DOI: 10.2478/sjdv-2025-0007

MELANOM I KARCINOM DOJKE – ISTRAŽIVANJE RETKE, ALI ZNAČAJNE KLINIČKE POVEZANOSTI – PRIKAZ SLUČAJA
MELANOMA AND BREAST CANCER – EXPLORING UNCOMMON BUT EMERGING CLINICAL ASSOCIATION – CASE REPORT

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UDK 616-006.81:618.19-006.6

Sažetak

Uvod. *Koegzistencija melanoma i karcinoma dojke predstavlja retku, ali klinički značajnu povezanost sa potencijalnim zajedničkim genetskim i hormonskim mehanizmima.* ***Prikaz slučaja.*** *Žena starosti 64 godine sa hormonski receptor–pozitivnim invazivnim duktalnim karcinomom desne dojke (HG2, ER Allred 8, PR Allred 7, HER2 1+, Ki-67 10%), lečena letrozolom i ribociklibom, razvila je diseminovanu papuloznu erupciju na trupu tokom palijativne radioterapije. Histopatološki pregled potvrdio je interfejs dermatitis u skladu sa lekom indukovanom kožnom reakcijom, koja se u potpunosti povukla uz primenu topikalne terapije. Istovremeno je u lumbosakralnoj regiji uočena pigmentovana lezija nepravilnih ivica, dermoskopski visokosuspektna na melanom, što je uslovilo upućivanje na široku lokalnu reeksciziju i biopsiju sentinelnog limfnog čvora.* ***Zaključak.*** *Ovaj prikaz naglašava važnost rutinskog dermatološkog pregleda kod pacijentkinja sa karcinomom dojke, radi ranog otkrivanja melanoma i adekvatnog multidisciplinarnog zbrinjavanja.*
Ključne reči: *melanom; tumori dojke; radioterapija; dermatitis; dermoskopija; rana dijagnoza tumora; klinički značaj; povezanost*

Abstract

Introduction. The coexistence of melanoma and breast cancer represents a rare but clinically significant association, potentially driven by shared genetic and hormonal mechanisms. **Case Report.** A 64-year-old woman with hormone receptor–positive invasive ductal carcinoma of the right breast (HG2, ER Allred 8, PR Allred 7, HER2 1+, Ki-67 10%), treated with letrozole and ribociclib, developed a disseminated papular eruption on the trunk during palliative radiotherapy. Histopathological examination confirmed interface dermatitis consistent with a treatment-related cutaneous reaction, which resolved completely with topical therapy. During the same evaluation, a pigmented lesion with irregular borders was identified in the lumbosacral region and was dermoscopically highly suspicious for melanoma, prompting referral for wide local reexcision and sentinel lymph node biopsy. **Conclusion.** This case underscores the importance of routine dermatologic examination in patients with breast cancer in order to facilitate early detection of melanoma and ensure appropriate multidisciplinary management.
Key words: Melanoma; Breast Neoplasms; Radiotherapy; Dermatitis; Dermoscopy; Early Diagnosis of Cancer; Clinical Relevance; Association

Uvod

Koegzistencija melanoma i karcinoma dojke, ranije smatrana retkom pojavom, danas se prepoznaje kao klinički značajniji fenomen nego što se pretpostavljalo. Ovi maligniteti neke zajednicke epidemiološke i biološke karakteristike, uključujući genetsku predispoziciju, hormonske uticaje i poremećaje imunološke regulacije. Mutacije gena kao što su BRCA2, CDKN2A (p16) i TP53 učestvuju u patogenezi oba tumora, dok estrogenski uticaji i faktori sredine dodatno povećavaju rizik. Koegzistencija se opisuje u 1–3% pacijenata, uz blago povećan obostrani rizik. Prepoznavanje ovog preklapanja važno je za praćenje pacijenata, genetsko savetovanje i terapijsko planiranje [1–4].

