LESER–TRÉLAT ZNAK KAO PARANEOPLASTIČNA MANIFESTACIJA MALIGNITETA: PREGLED LITERATURE

PREGLEDNI RAD

REVIEW ARTICLE

THE LESER–TRÉLAT SIGN AS A PARANEOPLASTIC MANIFESTATION OF MALIGNANCY: A REVIEW OF THE LITERATURE

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SAŽETAK

Uvod/Cilj: *Leser–Trélat* znak predstavlja paraneoplastičnu dermatozu koju karakteriše nagla i eruptivna pojava seboroičnih keratoza. Promene se najčešće javljaju u kratkom vremenskom intervalu, a često su praćene izraženim pruritusom, što dodatno skreće pažnju na mogućnost paraneoplastične etiologije. Patofiziološki mehanizam nije u potpunosti razjašnjen, ali se smatra da tumorske ćelije produkuju faktore rasta koji stimulišu proliferaciju keratinocita i dovode do naglog razvoja lezija. U literaturi se ovaj znak najčešće dovodi u vezu sa adenokarcinomima gastrointestinalnog trakta, među kojima se izdvaja adenokarcinom želuca, ali je opisana povezanost i sa drugim solidnim tumorima, kao i sa hematološkim malignitetima. Zbog moguće povezanosti sa neotkrivenom neoplazmom, pojava *Leser–Trélat* znaka zahteva ozbiljan klinički pristup i sistematsku dijagnostičku obradu, jer njegovo pravovremeno prepoznavanje može omogućiti otkrivanje osnovnog malignitetа u ranoj fazi bolesti. Cilj rada je analiza podataka iz dostupne literature o etiologiji, patogenezi i kliničkoj povezanosti *Leser–Trélat* znaka sa različitim malignitetima, kao i razmatranje njegovog dijagnostičkog i prognostičkog značaja u savremenoj kliničkoj praksi.

Metode: Izvršen je pregled literature pretragom baze podataka PubMed, pri čemu su obuhvaćeni dostupni originalni radovi, pregledni članci, prikazi slučaja i serije slučajeva. Pretraga je sprovedena korišćenjem sledećih ključnih reči: „Leser–Trélat sign", „paraneoplastic dermatosis", „seborrheic keratoses" i „malignancy".

Zaključak: Informisanje o *Leser–Trélat* znaku i multidisciplinarni pristup u otkrivanju njegove povezanosti sa malignitetima presudni su ranom otkrivanju neoplazmi. Prepoznavanje *Leser–Trélat* znaka može omogućiti dijagnostikovanje malignitetа u fazi kada je terapijski odgovor povoljniji, što značajno utiče na prognozu bolesti.

Ključne reči: seboroična keratoza, tumor, adenokarcinom

ABSTRACT

Introduction/Objective: The Leser–Trélat sign is a paraneoplastic dermatosis characterized by the sudden, eruptive appearance and rapid increase in number and size of multiple seborrheic keratoses, often accompanied by intense pruritus. This clinical presentation may raise suspicion of an underlying malignancy. Although its exact pathophysiological mechanism remains unclear, tumor-derived growth factors are believed to stimulate keratinocyte proliferation, contributing to the abrupt development of lesions. In the literature, the Leser–Trélat sign is most frequently associated with gastrointestinal adenocarcinomas, particularly gastric carcinoma, but it has also been reported in connection with other solid tumors and hematologic malignancies. Given its potential association with occult neoplasm, the appearance of the Leser–Trélat sign warrants a thorough clinical evaluation and systematic diagnostic workup, as timely recognition may facilitate early detection of the underlying malignancy. The aim of the paper is to analyze data from the available literature on the etiology, pathogenesis, and clinical associations of the Leser–Trélat sign with various malignancies, and to evaluate its diagnostic and prognostic significance in contemporary clinical practice.

Methods: A literature review was conducted using the PubMed database, including available original articles, review papers, case reports, and case series. The search was performed using the following keywords: "Leser–Trélat sign", "paraneoplastic dermatosis", "seborrheic keratoses", and "malignancy".

