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CASE REPORT

Leser-trelat sign in the diagnosis of occult neoplasms-case report

Vildana Jahić[1], Jagoda Balaban [2], Đuka Ninković Baroš[2,3], Darko Lukić[3], Darko Jović[3,4], Andrea Stanojević[5], Biljana Pavlovska[6]

[1]General Hospital Bijeljina, Bosnia and Herzegovina
[2]University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina
[3]University of Banja Luka, Faculty of Medicine, Bosnia and Herzegovina
[4]Health center S-tetic Banja Luka, Bosnia and Herzegovina
[5]General Hospital Doboj, Bosnia and Herzegovina
[6]General Hospital Gradiška, Bosnia and Herzegovina

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Correspondence to:
Vildana Jahić, MD
Srpske vojske 53, Bijeljina 76300, Bosna i Hercegovina
+38765/092-113
e-mail: dr.vildanajahic@gmail.com

Summary

Leser-Trélat (LT) sign (syndrome) is a rare, distinctive clinical phenomenon that is manifested by a sudden, eruptive, appearance of multiple itchy seborrheic keratoses (SK) that sometimes coincide with occult malignancy.

A 73-year-old patient came for examination of numerous, large seborrheic keratoses (SK) on the skin. According to the patient's statement, SK did not occur suddenly and "eruptively". Nevertheless, ultrasound and endoscopic evaluation were suggested to the patient to exclude the Leser-Trélat phenomenon. The patient was then diagnosed with an occult, asymptomatic rectal neoplasm.

The occurrence of numerous seborrheic keratoses (especially if they are "eruptive", large and bizarre in shape), should raise suspicion of LT phenomenon, or internal malignancy in the patient, and result in relevant diagnostic procedures to detect possible latent malignancy. It would be wise for the doctors of all disciplines to be acquainted with the existence of the LT sign (syndrome) and possible clinical implications of it.

Key words: Leser-Trélat sign; seborrheic keratosis; occult tumors; skin

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INTRODUCTION

Leser-Trélat sign (syndrome) is a distinctive clinical phenomenon that is manifested by a sudden, eruptive, appearance of multiple itchy seborrheic keratoses (SK) that sometimes coincide with occult malignancy. [1]

The LT sign is considered to be a rather rare paraneoplastic skin marker of internal malignancy. [2-5]

Seborrheic keratoses (SK) are very common benign skin changes in the population over 40 years old. SK are also found in completely healthy people. [6]

In the majority of published cases that describe Leser-Trélat (LT) syndrome, gastrointestinal adenocarcinoma is predominantly present, but the coincidence of SK has also been described with cancers of the lung, breast, esophagus, urinary bladder, larynx, ovary, prostate, as well as with melanoma, hepatocellular carcinoma, etc. [1,7]

The pathogenesis of the LT sign/syndrome remains unclear and continues to be the subject of prolonged observation. It is suspected that the release of cytokines and growth factors from the neoplasm stimulates the eruptive growth of seborrheic keratoses. In fact, overexpression of EGF-alpha and EGFR (epidermal growth factor receptor) may contribute to the eruptive nature of SK. [1-7]

CASE HISTORY

Patient M.O. 73 years old, came for the first time for a dermoscopic examination of the skin in June 2012 due to a change on the head, which was diagnosed as an intradermal nevus without significant elements. At the same time, in addition to this change, a non-melanocytic skin lesion was detected on the head, which turned out to be basocellular carcinoma (BCC). On that occasion, numerous seborrheic keratoses (31), of different sizes, were detected on the patient's chest. At the same time, according to the patient's claims, seborrheic keratoses occurred successively and without acute exacerbation in the form of eruptive growth. The BCC was then removed in the competent institution using an optimally radical method.

In the middle of January 2018, the patient came for examination again, this time due to the above mentioned seborrheic keratoses. The patient denied changes in number and size, although (by comparing previous pictures), it was clear that they were bigger. Seborrheic keratoses were larger in diameter, some having the form of irregular domes, atypical in appearance **(Figure 1)**. No skin changes that could be considered suspicious of malignancy were found.

Regardless of denying any changes in the SK themselves, the patient was recommended to undergo additional examination of the gastrointestinal tract in order to exclude possible Leser-Trélat phenomenon because of the impression that the SKs were larger and had unusual forms.

Initially, the patient showed no interest in additional examination because he did not see a possible link between skin changes and occult tumors. However, he finally obeyed and a few days after the above mentioned examination, he reported for further examination in a competent institution. On that occasion, the patient underwent ultrasound (US) examination of the abdomen and the results were as follows: 'Liver solid, isoechoic, fatty, pancreas humpbacked, fatty, without focal lesions, gallbladder, kidneys, spleen and retroperitoneum neat, prostate hypertrophic, homogenous with the volume of 63.3 ml. The colon meteoristic, sub-occluded.'