Prikaz slučaja

Prikazujemo slučaj 64-godišnje pacijentkinje koja se u oktobru 2025. godine javila na dermatološku konsultaciju zbog promena u vidu diseminovanih eritematoznih, jasno ograničenih papula lokalizovanih na trupu. Kliničkim pregledom i uvidom u medicinsku dokumentaciju utvrđeno je da je pacijentkinji prethodno dijagnostikovan invazivni karcinom desne dojke. Core needle biopsija potvrdila je invazivni duktalni karcinom, histološki gradus 2 (HG2). Imunohistohemijskim ispitivanjem utvrđeni su ER Allred skor 8, PR Allred skor 7, HER2 1+, uz Ki-67 proliferacioni indeks od 10%, što je u skladu sa biološkim profilom luminalnog tipa.

U skladu sa smernicama za lečenje hormonski receptor-pozitivnog karcinoma dojke, započeta je terapija letrozolom u kombinaciji sa CDK4/6 inhibitorom ribociklibom. Pacijentkinja je navela podatke o prethodnim reakcijama preosetljivosti na aspirin i metamizol.

Sedam dana pre pojave promena na koži započela je palijativnu radioterapiju torakalne kičme (segmenti Th3–Th10, ukupna doza 20 Gy u 5 frakcija, 3D tehnika), sa planiranom nastavnom iradijacijom regiona L3 i sakralne oblasti, uključujući obostrane sakroilijačne zglobove istim protokolom.

Međutim, dalji tok radioterapije privremeno je obustavljen nakon naglog razvoja diseminovanih jasno ograničenih eritematoznih papula na trupu, što je pobudilo sumnju na potencijalnu terapijski izazvanu kožnu reakciju ili paraneoplastičnu manifestaciju. Urađena je biopsija reprezentativne lezije. Histopatološki nalaz ukazao je na promene u vidu inter-

Introduction

The coexistence of melanoma and breast cancer, once considered uncommon, is now increasingly recognized as a clinically relevant association. These malignancies share several epidemiologic and biological features, including genetic susceptibility, hormonal influences, and alterations in immune regulation. Mutations in genes such as BRCA2, CDKN2A (p16), and TP53 contribute to the pathogenesis of both tumors, while estrogen exposure and environmental factors may further increase risk. The co-occurrence of these malignancies has been reported in approximately 1–3% of patients, with a modest bidirectional increase in incidence. Recognition of this overlap is essential for optimizing surveillance strategies, genetic counseling, and individualized therapeutic decision-making [1–4].

Case Report

We present the case of a 64-year-old woman who sought dermatologic consultation in October 2025 due to multiple erythematous, firm, non-tender papules on the trunk. Clinical evaluation and a detailed review of her medical history revealed that the patient had previously been diagnosed with invasive carcinoma of the right breast. Core needle biopsy performed on November 1, 2024 confirmed invasive ductal carcinoma, histological grade 2 (HG2). Immunohistochemical analysis demonstrated ER Allred score 8, PR Allred score 7, HER2 1+, and a Ki-67 proliferation index of 10%, consistent with luminal-type tumor biology.

In accordance with current guidelines for the treatment of hormone receptor–positive breast cancer, the patient initiated therapy with letrozole in combination with a CDK4/6 inhibitor ribociclib. The patient also reported a history of hypersensitivity reactions to aspirin and metamizole.

Seven days prior to the onset of cutaneous manifestations, the patient had begun palliative radiotherapy targeting the thoracic spine (segments Th3–Th10) with a total dose 20 Gy delivered in five fractions using a 3D technique. Continuation of radiotherapy to L3 and the sacral region, including the bilateral sacroiliac joints, was planned using the same regimen.

However, the scheduled radiotherapy course was temporarily suspended following the sudden appearance of multiple erythema-

face dermatitisa lihenoidnog tipa. Uvedena je lokalna terapija kortikosteroidima, nakon čega je došlo do potpunog povlačenja kožnih manifestacija, što je omogućilo nastavak planiranja onkološkog lečenja.