Conclusion: Awareness of the Leser–Trélat sign and a multidisciplinary approach to investigating its association with malignancies are crucial for the early detection of neoplasms. Recognition of the Leser–Trélat sign may enable the diagnosis of malignancy at a stage when therapeutic response is more favorable, thereby significantly improving disease prognosis.

Keywords: seborrheic keratosis, tumor, adenocarcinoma

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UVOD

Paraneoplastične dermatoze nalaze se na drugom mestu po učestalosti među svim paraneoplastičnim manifestacijama i mogu imati značajnu ulogu u ranom otkrivanju neoplazmi [1]. Često je, međutim, izuzetno izazovno odrediti uzročno-posledičnu vezu između visceralnog maligniteta i kožnih promena.

Leser–Trélat znak se izdvaja kao posebno značajan entitet u ovoj heterogenoj grupi dermatoza. On se manifestuje naglom pojavom i rapidnom proliferacijom seboroičnih keratoza [1,2]. One predstavljaju česte benigne kožne promene, posebno zapažene kod pacijenata starijih od 40 godina, sa porastom učestalosti u starijoj populaciji. Obično se manifestuju kao jasno ograničene, svetlosmeđe ili tamnije, pigmentisane makule, koje vremenom postaju blago izdignute papule ili plakovi [2].

Prve ideje o povezanosti kožnih promena sa visceralnim malignitetima nastale su u drugoj polovini 20. veka, kada su hirurzi *E. Leser* i *U. Trélat* ukazali na odnos između neoplazmi unutrašnjih organa i angioma kože [3]. Iako je eruptivnu pojavu seboroičnih keratoza usled postojanja visceralnog maligniteta dokumentovao Holander 1900. godine, naziv ovog znaka ostao je *Leser–Trélat*, u čast lekara koji su prvi ukazali na značaj paraneoplastičnih dermatoza [3].

Leser–Trélat znak je najčešće je povezan sa adenokarcinomima gastrointestinalnog trakta, posebno adenokarcinomom želuca i kolona, ali postoje i podaci o vezi sa tumorima dojke, materice, jajnika, mokraćne bešike, jetre, prostate, pluća, sarkomima, malignim melanomom, kao i sa hematološkim malignitetima, poput limfoma i leukemija [4]. Određena benigna stanja mogu dovesti do eruptivne pojave seboroičnih keratoza, što se naziva pseudo- *Leser–Trélat* znak [5].

Patogeneza ovog fenomena još uvek nije u potpunosti razjašnjena, ali se smatra da tumorske ćelije produkuju faktore rasta koji stimulišu snažnu proliferaciju keratinocita [1,4]. Podaci govore da u paraneoplastičnim humoralnim mehanizmima najznačajnije mesto zauzimaju epidermalni faktor rasta (*EGF*) i transformišući faktor rasta alfa (*TGF*-α), koji su odgovorni za proliferaciju keratinocita i dovode do brze pojave seboroičnih keratoza.

Klinički značaj *Leser–Trélat* znaka ogleda se u mogućnosti da predstavlja rani pokazatelj prisustva osnovnog maligniteta. Prepoznavanje ovog znaka može omogućiti rano otkrivanje neoplazmi, u fazi kada je terapijski odgovor povoljniji, čime se direktno utiče na prognozu.

Cilj ovog pregleda literature je sistematski prikaz etioloških i patofizioloških mehanizama, kliničke prezentacije, paraneoplastičnih asocijacija i dijagnostičkog značaja *Leser–Trélat* znaka.

INTRODUCTION

Paraneoplastic dermatoses rank second in frequency among all paraneoplastic manifestations and may play a significant role in the early detection of neoplasms [1]. However, determining the causal relationship between visceral malignancy and cutaneous changes is often extremely challenging.

The Leser–Trélat sign stands out as a particularly important entity within this heterogeneous group of dermatoses. It is characterized by the sudden onset and rapid proliferation of seborrheic keratoses [1,2]. These are common benign skin lesions, particularly observed in patients older than 40 years, with increasing prevalence in the elderly population. They usually present as well-demarcated, light-brown or darker pigmented macules that gradually evolve into slightly elevated papules or plaques [2].