The patient was hospitalized in the first week of March 2018 in a competent institution for further examination, which showed the following:

- gastroscopic examination: 'Esophagus of an appropriate lumen, with mild hyperemia above the cardia. The mucosa of the antral part is hyperemic and slightly edematous with linear non-bleeding erosions confluent towards the pylorus. Pylorus is circular and passable for the instrument, there is DG reflux. Mild hyperemia of the mucosa of the duodenal bulbus. Postbulbar finding neat, bile is present';
- digital rectal examination: 'An uneven polypoid hard infiltration is palpated';
- colonoscopic examination: 'Colonoscope inserted 30 cm into the rectum, 5 cm from the anocutaneous line tm infiltration, polypoid, hard, necrotic, covering 2/3 of the circumference 10 cm long. Taken forceps biopsy. At the exit, a wreath of hemorrhoidal nodules';
- pathohistological finding: Adenocarcinoma scirrhosum invasivum (particulae) ;
- MR of the pelvis: "A circular, irregular, soft-tissue thickening of the rectal wall can be seen, the distal end begins just above the junction of the levator anii and at a distance of about 5 cm from the anus. The cranial thickening of the wall involves the intestine in the length of about 5 cm. The described wall thickening is up to 15 mm in diameter, it shows postcontrast marginal amplification of signal intensity, affects all layers of the wall and is without certain signs of serosa breakthrough and perirectal adipose tissue infiltration. The differential diagnosis primarily corresponds to the infiltrative Neo process. There are no signs of infiltration of seminal vesicles, prostate and bladder. Locoregionally, in the perirectal adipose tissue on the right side at the "9h" position, there is an oval lymph node with a maximum diameter of 9.5 mm and slightly higher, on the left side, at the level of the rectosigmoid junction, two round nodes up to 5 mm in size. The urinary bladder is moderately filled with urine, without wall thickening and without pathological contents. The prostate is enlarged, 40X52X38mm in diameter, slightly lobular contours, heterogeneous internal structure. Seed vesicles symmetrical. There is no free fluid in the small pelvis. No enlarged first nodules were observed along the iliac blood vessels. There are no signs of infiltration on the visible bone structures;

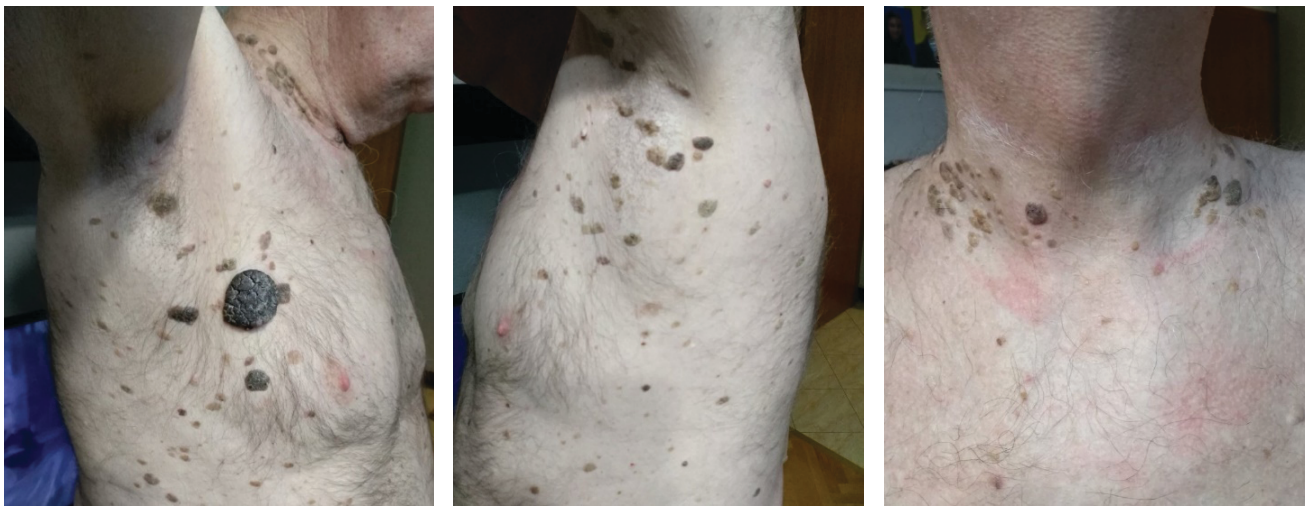

Figure 1. Seborrheic keratosis in patient M.O.

Conclusion: low infiltration of the rectal wall with locoregional lymphadenopathy.

The patient then underwent surgery for the mentioned neoplasm.

DISCUSSION

Seborrheic keratoses (SK) are very common (almost common), skin changes, especially in elderly population. Therefore, many authors suspect the existence of a correlation between SC and malignancies, that is, they believe that it is only a simple coincidence of the occurrence of SK and malignant tumors within Leser-Trélat syndrome (LTS).[8]

Although the pathogenesis of LTS is unclear, the clinical picture indicating LTS requires diagnostic processing to detect possible visceral malignancy.[1]

The case of possible LTS in our patient with rectal malignancy is also indicative, because it can, at least minimally, increase interest for skin changes, especially SK and the possibility of coincidental malignancy elsewhere.

