Case report

mucosa

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Is vulvar purpura a component of plasma cell vulvitis or mucosal porosis?

Vulvar purpura plazma hücreli vulvit ya da mukozal porozun bir komponenti olabilir mi?

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Abstract

Here, we presented six women with isolated vulvar purpura. No associated lesions such as sclerosis, atrophy, or hypopigmentation were observed. All patients were in postmenopausal period. In this case series, we discussed if a non-blanching purpura could be a component of plasma cell vulvitis or "mucosal porosis". The possibility of vulvar purpura was questioned as a mucosal equivalent of dermatoporosis which is an age-related degenerative process in the skin. While senile purpura is one of the morphological findings of dermatoporosis, vulvar purpura might be a part of "mucosal porosis". Rapid response to topical estrogen was remarkable in all patients.

Key words: *dermatoporosis, mucosa, plasma cell vulvitis, porosis, purpura, vulva*

Öz

Bu yazıda, izole vulvar purpurası olan altı hastayı sunduk. Hiçbir hastada eşlik eden skleroz, atrofi ya da hipopigmentasyon gibi bulgular gözlenmedi. Hastaların tümü postmenopozal dönemde idi. Bu vaka serisinde, vulvada görülen purpurik lezyonların plazma hücreli vulvitin bir komponenti ya da yeni bir antite "mukozal poroz" olma olasılığını tartıştık. Vulvada görülen purpuranın, yaşlanmaya bağlı olarak deride tanımlanan dermatoporozun "mukozal" eşdeğeri olabileceği fikri ilginç olabilir. Senil purpura, dermatoporozun morfolojik bir bulgusu ise, belki de vulvar purpura mukozal porozun bir göstergesidir. Tüm hastalarda topikal östrojenle hızlı bir düzelme gözlenmesi bu teoriyi destekler niteliktedir.

Anahtar kelimeler*: dermatoporoz, menopoz, mukoza, plazma hücreli vulvit, poroz, purpura, deri, vulva*

Introduction

Although vulvar purpura is mostly observed as a component of lichen sclerosus (LS), it has been also associated with plasma cell vulvitis (Zoon's vulvitis) (PCV),[1,2] PCV-lichen aureus overlap,[3] and chronic intrapelvic conges-

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tion with increased venous pressure possibly due to abdominal ptosis.[4]

Dermatoporosis is an umbrella term to define degenerative changes in the aged skin such as senile purpura, stellate pseudoscars, skin atrophy and laceration, and dissecting hematomas as well. Different mechanisms might have a role in the development of dermatoporosis.[5] Here, we presented six cases with isolated vulvar purpura and discussed the possibility of "vulvar mucosal porosis". However, it is crucial to consider if those cases were plasma cell vulvitis (PCV) which is a well-known entity with proposed criteria by Virgili et al.[1]

Case reports

Some characteristics of patients were summarized in Table 1. The patients were examined by both a dermatologist and a gynaecologist in the Vulvar Clinic. They were referred from Gynaecology Clinic. All patients had similar dermatologic findings characterized by non-blanching yellow-red, macular purpuric lesions in the introitus and/or the inner labia minora (Figs. 1a, 2a and 3) (Table 1). Oral mucosa and skin examinations were normal. HIV serology was negative in all patients. Case 3 denied biopsy, cases 4, 5 and 6 denied both photography and biopsy. They all were treated with topical estriol cream once a day for 2 weeks, then twice a week for 3 months.

Informed consents were obtained in all six patients.

Case 1

A 57-year-old female was seen with the complaint of progressive vulvar discoloration (Fig. 1a), dyspareunia, and mild pruritus for one year. Fasting glucose and HbA1c were 138 mg/dl (N: 74-106 mg/dl) and 6.6% (N: 4-6%), respectively. A punch biopsy was taken from the purpuric area. Histopathology showed focal atrophy at the epithelium, dense plasma cell infiltration, erythrocyte extravasation and congestion in the lamina propria. In addition, the Lozenge shape keratinocytes were obtained at the epithelium. There was a dense plasma cell infiltration which consists of more than 50% of the cells in the lamina propria with CD-38 immunohistochemical staining. These findings were obtained in the focal area (Figs. 1b and 1c). Le-