The first ideas regarding the association between skin changes and visceral malignancies emerged during the second half of the 20th century, when surgeons E. Leser and U. Trélat pointed out the relationship between internal organ neoplasms and cutaneous angiomas [3]. Although the eruptive appearance of seborrheic keratoses associated with visceral malignancy was documented by Hollander in 1900, the sign retained the name Leser–Trélat in honor of the physicians who first emphasized the importance of paraneoplastic dermatoses [3].

The Leser–Trélat sign is most commonly associated with gastrointestinal adenocarcinomas, especially gastric and colorectal adenocarcinoma, although associations with tumors of the breast, uterus, ovaries, urinary bladder, liver, prostate, lungs, sarcomas, malignant melanoma, and hematological malignancies such as lymphomas and leukemias have also been reported [4]. Certain benign conditions may also lead to the eruptive appearance of seborrheic keratoses, a phenomenon referred to as the pseudo–Leser–Trélat sign [5].

The pathogenesis of this phenomenon has not yet been fully elucidated, but it is believed that tumor cells produce growth factors that strongly stimulate keratinocyte proliferation [1,4]. Data suggest that epidermal growth factor (EGF) and transforming growth factor alpha (TGF-α) play the most important role in paraneoplastic humoral mechanisms, being responsible for keratinocyte proliferation and the rapid development of seborrheic keratoses.

The clinical significance of the Leser–Trélat sign lies in its potential to represent an early indicator of an underlying malignancy. Recognition of this sign may enable early detection of neoplasms at a stage when therapeutic response is more favorable, thereby directly influencing prognosis.

EPIDEMIOLOGIJA

Leser–Trélat znak najčešće se javlja kod pacijenata starije životne dobi, pri čemu je prosečna starost obolelih 61 godina [6]. U literaturi nema podataka o njegovoj pojavi kod dece mlađe od 10 godina, dok su sporadični slučajevi opisani u uzrasnoj grupi od 10 do 20 godina [7,8]. Dostupne studije ukazuju da se znak javlja podjednako kod muškaraca i žena [5,6]. Kada se govori o uticaju profesionalne izloženosti na naglu pojavu seboroičnih keratoza, ne postoje podaci koji bi ukazivali da na pojavu *Leser–Trélat* znaka utiče zanimanje.

ETIOLOGIJA I PATOFIZIOLOŠKI MEHANIZMI

Seboroične keratoze nastaju usled proliferacije nezrelih keratinocita, međutim, naučnici još uvek nisu saglasni oko jedinstvenog mehanizma koji dovodi do eruptivnog nastanka seboroičnih keratoza u *Leser–Trélat* znaku. Studije govore da je najverovatniji mehanizam nastanka stimulacija keratinocita različitim citokinima i faktorima rasta koje produkuju tumorske ćelije [8,9]. Krajem dvadesetog veka naučnici su ustanovili da tumorske ćelije produkuju transformišući faktor rasta-alfa (*TNF*-α), epidermalni faktor rasta-alfa (*EGF*-α) i amfiregulin, koji mogu dovesti do stimulacije mitoze keratinocita [9]. Studija sprovedena 2011. godine ukazuje da pored ovih molekula, i insulinu sličan faktor rasta, katalička podjedinica fosfatidil-inozitol 3-kinaze (*PIK3CA*) i receptor-3 faktora rasta fibroblasta (*FGFR3*) imaju ulogu u nastanku seboroičnih keratoza u okviru *Leser–Trélat* znaka [10]. Svi ovi molekulu intenzivno stimulišu proliferaciju keratinocita, što se prezentuje eruptivnim rastom seboroičnih keratoza. Pored toga, postavljene su i imunološke teorije, koje govore o postojanju reakcija posredovanih tumorskim antigenima i citokinima, koji dovode do hiperproliferacije keratinocita [1,3,4].

