoms as fatigability, loss of appetite and libido, social withdrawal, difficulties at work and sleep disorders [34, 35].

It is believed that depression and chronic pain may have a common pathomechanism. Pain is related to the activation of an integrated neuromatrix called the pain neuromatrix. It consists of the primary and secondary somatosensory cortex – involved in the perception and discrimination of nociceptive stimuli, and the prefrontal cortex, the anterior cingulate gyrus, the insula, the amygdaloid nucleus, nucleus accumbens and thalamus – areas associated with the emotional and motivational aspects of pain [36, 37]. Together with the chronification of pain, the neural activation is shifted to the areas associated with emotions and motivation [38]. In individuals with chronic pain a reduction has been observed in the volume of grey matter in the anterior cingulate gyrus, the insula and the prefrontal cortex [39]. The neural areas and circuits participating in the processing of pain stimuli overlap with those that play a key role in the pathogenesis of depression. The deregulation of the reward circuitry, with nucleus accumbens being one of its elements, conditions anhedonia. The prefrontal cortex and the anterior cingulate gyrus are involved in processing negative emotional states, and the amygdaloid nucleus and hippocampus play a role in forming and recovering memories with a negative emotional content [40]. In experimental conditions the brain activity pattern in healthy volunteers experiencing intensive social rejection complies with the pattern observed in people subjected to pain stimuli. The results suggest that the key element linking pain and depression is the accompanying suffering – physical in the case of pain and mental in the event of depression [41, 42].

The pain-modifying corticofugal system is a complex neural network linking the brain stem with the spinal cord. Signals from nociceptive pathways and limbic structures such as the amygdala and the limbic cortex are integrated in the area of the periaqueductal gray, which then send projections to the brain stem nuclei and the rostral ventromedial medulla, activating the corticofugal pain-inhibiting pathways. The neurons of the corticofugal pain-inhibiting pathways end with projection neurons of the spinal cord dorsal horn. Some of the corticofugal pain-inhibiting pathways produce endorphins. Two other pathways are the spinal noradrenergic pathway starting at locus coeruleus and the corticofugal serotonergic pathway starting at raphe nuclei. Serotonin causes the hyperpolarization of the dorsal horn neurons through 5-HT1B/D presynaptic receptors, and noradrenaline – through α2 receptors. The physiological function of corticofugal serotonergic and noradrenergic pain-inhibiting pathways is to mask the perception of insignificant nociceptive stimuli. As in depression there is a deficit in monoaminergic transmission, normal stimuli which would otherwise be ignored can be perceived as nociceptive stimuli [36, 37].

Antidepressants from the group of selective reuptake inhibitors of serotonin and noradrenaline (duloxetine, venlafaxine) and tricyclic antidepressants have a proven effectiveness in the treatment of chronic pain. Serotonin reuptake inhibitors have a slightly lesser analgesic effect [36, 37, 43, 44]. The results of experimental and laboratory studies demonstrate that their analgesic effect is independent of the mood-regulating effect and is probably related to reinforcing noradrenergic and serotonergic transmission in the corticofugal pain-inhibiting system. Furthermore, the doses of antidepressants used as analgesics are usually lower (amitriptyline 50–100 mg and an equivalent of this dose) than doses used for depression. The analgesic effect usually appears earlier than the antidepressant effect [43, 44]. Another group of drugs used in the treatment of chronic neuropathic pain are anticonvulsants such as carbamazepine, pregabalin and gabapentin [44]. Their analgesic effect is related to blocking ion channels, which leads to the hyperpolarization of spinal cord dorsal horn neurons [37]. Antidepressants and anticonvulsants are commonly used in the treatment of vulvodynia. Despite the fact that there are satisfactory effects of treating vulvodynia with these drugs, meta-analyses do not provide grounds for recommending them for general application [45–47]. Among the treatments used in vulvodynia there are local analgesics, estrogen creams, and also couple psychotherapy, individual and group psychotherapy aimed at dealing with pain and sexual issues.

In patients with hypertonia of pelvic floor muscles, myofascial therapy can be particularly effective, supplemented with learning muscle contraction and relaxation with the use of biofeedback. In difficult cases resistant to conservative treatment, the following procedures are carried out: vestibulectomy, perineoplasty or pudendal nerve block [28, 47, 48]. In the analyzed clinical case, the effects of clomipramine, venlafaxine and escitalopram were satisfactory but impermanent. During the last hospitalization vulvar pain and depression resolved simultaneously already after three weeks from adding gabapentin to the duloxetine therapy at a relatively low dose of 1,200 mg/d. A similar effect could have been achieved through duloxetine monotherapy, but an attempt to increase the dose from 60 mg/d to 90 mg/d caused urinary retention.