Table 1. Clinical and laboratory characteristics of the patients

	Menopause	Location	Associated symptoms/findings	Comorbidity	Laboratory*
Case 1 Age 57	8 years	Introitus	Dyspareunia Mild pruritus	DM	Glucose ↑ HbA1C ↑ Others: N
Case 2 Age 50	5 months	Introitus	Pruritus	DM	N
Case 3 Age 48	1 year	Introitus	Pruritus	DM	Insulin ↑ Others: N
Case 4 Age 54	5 years	Introitus Inner aspects of labia minora	Dyspareunia Fissuration	No	N
Case 5 Age 57	7 years	Introitus	No	DM HT	N
Case 6 Age 52	4 years	Introitus	No	HT Cholecystectomy	N

* Fasting glucose, HbA1C, complete blood count, sedimentation rate, hepatic and renal functions, coagulation tests, Hepatitis B, C and HIV serologies; DM, Diabetes mellitus; HT, Hypertension

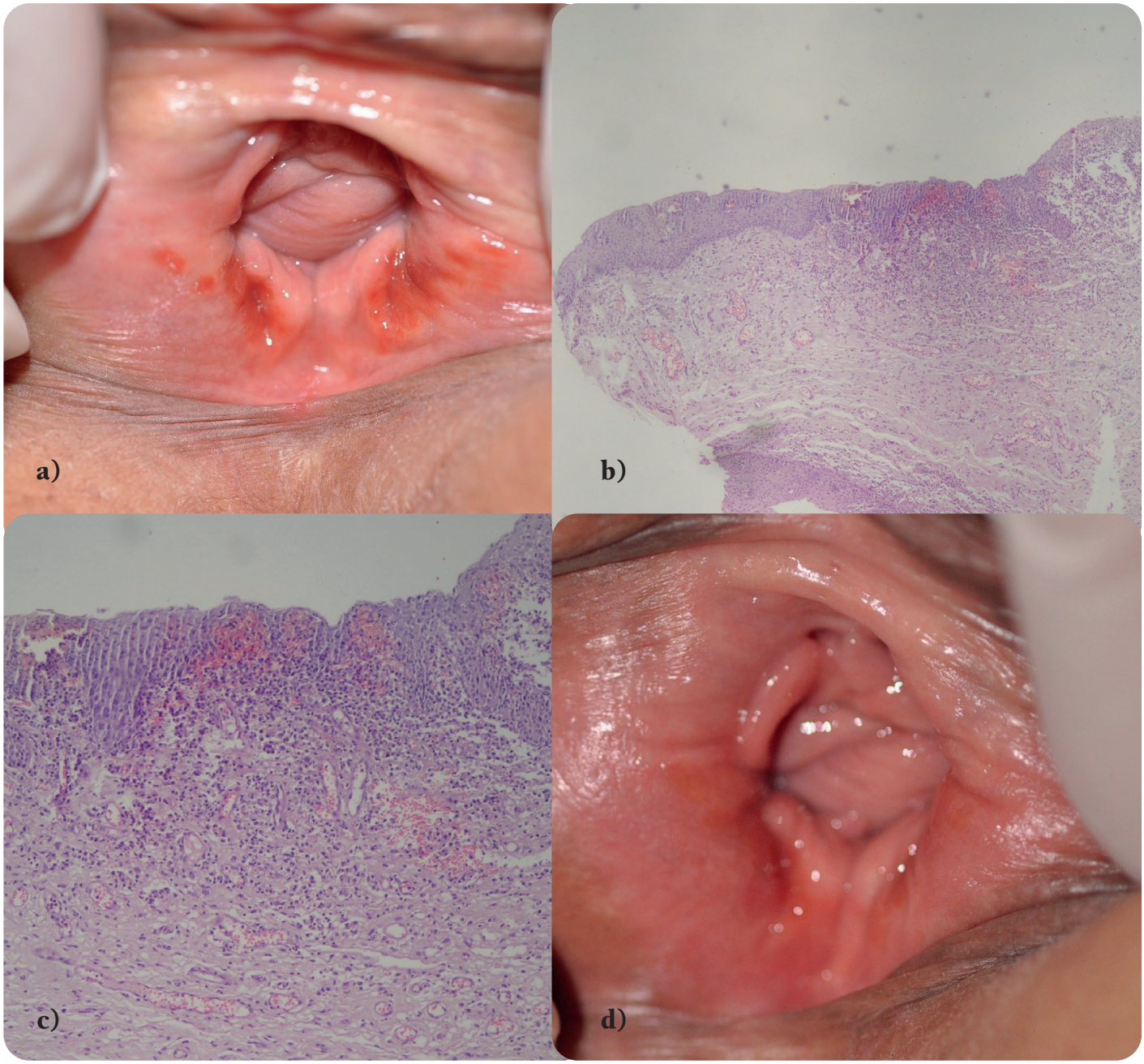

Fig. 1a. Vulvar purpuric discoloration, **1b.** Focal atrophy at the epithelium, dense plasma cell infiltration, erythrocyte extravasation and congestion in the lamina propria. (H.E.x4) **1c.** A dense plasma cell infiltration which consists of more than 50% of the cells in the lamina propria with CD-38 immunohistochemical staining. (H.E.x40) **1d.** Subsided lesions two weeks later with topical estrogen cream

sions subsided in the 2nd week of follow-up with estrogen cream (Fig. 1d).