Postoje studije koje govore o tzv. pseudo-*Leser–Trélat* znaku, gde pojava seboroičnih keratoza prati izvesna benigna stanja, kao što je trudnoća, infekcija virusom *HIV* i stanja nakon transplantacije [11]. Postoje podaci o pojavi pseudo-*Leser–Trélat* znaka i prilikom infekcije virusom *COVID-19* [5].

KLINIČKA SLIKA

Seboroične keratoze su izuzetno česte benigne promene kože koje imaju dugogodišnju evoluciju i karakterističan izgled smeđih, pigmentovanih i jasno ograničenih makula, koje najčešće evoluiraju u tamne, baršunaste papule ili plakove, zalepljenog, voštanog izgleda [12,13].

Dok se benigna forma seboroične keratoze razvija u vremenskom periodu od nekoliko godina, seboroič-

The aim of this literature review is to provide a systematic overview of the etiological and pathophysiological mechanisms, clinical presentation, paraneoplastic associations, and diagnostic significance of the Leser–Trélat sign.

EPIDEMIOLOGY

The Leser–Trélat sign most commonly occurs in elderly patients, with the average age of affected individuals being 61 years [6]. There are no reports in the literature of its occurrence in children younger than 10 years, whereas sporadic cases have been reported in the 10–20-year age group [7,8]. Available studies indicate that the sign occurs equally in men and women [5,6]. Regarding the influence of occupational exposure on the sudden appearance of seborrheic keratoses, there is no evidence that occupation affects the occurrence of the Leser–Trélat sign.

ETIOLOGY AND PATHOPHYSIOLOGICAL MECHANISMS

Seborrheic keratoses arise as a result of immature keratinocyte proliferation; however, scientists still have not reached consensus regarding a single mechanism responsible for the eruptive onset of seborrheic keratoses in the Leser–Trélat sign. Studies suggest that the most likely mechanism involves stimulation of keratinocytes by various cytokines and growth factors produced by tumor cells [8,9]. At the end of the twentieth century, researchers established that tumor cells produce transforming growth factor-alpha (TNF-α), epidermal growth factor-alpha (EGF-α), and amphiregulin, all of which may stimulate keratinocyte mitosis [9]. A study conducted in 2011 indicated that, in addition to these molecules, insulin-like growth factor, the catalytic subunit of phosphatidylinositol 3-kinase (PIK3CA), and fibroblast growth factor receptor 3 (FGFR3) also play a role in the development of seborrheic keratoses within the Leser–Trélat sign [10]. All these molecules intensely stimulate keratinocyte proliferation, clinically presenting as eruptive growth of seborrheic keratoses. Furthermore, immunological theories have been proposed, suggesting the existence of tumor antigen- and cytokine-mediated reactions that lead to keratinocyte hyperproliferation [1,3,4].

There are studies describing the so-called pseudo–Leser–Trélat sign, in which seborrheic keratoses occur in association with certain benign conditions such as pregnancy, HIV infection, and post-transplantation states [11]. Reports also exist regarding the occurrence of the pseudo–Leser–Trélat sign during COVID-19 infection [5].

ne keratoze u okviru *Leser–Trélat* znaka imaju izuzetno kratak interval između inicijalnog pojavljivanja i eruptivnog širenja, koji može biti i kraći od godinu dana [14]. Ove seboroične keratoze se najčešće pojavljuju na leđima i imaju karakterističan raspored, koji se u literaturi opisuje kao grane na božičnoj jelci ili kapi kiše [14]. Ređe zastupljene lokacije su vrat, pazušna jama i ekstremiteti [13].

Kako je *Leser–Trélat* znak paraneoplastična dermatoza, možemo očekivati i pojavu drugih simptoma u okviru paraneoplastičnog sindroma. Pacijenti često navode pojavu generalizovanog svraba i značajnog gubitka kilograma u kratkom vremenskom periodu [14,15]. Možemo uočiti i pojavu drugih paraneoplastičnih dermatoza, kao što je *Acantosis nigricans*, koja se sreće kod 20% pacijenata sa *Leser–Trélat* znakom [16].