Tokom iste konsultacije, uočena je pigmentovana ploča u lumbalnoj regiji ***(Slika 1).*** *Dermoskopski pregled pokazao je izraženu asimetriju sa atipičnom pigmentnom mrežom, radijalnim linijama i naglašenim radijalnim širenjem, uz prisustvo plavobelog vela, što je ukazivalo na visoku sumnju na melanom* ***(Slika 2)****. Pacijentkinja je hitno upućena na hiruršku ekscisiju lezije. Histopatološka analiza potvrdila je superficijalno širući melanom, Clark nivo II, Breslow debljina 1,2 mm, stadijum pT2a* ***(Slika 3)****. U skladu sa preporukama za lečenje melanoma, pacijentkinja je potom upućena na široku lokalnu reekscisiju i biopsiju limfnog čvora straža (SLNB).*

Klinički gledano, nedovoljno prepoznavanje ove veze ima praktične posledice. Preživeli nakon karcinoma dojke retko se rutinski upućuju na dermatološki pregled, dok se kod obolelih od melanoma retko koristi procena rizika specifična za karcinom dojke. Povećanje svesti o ovoj asocijaciji može doprineti ranijem otkrivanju, boljoj koordinaciji između različitih specijalnosti i unapređenju genetskog savetovanja.

Diskusija

Koegzistencija melanoma i karcinoma dojke i dalje nije široko prepoznata u kliničkoj praksi. Iako su oba maligniteta pojedinačno česta, njihova istovremena pojava kod istog pacijenta često se smatra slučajnom i stoga se nedovoljno razmatra u dijagnostičkom i terapijskom procesu. Najnoviji podaci ukazuju da povezanost ova dva tumora može biti značajnija nego što se ranije pretpostavljalo, što naglašava potrebu za većom pažnjom među onkolozima, dermatolozima i lekarima za genetsko savetovanje [1–3].

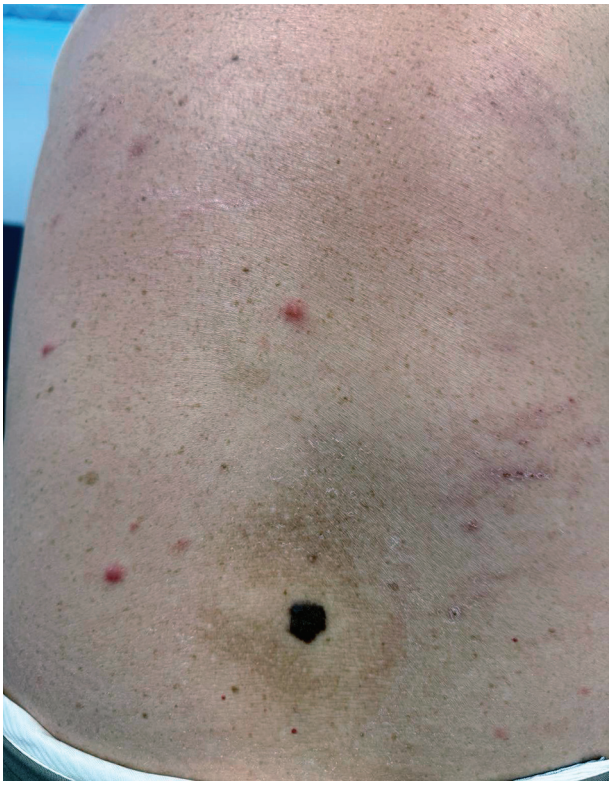
Nekoliko zajedničkih mehanizama može doprineti ovoj asocijaciji. Germinativne varijante gena BRCA2, CDKN2A (p16) i TP53 mogu povećati predispoziciju za razvoj oba tumora [4–8].