Currently gabapentin is registered by the FDA for the treatment of focal seizures and chronic neuropathic pain. A review of the studies shows that gabapentin applied in doses from 1,200 mg to 3,000 mg per 24 hours can significantly reduce vulvar pain in 50–85% of patients with localized or generalized vulvodynia [49]. Due to the methodological limitations of the available data (a small study group, non-random sampling, no placebo control, a short observation period), gabapentin has not been registered for the treatment of vulvodynia and so far has been used off-label [49]. However, the authors are expecting the results of a multicentre, randomized, placebo-controlled, double-blind trial for the effectiveness of gabapentin in the treatment of provoked vestibulodynia [50]. In the described patient, gabapentin therapy contributed to remission also in terms of depressive symptoms and catastrophism related to pain. The literature on the subject includes case studies and open-label studies in which gabapentin proved successful in the treatment of drug-resistant depression [51], coexisting with pain and somatization [52], in patients with epilepsy [53] or depression in bipolar affective disorders [54–56]. However, the results of randomized double-blind trials demonstrate that gabapentin used in monotherapy [57, 58] or as an add-on therapy [59] is no more effective than placebo in treating drug-resistant depression in the course of BAD [57–59] and UAD [57, 58]. There are also individual reports confirming the anxiolytic properties of gabapentin in social phobia [60], perioperative anxiety and catastrophism related to post-operative pain [61, 62]. In the context of a rapidly increasing number of studies confirming the effectiveness of pregabalin in treating generalized anxiety disorders (GAD) [63], it is surprising that there are no corresponding scientific findings on gabapentin. As the molecular mechanism of these two drugs is similar (blocking voltage-gated calcium channels), it can be expected that gabapentin is at least as effective in GAD treatment as pregabalin.

The patient in question was eventually diagnosed with vulvodynia and recurring depressive disorder. The diagnosis was based on the following:

1) the nature of the reported vulvar pain met the criteria for vulvodynia, which was confirmed by a gynecologist specializing in the field;
2) mood disorders co-occurring with the pain met the criteria for depressive episodes according to the ICD-10;
3) the course of mood disorders with remission and relapse period of at least 2 months;
4) persisting symptoms of a depressive episode and a suicide attempt despite the pain subsiding during the third hospitalization;
5) the necessity to use high doses of antidepressants to achieve the remission of mood disorders and pain symptoms;
6) a high probability of a hereditary background of mood disorders.

The aforementioned diagnosis will be fully confirmed if in the future the patient experiences a depressive episode independent of pain. Due to a satisfactory response to gabapentin, a differential diagnosis with anxiety disorders was also provided. It cannot be ruled out that the patient in fact suffers from bipolar affective disorders. However, the current clinical trials at this point do not validate such a diagnosis. Table 2 contains arguments speaking against the above findings. However, it should be

emphasized that the diagnosis was based on the analysis of the medical documentation and a detailed clinical examination of the patient. Structured clinical interviews based on diagnostic criteria were not used in this case, which constitutes a limitation of the presented case study.

Table 2. **Differential diagnosis**

Bipolar affective disorder	– no history of manic, hypomanic or mixed episodes
Generalized anxiety disorders	– a clear predominance of severity of symptoms of depressive syndrome over severity of anxiety symptoms; – anxiety was not generalized but related to the catastrophism associated with pain; – lack of chronically persistent vegetative disorders
Somatization disorder	– the criterion of the number of somatic complaints necessary for diagnosis (≥ 6 symptoms in the scope of at least two separate groups) has not been met; – diagnosis of somatic disease (vulvodynia) was made in relation to vulva pain; – lack of persistent demand for further consultations with various specialists after diagnosis (diagnosis was not deepened under the pressure of the patient)
Hypochondriacal disorder	– lack of permanent conviction about the occurrence of at least one somatic disease clearly defined by the patient and explaining the occurrence of the reported symptoms
Persistent psychogenic pain	– the genesis of vulvar pain was determined in gynecological examination

Conclusions

1. Vulvodynia often coexists with depressive disorders.
2. Depressive disorders may constitute a risk factor for vulvodynia and occur as a secondary condition to pain.
3. The frequency of other functional pain syndromes such as fibromyalgia and temporomandibular joint syndrome is much higher in patients with vulvodynia than in the general female population.
4. The risk of suicide in vulvodynia, similarly to other chronic pain syndromes, is relatively high, especially with coexisting depressive symptoms.