MALIGNITETI

Leser–Trélat znak najčešće ukazuje na prisustvo karcinoma gastrointestinalnog trakta (kod 32% svih pacijenata sa ovim znakom ustanovljeno je prisustvo gastrointestinalnih tumora) [17,18]. Pored ovih tumora, postoje podaci o povezanosti sa karcinomom pluća, dojke, materice, jajnika, prostate, malignim melanomom, multiplim mijelomom, leukemijama, limfomima, hepatocelularnim karcinomom i sarkomima [17–42].

Leser–Trélat znak i gastrointestinalni tumori

Prva studija koja govori o povezanosti *Leser–Trélat* znaka sa gastrointestinalnim tumorima objavljena je 1980. godine, a poslednji podaci su iz januara 2026. godine. Više od trećine pacijenata sa ovim znakom poseduje tumore gastrointestinalnog trakta [17]. Najzastupljeniji gastrointestinalni tumori su gastrični adenoakarcinomi, a pored njih prisutni su i karcinomi kolona i rektuma, kao i karcinom jednjaka i pankreasa [18–20].

Leser–Trélat znak i karcinom dojke

Podaci o povezanosti *Leser–Trélat* znaka i karcinoma dojke prvi put su zabeleženi 1982. godine, dok su najnoviji izveštaji objavljeni u januaru 2026. godine. U literaturi su opisane kako serije slučajeva, tako i pojedinačni prikazi koji dovode u vezu eruptivnu pojavu seboroičnih keratoza sa malignitetom dojke, pri čemu je invazivni duktalni karcinom najčešće registrovani histološki tip [21–23].

Iako se većina slučajeva odnosi na pacijentkinje, dostupni su i podaci o pojavi *Leser–Trélat* znaka kod muškaraca sa dijagnostikovanim karcinomom dojke [24]. Posebnu pažnju privlači i opis porodične pojave – majke i ćerke sa eruptivnim seboroičnim keratozama, kod kojih je naknadno potvrđen karcinom dojke [25].

CLINICAL PRESENTATION

Seborrheic keratoses are extremely common benign skin lesions characterized by long-term evolution and the characteristic appearance of brown, pigmented, well-demarcated macules that most commonly evolve into dark, velvety papules or plaques with a "stuck-on," waxy appearance [12,13].

While the benign form of seborrheic keratosis develops over several years, seborrheic keratoses associated with the Leser–Trélat sign demonstrate an extremely short interval between initial appearance and eruptive spread, often shorter than one year [14]. These seborrheic keratoses most commonly appear on the back and display a characteristic distribution described in the literature as resembling "branches of a Christmas tree" or "raindrops" [14]. Less frequently affected sites include the neck, axillae, and extremities [13].

Since the Leser–Trélat sign is a paraneoplastic dermatosis, the presence of additional symptoms within the paraneoplastic syndrome is also expected. Patients frequently report generalized pruritus and significant weight loss over a short period [14,15]. Other paraneoplastic dermatoses may also be observed, such as acanthosis nigricans, which occurs in approximately 20% of patients with the Leser–Trélat sign [16].

MALIGNANCIES

The Leser–Trélat sign most commonly indicates the presence of gastrointestinal tract carcinoma (gastrointestinal tumors are identified in 32% of all patients with this sign) [17,18]. In addition to these tumors, associations have also been reported with lung, breast, uterine, ovarian, and prostate carcinoma, malignant melanoma, multiple myeloma, leukemias, lymphomas, hepatocellular carcinoma, and sarcomas [17–42].

Leser–Trélat Sign and Gastrointestinal Tumors

The first study describing the association between the Leser–Trélat sign and gastrointestinal tumors was published in 1980, while the most recent data date from January 2026. More than one-third of patients with this sign have gastrointestinal tract tumors [17]. The most common gastrointestinal tumors are gastric adenocarcinomas, followed by colorectal carcinoma, as well as esophageal and pancreatic carcinoma [18–20].