U porodicama sa BRCA2 mutacijama opisan je blago povećan rizik za melanom [5], dok su CDKN2A mutacije – najpoznatije po ulozi u hereditarnom melanomu – takođe identifikovane kod pacijentkinja sa karcinomom dojke

tous papules on the trunk, raising concern for a possible treatment-related cutaneous adverse reaction or a paraneoplastic dermatologic manifestation. A targeted dermatologic evaluation was performed, and a biopsy of a representative lesion was obtained.

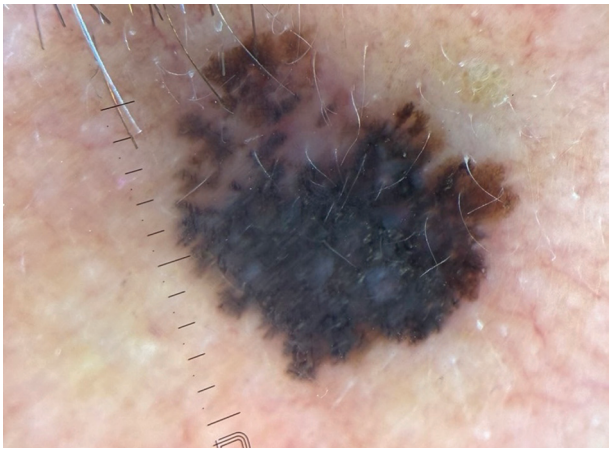
Histopathological examination demonstrated findings consistent with lichenoid interface dermatitis, thereby excluding a paraneoplastic process. The patient initiated topical corticosteroid therapy, which resulted in complete clinical resolution of the lesions, allowing continuation of the planned oncologic treatment.

During the same dermatologic consultation, a pigmented plaque in the lumbar region was incidentally identified **(Figure 1)**. Dermoscopic examination revealed marked asymmetry, an atypical pigment network, radial



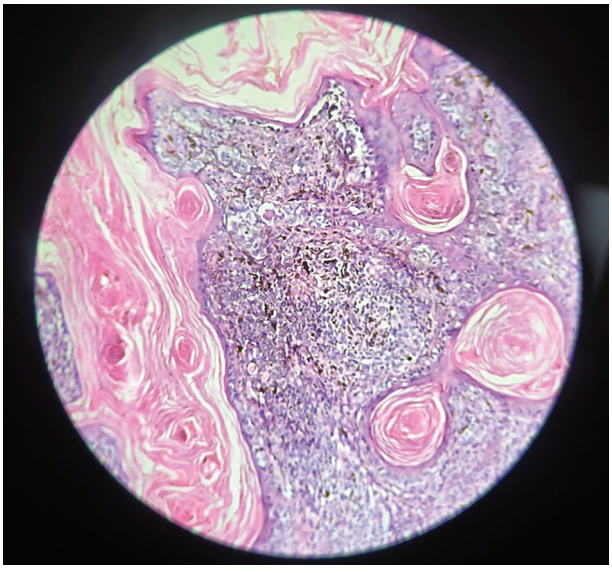
Slika 1. *U predelu lumbosakralne regije tamnosmeđi plak nepravilnog oblika promera oko 1.5 cm neravnih ivica, visoko suspektan za melanom.*

Figure 1. In the lumbosacral region, a dark-brown plaque of irregular shape and uneven borders, measuring approximately 1.5 cm in diameter, highly suggestive of melanoma



Slika 2. *Dermoskopski pregled pigmentne promene na leđima. Asimetrija sa atipičnom mrežom pigmenata, radijalnim linijama i izraženim radijalnim strujanjem, uz prisustvo plavobelog vela.*
Figure 2. Dermoscopic examination of the pigmented lesion on the back. Asymmetry with an atypical pigment network, radial lines and prominent radial streaming (-), with the presence of a blue-white veil (*)

[7]. Uprkos ovim nalazima, genetski paneli namenjeni proceni rizika za melanom retko uključuju gene vezane za karcinomdojke, što ukazuje na nedovoljno integrisan pristup genetskoj evaluaciji.