References

1. http://www.iasp-pain.org/Taxonomy#Pain [retrieved: 4.09.2017].
2. Gatchel RJ. *Comorbidity of chronic pain and mental health disorders: The biopsychosocial perspective*. Am. Psychol. 2004; 59(8): 795–805.

3. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. *Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment*. Eur. J. Pain 2006; 10(4): 287–333.
4. Lindsay PhG, Wyckoff M. *The depression-pain syndrome and its response to antidepressants*. Psychosomatics. 1981; 22(7): 571–577.
5. Bair MJ, Robinson RL, Katon W, Kroenke K. *Depression and pain comorbidity: A literature review*. Arch. Intern. Med. 2003; 163(20): 2433–2445.
6. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. *Chronic pain-associated depression: Antecedent or consequence of chronic pain? A review*. Clin. J. Pain 1997; 13(2): 116–137.
7. Ohayon MM. *Specific characteristics of the pain/depression association in the general population*. J. Clin. Psychiat. 2004; 65(Suppl. 12): 5–9.
8. Agüera L, Failde I, Cervilla JA, Díaz-Fernández P, Mico JA. *Medically unexplained pain complaints are associated with underlying unrecognized mood disorders in primary care*. BMC Fam. Pract. 2010; 11(3): 17.
9. Katona C, Peveler R, Dowrick C, Wessley S, Feinmann C, Gask L et al. *Pain symptoms in depression: Definition and clinical significance*. Clin. Med. (Lond.) 2005; 5(4): 390–395.
10. Merskey H, Bogduk N. *Classification of chronic pain*. Seattle: IASP Press; 1994.
11. Bornstein J, Goldstein AT, Stockdale CK, Berqeron S, Pukall C, Zolnoun D et al. *2015 ISSVD, ISSWSH, and IPPS Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia*. J. Sex. Med. 2016; 13(4): 607–612.
12. Arnold LD, Bachmann GA, Rosen R, Rhoads GG. *Assessment of vulvodynia symptoms in a sample of US women: A prevalence survey with a nested case control study*. Am. J. Obstet. Gynecol. 2007; 196(2): 128.e1–6.
13. Harlow BL, Stewart EG. *A population-based assessment of chronic unexplained vulvar pain: Have we underestimated the prevalence of vulvodynia?* J. Am. Med. Womens Assoc. 2003; 58(2): 82–88.
14. Reed BD, Crawford S, Couper M, Cave M, Haefner HK. *Pain at the vulvar vestibule: A web-based survey*. J. Low. Genit. Tract Di. 2004; 8(1): 48–57.
15. Reed BD, Harlow SD, Sen A, Legocki LJ, Edwards RM, Arato N et al. *Prevalence and demographic characteristics of vulvodynia in a population-based sample*. Am. J. Obstet. Gynecol. 2012; 206(2): 170.e1–9.
16. Reed BD, Harlow SD, Plegue MA, Sen A. *Remission, relapse, and persistence of vulvodynia: A longitudinal population-based study*. J. Womens Health 2016; 25(3): 276–283.
17. Nguyen RH, Ecklund AM, MacLehose RF, Veasley C, Harlow BL. *Co-morbid pain conditions and feelings of invalidation and isolation among women with vulvodynia*. Psychol. Health Med. 2012; 17(5): 589–598.
18. Goldstein AT, Burrows L. *Vulvodynia*. J. Sex. Med. 2008; 5(1): 5–14.
19. Chou KL. *Reciprocal relationship between pain and depression in older adults: Evidence from the English Longitudinal Study of Ageing*. J. Affect Disorders 2007; 102(1): 115–123.
20. Meyer T, Cooper J, Raspe H. *Disabling low back pain and depressive symptoms in the community-dwelling elderly: A prospective study*. Spine. 2007; 32(21): 2380–2386.
21. Magni G. *Review article on the relationship between chronic pain and depression when there is no organic lesion*. Pain 1987; 31: 1–21.
22. Masheb RM, Wang E, Lozano C, Kerns RD. *Prevalence and correlates of depression in treatment-seeking women with vulvodynia*. J. Obstet. Gynaecol. 2005; 25(8): 786–791.