Leser–Trélat Sign and Breast Cancer

Data regarding the association between the Leser–Trélat sign and breast cancer were first reported in 1982, while the most recent reports were published in January 2026. Both case series and individual case reports describing eruptive seborrheic keratoses asso-

Leser–Trélat znak i karcinom pluća

Prvi podaci o povezanosti eruptivne pojave seboroičnih keratoza i tumora pluća objavljeni su 1977. godine. Pojava *Leser–Trélat* znaka kod pacijenata sa tumorom pluća sreće se u 5–10% slučajeva, a najčešće je u vezi sa nesitnoćelijskim karcinomom pluća, skvamocelularnim i adenokarcinomom [26–29].

Leser–Trélat znak i maligni melanom

Prvi podaci i pojavi *Leser–Trélat* znaka kao paraneoplastične manifestacije malignog melenoma potiču iz 1970 godine. Eruptivna pojava seboroičnih keratoza nije česta kod malignog melanoma, ali je izuzetno značajna jer je povezana sa uznapredovalim stadijumima ovog karcinoma, kod kojih je *Breslov* indeks veći od 2,4 mm [30,32]. U literaturi postoje podaci o pojavi *Leser–Trélat* znaka kod primarnih tumora, ali i kod metastaza [31,32].

Leser–Trélat znak i limfoproliferativne bolesti

Iako je *Leser–Trélat* znak najćešće povezan sa solidnim tumorima, postoje podaci koji govore o vezi sa limfoproliferativnim bolestima. Prvi opisi hematoloških maligniteta u vezi sa *Leser–Trélat* znakom pojavljuju se sredinom 20. veka u vidu prikaza slučaja limfoma i leukemija praćenih eruptivnom pojavom seboroičnih keratoza. Najčešće opisana limfoproliferativna bolest povezana sa ovim znakom je *Mycosis fungoides*, koji predstavlja najčešći oblik kutanog *t*-ćelijskog limfoma (*CTCL*) [36]. U literaturi je opisano više slučajeva u kojima je nagla eruptivna pojava seboroičnih keratoza pratila progresiju ili relaps bolesti. U većini tih slučajeva radilo se o uznapredovalim stadijumima bolesti [36–39].

Drugi po učestalosti je *Sézary* sindrom, leukemijska varijanta kutanog *t*-ćelijskog limfoma. Kod ovih pacijenata se *Leser–Trélat* znak najčešće javlja udružen sa eritrodermijom, a u pojedinim slučajevima je primećeno povlačenje keratoza nakon uspešne terapije [40].

Pored kutanog *t*-ćelijskog limfoma, *Leser–Trélat* znak srećemo i kod hronične limfocitne leukemije, *non-Hodgkin* i *Hodgkin* limfoma i vrlo retko kod akutnih leukemija [41].

DIJAGNOZA

Eruptivna pojava seboroičnih keratoza u kratkom vremenskom periodu (često kraćem od godinu dana) budi sumnju na postojanje paraneoplastične dermatoze – *Leser–Trélat* znaka.

U literaturi se navode postulati koji nam mogu pomoći u dijagnostikovanju paraneoplastične dermatoze (Tabela 1).

ciated with breast malignancy have been documented in the literature, with invasive ductal carcinoma being the most frequently reported histological type [21–23].

Although most cases involve female patients, reports also exist describing the occurrence of the Leser–Trélat sign in men diagnosed with breast cancer [24]. Particularly noteworthy is the description of familial occurrence–mother and daughter presenting with eruptive seborrheic keratoses who were subsequently diagnosed with breast cancer [25].

Leser–Trélat Sign and Lung Cancer

The first reports describing the association between eruptive seborrheic keratoses and lung tumors were published in 1977. The occurrence of the Leser–Trélat sign in patients with lung tumors is observed in 5–10% of cases and is most commonly associated with non-small cell lung carcinoma, squamous cell carcinoma, and adenocarcinoma [26–29].

Leser–Trélat Sign and Malignant Melanoma

The first reports of the Leser–Trélat sign as a paraneoplastic manifestation of malignant melanoma date back to 1970. The eruptive appearance of seborrheic keratoses is uncommon in malignant melanoma but is extremely important because it is associated with advanced stages of this malignancy, particularly when the Breslow index exceeds 2.4 mm [30,32]. The literature contains reports of the Leser–Trélat sign occurring in both primary tumors and metastatic disease [31,32].