Slika 3. *Histopatološki potvrđen melanom, HE bojenje, uvećanje x100*
Figure 3. Histopathologically confirmed melanoma, H&E staining, ×100 magnification

lines with prominent radial streaming, and the presence of a blue-white veil, all highly suggestive of melanoma **(Figure 2)**. The patient was promptly referred for surgical excision of the lesion. Histopathological analysis **(Figure 3)** confirmed superficial spreading melanoma, Clark level II, with a Breslow thickness of 1.2 mm, corresponding to stage pT2a. In accordance with established melanoma management guidelines, the patient was subsequently referred for wide local re-excision and sentinel lymph node biopsy (SLNB).

Discussion

The coexistence of melanoma and breast cancer remains insufficiently recognized in routine clinical settings. Although both malignancies are common individually, their occurrence in the same patient has traditionally been regarded as coincidental and has therefore received limited attention. However, recent studies suggest that the relationship between these cancers may be stronger than previously assumed, highlighting the need for increased awareness among clinicians involved in oncologic care [1–3].

Several shared biological mechanisms may contribute to this association. Inherited pathogenic variants in *BRCA2*, *CDKN2A (p16)*, and *TP53* has been implicated in the development of both malignancies [4–8]. Families carrying BRCA2 mutations demonstrate a modestly increased risk of melanoma [5], while CDKN2A mutations, classically associated with hereditary melanoma syndromes, have also been reported in patients with breast cancer [7]. Despite this genetic overlap, contemporary genetic testing panels for melanoma rarely include genes typically associated with breast cancer susceptibility, underscoring an important gap in current genetic evaluation strategies.

Hormonal and immunologic factors may also contribute to the observed association. Estrogen signaling pathways, which play a key role in breast cancer pathogenesis, can stimulate melanocyte proliferation and may influence melanoma development and progression [9,10]. Furthermore, breast cancer treatments – including radiotherapy and systemic therapies – may modify local immune responses within the skin, potentially increasing susceptibility to the development of a sec-

Hormonski i imunološki faktori takođe mogu imati ulogu. Estrogenski signalni putevi, ključni u patogenezi karcinoma dojke, mogu stimulisati proliferaciju melanocita i potencijalno uticati na biološko ponašanje melanoma [9,10]. Pored toga, onkološke terapije poput radioterapije i sistemskih tretmana mogu narušiti kožnu imunološku homeostazu, što u određenim situacijama može povećati rizik za nastanak drugog primarnog melanoma, iako su podaci koji to potvrđuju još ograničeni [3,10]. Ove interakcije nisu u potpunosti obuhvaćene postojećim smernicama iz oblasti onkologije i dermatologije.

Zaključak

Iako je koegzistencija melanoma i karcinoma dojke retka, verovatno je nedovoljno prepoznata i dijagnostikovana. Prepoznavanje ove povezanosti važno je za sveobuhvatno onkološko zbrinjavanje jer zajednički molekularni i hormonski mehanizmi mogu doprineti unapređenju strategija nadzora i prevencije kod pacijenata sa rizikom.

ond primary melanoma, although current evidence remains limited [3,10].

The clinical implications of this relationship are significant. Breast cancer survivors are not routinely referred for dermatologic screening, while patients with melanoma are rarely evaluated using breast cancer–specific risk assessment tools. Greater recognition of this association could facilitate earlier diagnosis, improve interdisciplinary collaboration, and enhance genetic counseling and surveillance strategies.

Conclusion

Although the coexistence of melanoma and breast cancer is relatively rare, it is likely underrecognized in clinical practice. Awareness of this association is important for comprehensive oncologic care, as shared molecular and hormonal mechanisms may influence future strategies for surveillance, prevention, and personalized management.

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Received 24.12.2025.
Accepted 26.02.2026.