23. Khandker M, Brady SS, Vitonis AF, Maclehose RF, Stewart EG, Harlow BL. *The influence of depression and anxiety on risk of adult onset vulvodynia*. J. Womens Health 2011; 20(10): 1445–1451.
24. Tang NK, Crane C. *Suicidality in chronic pain: A review of the prevalence, risk factors and psychological links*. Psychol. Med. 2006; 36(5): 575–586.
25. Edwards RR, Bingham CO, Bathon J, Haythornthwaite JA. *Catastrophizing and pain in arthritis, fibromyalgia, and other rheumatic diseases*. Arthritis Rheumatol. 2006; 55(2): 325–332.
26. Smith KB, Waxman S, Chamberlain SM, Pukall CF, Segal S. *Fear of pain and catastrophising among women with vulvodynia*. In: SSTAR (Society for Sex Therapy and Research) 2008: 33rd Annual Meeting (p. 107).
27. Gracely RH, Geisser ME, Giesecke T, Grant MA, Petzke F, Williams DA, Clauw DJ. *Pain catastrophizing and neural responses to pain among persons with fibromyalgia*. Brain 2004; 127(4): 835–843.
28. Zolnoun D, Hartmann K, Lamvu G, As-Sanie S, Maixner W, Steege J. *A conceptual model for the pathophysiology of vulvar vestibulitis syndrome*. Obstet. Gynecol. Surv. 2006; 61(6): 395–401.
29. Lovell RM, Ford AC. *Effect of gender on prevalence of irritable bowel syndrome in the community: Systematic review and meta-analysis*. Am. J. Gastroenterol. 2012; 107(7): 991–1000.
30. Queiroz LP. *Worldwide epidemiology of fibromyalgia*. Curr. Pain Headache R. 2013; 7(8): 1–6.
31. Davis NF, Brady CM, Creagh T. *Interstitial cystitis/painful bladder syndrome: Epidemiology, pathophysiology and evidence-based treatment options*. Eur. J. Obstet. Gyn. R. B. 2014; 175: 30–37.
32. Fariello JY, Moldwin RM. *Similarities between interstitial cystitis/bladder pain syndrome and vulvodynia: Implications for patient management*. Trans. Androl. Urol. 2015; 4(6): 643–652.
33. Wilson KG, Mikail SF, D'Eon JL, Minns JE. *Alternative diagnostic criteria for major depressive disorder in patients with chronic pain*. Pain 2001; 91(3): 227–234.
34. Peveler R, Katona C, Wessely S, Dowrick Ch. *Painful symptoms in depression: Under-recognised and under-treated?* Brit. J. Psychiat. 2006; 188(3): 202–203.
35. Morley S, Williams ACDC, Black S. *A confirmatory factor analysis of the Beck Depression Inventory in chronic pain*. Pain 2002; 99(1): 289–298.
36. Denk F, McMahon SB, Tracey I. *Pain vulnerability: A neurobiological perspective*. Nat. Neurosci. 2014; 17(2): 192–200.
37. Stahl SM. *Podstawy farmakologii. Teoria i praktyka*, Vol. 4. Gdansk: Via Medica; 2004.
38. Hashmi JA, Baliki MN, Huang L, Baria AT, Torbey S, Hermann KM et al. *Shape shifting pain: Chronification of back pain shifts brain representation from nociceptive to emotional circuits*. Brain 2013; 136(9): 2751–2768.
39. Bushnell MC, Čeko M, Low LA. *Cognitive and emotional control of pain and its disruption in chronic pain*. Nat. Rev. Neurosci. 2013; 14(7): 502–511.
40. Ressler KJ, Mayber HS. *Targeting abnormal neural circuits in mood and anxiety disorders: From the laboratory to the clinic*. Nat. Neurosci. 2007; 10(9): 1116–1124.
41. Kross E, Berman MG, Mischel W, Smith EE, Wager TD. *Social rejection shares somatosensory representations with physical pain*. P. Natl. Acad. Sci. USA. 2011; 108(15): 6270–6275.
42. Eisenberger NI, Lieberman MD, Williams KD. *Does rejection hurt? An fMRI study of social exclusion*. Science 2004; 302(5643): 290–292.
43. Mico JA, Ardid D, Berrocoso E, Eschalier A. *Antidepressants and pain*. Trends Pharmacol. Sci. 2006; 27(7): 348–354.