Leser–Trélat Sign and Lymphoproliferative Diseases

Although the Leser–Trélat sign is most commonly associated with solid tumors, reports also indicate an association with lymphoproliferative diseases. The first descriptions of hematological malignancies associated with the Leser–Trélat sign appeared in the mid-20th century as case reports of lymphomas and leukemias accompanied by eruptive seborrheic keratoses. The most commonly described lymphoproliferative disease associated with this sign is mycosis fungoides, the most common form of cutaneous *t*-cell lymphoma (CTCL) [36]. Several cases have been reported in which sudden eruptive seborrheic keratoses accompanied disease progression or relapse. In most of these cases, the disease was advanced [36–39].

The second most frequent association is Sézary syndrome, the leukemic variant of cutaneous *t*-cell lymphoma. In these patients, the Leser–Trélat sign most commonly occurs together with erythroderma, and in some cases, regression of the keratoses has been observed following successful therapy [40].

Tabela 1. Curthovi postulati kao kriterijumi za dijagnostiku paraneoplastičnih dermatoza

Table 1. Curth's postulates as criteria for the diagnosis of paraneoplastic dermatoses

Curthovi postulati / *Curth's postulates*
Neoplastični i paraneoplastični proces počinju istovremeno / *Both the neoplastic and paraneoplastic processes began concurrently*
Neoplastični i paraneoplastični proces imaju paralelan tok bolesti (odnosno, paraneoplastična manifestacija se povlači nakon lečenja osnovnog maligniteta i ponovo se javlja ukoliko dođe do relapsa tumora) / *Both the neoplastic and paraneoplastic processes have a parallel disease course (ie, the paraneoplastic process resolves with treatment of the underlying malignancy, and the paraneoplastic process relapses if the malignancy returns).*
Paraneoplastični proces je povezan sa specifičnim tipovima maligniteta / *The paraneoplastic process is associated with specific types of malignancy*
Kožne lezije nisu povezane ni sa jednim genetskim sindromom / *The skin lesions are not associated with any potential underlying genetic syndromes*
Kožne lezije nisu česte u opštoj populaciji / *The skin lesions are not common in the general population*

Kako znamo da ovo može biti prvi indikator maligniteta, ukoliko postoji sumnja da klinička slika odgovara *Leser–Trélat* znaku, neophodno je dalje primeniti adekvatne dijagnostičke procedure u cilju otkrivanja maligniteta. Procena započinje detaljnom anamnezom i kompletnim fizikalnim pregledom, pri čemu je izuzetno značajno zabeležiti postojanje značajnog gubitka kilograma, svraba, povišene telesne temperature, anemije, malaksalosti i drugih simptoma koji nam mogu ukazati na postojanje neotkrivene neoplazme [15,42].

Osnovna laboratorijska dijagnostika obuhvata kompletnu krvnu sliku i biohemijske analize, dok se skrining testovi (mamografija, *Papanikolau* test, *PSA*) sprovode prema polu, uzrastu i indikaciji [15,16]. Najčešće se koriste rendgen grudnog koša i ehosonografija grudnog koša, abdomena i karlice. Kako je najviše pacijenata sa *Leser–Trélat* znakom obolelo od tumora gastrointestinalnog trakta, neophodno je fokusirati se na detaljan pregled ovog sistema organa, koristeći endoskopske metode i kompjuterizovanu tomografiju [15,16].

TERAPIJSKE PROCEDURE

Lečenje *Leser–Trélat* znaka prvenstveno podrazumeva terapiju osnovnog maligniteta, nakon čega se kod oko 50% pacijenata beleži povlačenje seboroičnih keratoza [6]. Ove kožne promene mogu se ublažiti metodama poput krioterapije, kiretaže lezija ili elektrodesikacije [43].