Case 2

A 50-year-old female was referred for genital pruritus. Dermatologic examination was also consistent with lichen simplex chronicus in the supraclitoral area. Her past medical history was remarkable for diabetes mellitus. Histopathology of a punch biopsy showed similar findings except more atrophy in the epithelium than Case 1 (Fig. 2b). CD-38 staining showed plasma cells consisted of nearly 40% of whole infiltration (Fig.

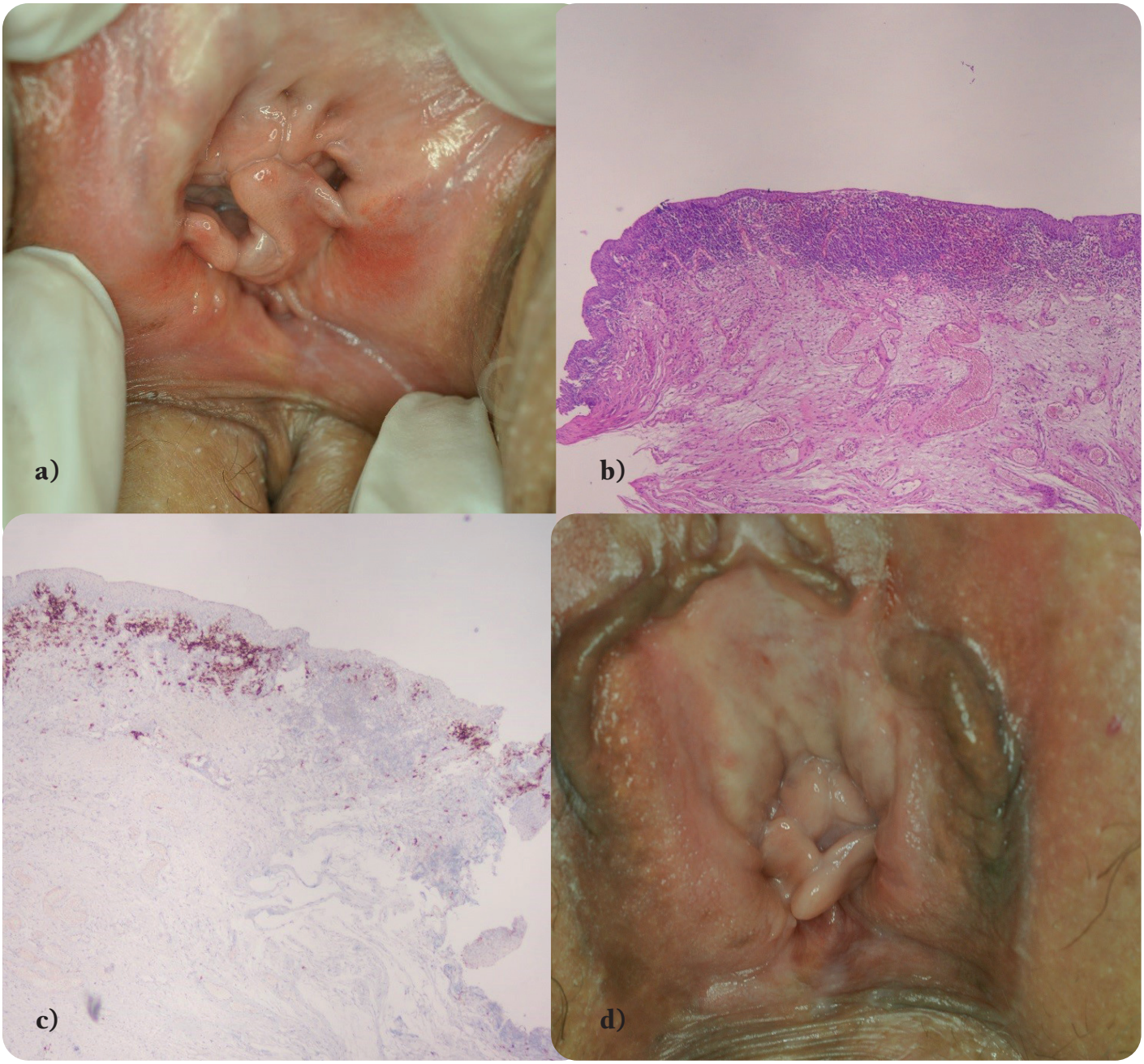

Fig. 2a. Vulvar purpuric discoloration **2b.** More atrophic epithelium and similar findings with case 1. (H.E.x4) **2c.** CD-38 staining showed plasma cells consisted of nearly 40% of whole infiltration (H.E.x40) **2d.** Almost clear examination two weeks later with topical estrogen