Even when the Leser-Trélat sign (syndrome) is not anamnestically and diagnostically confirmed, it seems that patients affected by suspected SK should be closely monitored, due to potential occult malignancy.[8]

Leser-Trélat sign is usually associated with adenocarcinoma, most often of the colon or stomach, but also the liver, kidneys, pancreas. Then, there was a coincidence with hepatocellular carcinoma, lung, breast, urinary bladder, prostate carcinoma, as well as with malignancies of the esophagus, larynx and ovaries, melanoma, mycosis fungoides, nasopharyngeal carcinoma, etc.[7,8] In over 60% of the cases, the disease was detected in an advanced (metastatic) phase.[1] LTS has been described in woman with osteogenic sarcoma, then in a man diagnosed with germ, etc.[1]

Our patient with asymptomatic malignancy on the rectum was referred for further evaluation, precisely on the basis of suspicion of LTS, despite the possible coincidence of SK with visceral neoplasms. The supplementary evaluation proved to be justified. Namely, it is clear that the patient would only appear later with problems related to malignancy.

Suspicion of LTS should be based primarily on the sudden eruption of SK and/or the size and change in the number of SK.[8]

Probably justifiably, there is a suggestion that the importance of LTS is underestimated, that is, that the importance of the occurrence of multiple SKs is largely minimized.

In everyday clinical practice, multiple SKs may be neglected or misdiagnosed. There is a proposal that in all cases of sudden eruption or intensification of the appearance of SK, an adequate dermatological evaluation is performed, in order to more accurately assess the frequency of association of SK with occult neoplasms.[8]

At the same time, malignant acanthosis nigricans, characterized by velvety, symmetrical hyperpigmentation, anywhere on the body (more often at intertriginous parts), occurs simultaneously in about 20% of cases showing the Leser-Trélat sign and should increase the suspicion of coincidental malignancy.

It has been observed that in many patients who show the Leser-Trélat sign, another paraneoplastic disease occurs at the same time, so that a careful examination and precise anamnesis cannot be assessed.[2-7]

As epidermal growth factor (EGF) receptors are present on basal keratinocytes, it has been suggested that greater importance should be given to combining molecular characteristics of multiple SKs with immunohistochemical analyzes of EGFR proteins to determine the likelihood of Leser-Trélat syndrome and consequently a high risk of disease.[8]

At the same time, it is suggested for EGFR immunohistochemical analysis to be limited, i.e, to indicate the presence of LTS only when some additional clinical manifestations are present, such as: acute morphological changes in long-standing multiple SK, sudden, multiple

"eruption" of SK, association with acanthosis or other paraneoplastic manifestations of the skin, a younger age of the patient at the onset of SK, and malignancies in personal and/or family history.[8]

Experience with our patient has shown that it makes sense to ask for careful observation, ultrasound and endoscopic examination, even when the patient himself denies a sudden increase in volume or number of SKs, if their number and appearance are objectively suspicious.

CONCLUSION

Occurrence of numerous seborrheic keratoses (especially if they are "eruptive", large and bizarre in shape[1-7]), should raise suspicion of LT phenomenon, or internal malignancy in the patient, and result in relevant diagnostic procedures to detect possible latent malignancy. It would be wise for the doctors of all disciplines to be acquainted with the existence of the LT sign (syndrome) and the possible clinical implications of it.

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LESER TRELAT ZNAK U DIJAGNOZI OKULTNIH NEOPLAZMI-PRIKAZ SLUČAJA

Vildana Jahić[1], Jagoda Balaban[2], Đuka Ninković Baroš[2,3], Darko Lukić[3], Darko Jović[3,4], Andrea Stanojević[5], Biljana Pavlovska[6]

Sažetak

Leser-Trelat (LT) znak (sindrom) je rijedak, karakterističn klinički fenomen koji se manifestuje iznenadnom, eruptivnom, pojavom višestrukih svrbećih seboroičnih keratoza (SK), koje ponekad koincidiraju sa okultnim malignitetom.

Pacinet star 73 godine javio se na pregled brojnih, velikih seboroičnih keratoza (SK) na koži. Prema izjavi pacijenta, SK nisu nastale naglo i „eruptivno". Ipak, savjetovana mu je ultrazvučna i endoskopska evaluacija, radi isključenja Leser-Trelat fenomena. Pacijentu je potom otkrivena okultna, asimptomatska neoplazma rektuma.

Pojava brojnih seboroičnih keratoza (naročito ukoliko su „eruptivne",velike i bizarnog oblika), trebalo bi da pokrene sumnju na LT fenomen, ondosno, na unutrašnji malignitet kod pacijenta, te da rezultuje relevantnim dijagnostičkim procedurama radi otkrivanja eventualnog skrivenog maligniteta. Bilo bi mudro da se doktori medicine svih disciplina upoznaju sa postojanjem LT znaka (sindroma) i mogućim kliničkim implikacijama istog.

Ključne reči: Leser-Trelat znak, seboroične keratoze, okultni tumori, koža

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