44. Kroenke K, Krebs EE, Bair MJ. *Pharmacotherapy of chronic pain: A synthesis of recommendations from systematic reviews*. Gen. Hosp. Psychiat. 2009; 31(3): 206–219.
45. Leo RJ, Dewani S. *A systematic review of the utility of antidepressant pharmacotherapy in the treatment of vulvodynia pain*. J. Sex. Med. 2013; 10(10): 2497–2505.
46. Leo RJ. *A systematic review of the utility of anticonvulsant pharmacotherapy in the treatment of vulvodynia pain*. J. Sex. Med. 2013; 10(8): 2000–2008.
47. De Andres J, Sanchis-Lopez N, Asensio-Samper JM, Fabregat-Cid G, Villanueva-Perez VL, Monsalve Dolz V et al. *Vulvodynia – An evidence-based literature review and proposed treatment algorithm*. Pain Pract. 2016; 16(2): 204–236.
48. Pasek J, Baszak-Radomańska E, Nowosad M, Błazik L, Sieroń A. *Wulwodynia jako zespół bólowy spowodowany dysfunkcją mięśni dna miednicy*. Annales Academiae Medicae Silesiensis. 2015; (69): 49–53.
49. Spoelstra SK, Borg C, Weijmar Schultz WC. *Anticonvulsant pharmacotherapy for generalized and localized vulvodynia: A critical review of the literature*. J. Psychosom. Obst. Gyn. 2013; 34(3): 133–138.
50. Brown CS, Foster DC, Wan JY, Rawlinson LA, Bachmann GA. *Rationale and design of a multicenter randomized clinical trial of extended release gabapentin in provoked vestibulodynia and biological correlates of response*. Contemp. Clin. Trials. 2013; 36(1): 154–165.
51. Yasmin S, Carpenter LL, Leon Z, Siniscalchi JM, Price LH. *Adjunctive gabapentin in treatment-resistant depression: A retrospective chart review*. J. Affect. Disorders 2001; 63(1): 243–247.
52. Maurer I, Volz H, Sauer H. *Gabapentin leads to remission of somatoform pain disorder with major depression*. Pharmacopsychiatry 1999; 32(6): 255–257.
53. Harden CL, Lazar LM, Pick LH, Nikolov B, Goldstein MA, Carson D et al. *A beneficial effect on mood in partial epilepsy patients treated with gabapentin*. Epilepsia 1999; 40(8): 1129–1134.
54. Ghaemi SN, Goodwin FK. *Gabapentin treatment of the non-refractory bipolar spectrum: An open case series*. J. Affect. Disorders 2001; 65(2): 167–171.
55. Wang PW, Santosa C, Schumacher M, Winsberg ME, Strong C, Ketter TA. *Gabapentin augmentation therapy in bipolar depression*. Bipolar Disord. 2002; 4(5): 296–301.
56. Vieta E, Martinez-Aran A, Nieto E, Colom F, Reinares M, Benabarre A et al. *Adjunctive gabapentin treatment of bipolar disorder*. Eur. Psychiat. 2000; 15(7): 433–437.
57. Frye MA, Ketter TA, Kimbrell TA, Dunn RT, Speer AM, Osuch EA et al. *A placebo-controlled study of lamotrigine and gabapentin monotherapy in refractory mood disorders*. J. Clin. Psychopharm. 2000; 20(6): 607–614.
58. Obrocea GV, Dunn RM, Frye MA, Ketter TA, Luckenbaugh DA, Leverich GS et al. *Clinical predictors of response to lamotrigine and gabapentin monotherapy in refractory affective disorders*. Biol. Psychiat. 2002; 51(3): 253–260.
59. Pande AC, Crockatt JG, Janney CA, Werth JL, Tsaroucha G. *Gabapentin in bipolar disorder: A placebo-controlled trial of adjunctive therapy*. Bipolar Disord. 2000; 2(3p2): 249–255.
60. Pande AC, Davidson JR, Jefferson JW, Janney CA, Katzelnick DJ, Weisler RH et al. *Treatment of social phobia with gabapentin: A placebo-controlled study*. J. Clin. Psychopharm. 1999; 19(4): 341–348.
61. Clarke H, Kirkham KR, Orser BA, Katznelson R, Mitsakakis N, Ko R et al. *Gabapentin reduces preoperative anxiety and pain catastrophizing in highly anxious patients prior to major surgery: A blinded randomized placebo-controlled trial*. Can. J. Anesth. 2013; 60(5): 432–443.

62. Tirault M, Foucan L, Debaene B, Frasca D, Lebrun T, Bernard JC et al. *Gabapentin premedication: Assessment of preoperative anxiolysis and postoperative patient satisfaction*. Acta Anaesthesiol. Belg. 2010; 61(4): 203.
63. Boschen MJ. *A meta-analysis of the efficacy of pregabalin in the treatment of generalized anxiety disorder*. Can. J. Psychiat. 2011; 56(9): 558–566.

Address: Ewelina Soroka
2nd Department of Psychiatry and Psychiatric Rehabilitation,
Medical University of Lublin
20-439 Lublin, Głuska Street 1