2c). The patient was lesion free in the 2nd week of follow-up with topical estrogen (Fig. 2d).

Case 3

A 48-year-old female was referred for genital pruritus. Dermatologic examination was also consistent with lichen simplex chronicus in the labium majus. Her past medical history was remarkable for diabetes mellitus. The patient had no lesion in the 3rd week of follow-up with topical estrogen.

Case 4

A 54-year-old female presented with dyspareunia and burning of the vulva started one year ago. A fissure

was also noticed in the lower part of the vulva in addition to purpuric lesions mentioned above. The lesions were disappeared after one month of treatment with estrogen cream.

Case 5

A 57-year-old female was referred for asymptomatic vulvar lesions. The patient was lesion-free after being treated with estrogen cream for two months.

Case 6

A 52-year-old female was referred for asymptomatic, purplish lesions in the vulva. The patient was lesion-free in 2nd month of applying estrogen cream.

Discussion

"Dermatoporosis" is a similar entity as osteoporosis defining a chronic fragility syndrome in the aging skin.[5] It is seen in elderly usually after the age of 60. Potential underlying mechanisms of fragile skin in dermatoporosis might be related to loss of extracellular matrix (ECM), alterations in skin viscoelasticity, ultraviolet light (UVL)-mediated effects, and hyaluronate-and CD44-dependent growth factor signalization defects.[5] Senile purpura is one of the morphological markers of dermatoporosis and results from spontaneously or repetitive minimal trauma causing dermal haemorrhage in the absence of coagulation defects.[5] Although mucosal equivalent of dermatoporosis has not been previously reported, it is likely that all the mentioned mechanisms except for the effect of UVL may cause vulvar degenerative process. Estrogen deficiency due to menopause might have an additional contributing factor for vulva. Therefore, "vulvar mucosal porosis" is a reasonable term to define vulvar degenerative changes such as purpura seen in our patients. Vulvar purpura might be a mucosal type of senile purpura classified as a morphological type of dermatoporosis. Frictional trauma together with postmenopausal atrophy and vulvar xerosis may induce purpura. The presence of introitus involvement (all cases) and dyspareunia (two cases) suggest that coitus might be a contributing trauma as well.

Presented cases were between the ages of 48 and 57 years (Table 1). Considering dermatoporosis starts after the age of 60 years,[5] it is reasonable to hypothesize that mucosal fragility may develop earlier than skin. Furthermore, decreased physical activity and sexual intercourse in elderly may decrease frictional trauma and subsequent purpura.

Vulvar purpura is mostly observed as a component of LS. Unlike LS, none of our patients had sclerosis, atrophy, and hypopigmentation. Of interest, our patients only presented with nonpalpable purpura contrary to Henoch-Schönlein vasculitis. All patients denied prior usage of systemic or topical steroid, which could also cause cutaneous purpura. Interestingly, lichen aureus associated with PCV was reported as a rare cause of localized purpura in the vulva.[3] Authors emphasized trauma might have a possible role of both entities.[3] In consideration to the similarities with PCV, it is questionable if mucosal porosis is a real entity (Table 2). PCV is a rare but well-known entity of ISSVD (International Society for The Study of Vulvovaginal Disease) classification, whereas mucosal porosis is a hypothesis we suggest as a result of a degenerative process. We presented six cases totally with three cases had a clinical picture and only two had histopathological examination. Clinical similarities and rapid efficacy of topical estrogen in all six patients might support and raise a question the possibility of a new entity (Table 2). Histopathological findings in our patients should be interpreted scrupulously. Although Virgili et al.[1,2] defined histopathologic criteria in PCV and emphasized plasma cell infiltration should be more than 25%, plasma cell infiltration could be less than usual as in some cases of plasma cell balanitis.[6] We found dense lichenoid subepithelial infiltrate composed largely (more than 50% in the first case, 40% in the second case) of plasma cells. Our findings obtained in the epithelium and the lamina propria at the focal area. Virgili et al.[1] also proposed erythrocyte extravasation is not a specific finding of PCV, since micro trauma or biopsy may induce it. Instead, they emphasized the importance of hemosiderin deposition which we did not observe.[1] Focal concurrence of both epithelial atrophy and