ZAKLJUČAK

Leser–Trélat znak predstavlja klinički entitet od posebnog značaja u okviru paraneoplastičnih dermatoza, budući da može biti prvi, a ponekad i jedini vidljivi pokazatelj postojanja maligniteta. Iako su seboroične kera-

In addition to cutaneous *t*-cell lymphoma, the Leser–Trélat sign has been reported in chronic lymphocytic leukemia, non-Hodgkin and Hodgkin lymphoma, and, very rarely, in acute leukemias [41].

DIAGNOSIS

The abrupt appearance of seborrheic keratoses within a short period (often less than 1 year) raises suspicion of a paraneoplastic dermatosis–the Leser–Trélat sign.

The literature describes postulates that may aid in diagnosing paraneoplastic dermatoses (Table 1).

Since this sign may represent the first indicator of malignancy, if the clinical presentation suggests the Leser–Trélat sign, it is necessary to proceed with appropriate diagnostic procedures to identify the underlying malignancy. Evaluation begins with a detailed medical history and complete physical examination, with particular emphasis on documenting significant weight loss, pruritus, fever, anemia, fatigue, and other symptoms suggestive of an occult neoplasm [15,42].

Basic laboratory diagnostics include complete blood count and biochemical analyses, while screening tests (mammography, Papanicolaou test, PSA) are performed according to sex, age, and indication [15,16]. Chest radiography and ultrasonography of the thorax, abdomen, and pelvis are most commonly used. Since the majority of patients with the Leser–Trélat sign have gastrointestinal tract tumors, it is necessary to focus on detailed examination of this organ system using endoscopic methods and computed tomography [15,16].

THERAPEUTIC PROCEDURES

Treatment of the Leser–Trélat sign primarily involves therapy directed at the underlying malignancy, after

toze izuzetno česte u opštoj populaciji starijeg životnog doba, njihova nagla pojava i rapidna progresija, praćena intenzivnim pruritusom, zahtevaju dodatno ispitivanje. Ovaj znak najčešće upućuje na gastrointestinalne adenokarcinome, posebno karcinomom želuca, kolona i rektuma, ali su u literaturi dokumentovane i asocijacije sa tumorima dojke, materice, jajnika, mokraćne bešike, pluća, hepatocelularnim karcinomom, malignim melanomom, sarkomima i limfoproliferativnim bolestima.

Adekvatno poznavanje kliničkih karakteristika *Leser–Trélat* znaka i multidisciplinarni dijagnostički pristup imaju ključnu ulogu u pravovremenom otkrivanju potencijalno udruženih maligniteta. Sistematska evaluacija pacijenata sa eruptivnim seboroičnim keratozama doprinosi ranom postavljanju dijagnoze osnovne neoplazme, često u fazi kada je terapijski odgovor povoljniji. Takav pristup značajno utiče na tok bolesti i prognozu.

Sukob interesa: Nije prijavljen.

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which regression of seborrheic keratoses is observed in approximately 50% of patients [6]. These skin lesions may additionally be alleviated using methods such as cryotherapy, lesion curettage, or electrodesiccation [43].

CONCLUSION

The Leser–Trélat sign represents a clinically significant entity within the spectrum of paraneoplastic dermatoses, as it may be the first, and sometimes the only visible indicator of an underlying malignancy. Although seborrheic keratoses are extremely common in the elderly general population, their sudden onset and rapid progression, particularly when accompanied by intense pruritus, require further investigation. This sign most commonly suggests gastrointestinal adenocarcinomas, especially gastric, colonic, and rectal carcinoma; however, associations with breast, uterine, ovarian, urinary bladder, lung, hepatocellular carcinoma, malignant melanoma, sarcomas, and lymphoproliferative diseases have also been documented in the literature.

Adequate knowledge of the clinical features of the Leser–Trélat sign and a multidisciplinary diagnostic approach are key to the timely detection of potentially associated malignancies. Systematic evaluation of patients with eruptive seborrheic keratoses contributes to early diagnosis of the underlying neoplasm, often at a stage when therapeutic response is more favorable. Such an approach significantly influences disease course and prognosis.

Conflict of interest: None declared.

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