Table 2. Detailed comparison of the features of plasma cell vulvitis and our patients

	Plasma cell vulvitis (PCV)	Presented cases
Age of diagnosis	54.9 (49-74)	53 (48-57)
Symptoms	Asymptomatic (16.7%)[2] Pruritus (44.4%)[2] Dyspareunia (52.8%)[2] Burning (80.6%)[2]	Asymptomatic (2 cases) Pruritus (3 cases) Dyspareunia (2 cases)
Clinical features	Solitary sharply defined red-brown glistening patch, 1-3 cm Occasionally multiple, pinpoint purpuric spots and erosive lesions	Bilateral, macular non-blanching purpuric, yellow-red patches
Locations	Mainly inner surface of labia minora and periurethral area. Introitus can be involved	Introitus (6 cases) Inner surface of the labia minora (2 cases)
Histopathology		
Epithelial atrophy	Yes (13/18)[1]	Focal in inflammatory area, acanthosis in noninflammatory area (Case 1,2)
% plasma cell infiltration	Yes ≥50%: 11/18[1] 25-50: 5/18[1] <25%: 2/18[1]	Focal >50% (Case 1) ~%40 (Case 2)
Lozenge-shaped keratinocytes	2/18[1]	1/2
Slight spongiosis	Yes[1]	No (Case 1,2)
Vascular dilation	Yes[1]	Yes (Case 1,2)
Erythrocyte extravasation	Nonspecific[1]	Yes (case 1,2)
Hemosiderin deposition	Yes (15/18)[1]	No (Case 1,2)
Treatment	Lack of evidence for estrogen efficacy Estrogen as a treatment only in one study (improvement in only 16% of 36 patients)	Rapid improvement with topical estrogen in all patients

inflammation has not been mentioned in PCV. All of these histopathological findings seen in Case 1 and 2 could be a feature of a degenerative process (Table 2).

We observed a rapid improvement with topical estrogen in all patients. PCV has a chronic course and no effective treatment regimens have been established.[2] Topical steroids and calcineurin inhibitors are effective improving PCV symptoms rather than clinical signs.[7] There is no evidence estrogen is effective in PCV, although Virgili et al.[2] found estrogen is effective in only 16% of 36 PCV patients. Li et al.[3] reported topical estrogen increased the lesions in their PCV and lichen aureus overlap case, and they suggested this could be due to delayed type hypersensitivity reaction. Topical and systemic estrogens have not been mentioned for the treatment of dermatoporosis since there is no data about estrogen deficiency in dermatoporosis. However, estrogen might be the only reasonable agent

in estrogen-sensitive areas such as vulva in mucosal porosis.

Genitourinary syndrome of menopause (GSM) is a relatively new term describing signs and symptoms of genital, sexual and lower urinary tract of menopause. Tissue fragility, fissures and petechia have been reported among the signs of GSM.[8] Unlike our observation in patients, those symptoms are progressive and do not to resolve spontaneously.[9] Although changes of vaginal mucosa were well-described, vulvar histopathological findings were not mentioned. Nevertheless, vulvar porosis may basically define the similar entity of this spectrum with histopathological findings.

In conclusion, vulvar purpura in postmenopausal women may result from different mechanisms. Firstly, clinicians should exclude LS as an important cause of vulvar purpura. PCV is another cause. In case of an isolated vulvar purpura, decreased estrogen levels leading to vulvovaginal atrophy and xerosis may have a contributing role as in dermatoporosis. We are aware of the tendency of ISSVD to simplify and clarify the diagnostic categories of vulvar conditions. Suggestion of a new diagnostic category will need to be extremely well defined, including multiple histopathologic and gross examples, and describe a clear pathophysiologic mechanism to be considered as a novel category. However, these cases did not show an exact match for PCV or another entity. Mucosal porosis might be resulted in the presence of estrogen deficiency and contributing comorbidities such as diabetes mellitus (four cases) (Table 1). Further reports particularly ultra structural ones as in the study of Kaya et al.[5] in dermatoporosis might reveal if mucosal porosis is a novel entity or associated or a triggering factor of PCV. Vulvar purpura or "vulvar mucosal porosis" may be a common but neglected entity due to its minor symptoms or asymptomatic character mostly.

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