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CASE REPORT

Cadaveric Study: Sign of Leser-Trélat Associated with Breast Cancer

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Abstract

INTRODUCTION: Seborrheic keratoses (SK) is considered the most common benign skin lesions found in individuals that are middle aged and older. In dermatology practice, these lesions pose no threat to the individual but can be concerning for cosmetic and underlying malignancy reasons when they cover most of the skin surface. Of specific concern is the sign of Leser-Trélat, which has been documented as a cutaneous harbinger of underlying malignancy associated with proliferation of the size and/or number seborrheic keratoses. The rare sign is usually caused by malignancies such as gastrointestinal adenocarcinoma, but also lung, kidney, liver, or pancreatic cancer. This case report will describe the histology of the skin lesions in Lesar Trélat and analyze the current literature regarding its association with breast cancer, which is quite rare.

RESOURCES: For this case study, a cadaver from the body donor program in Philadelphia College of Osteopathic Medicine (PCOM), South Georgia was used. Skin samples were sent to Colquitt Regional Center for processing, where sections were embedded in paraffin and were stained with H&E stain. A pathologist reported histopathological findings of the skin lesions and the breast tissue samples.

DESCRIPTION: Multiple SK lesions covering the face, abdomen, back, as well as both upper and lower extremities were observed in one of the cadavers in the gross anatomy laboratory. Due to the significant number of pigmented, verrucous lesions, the sign of Leser-Trélat was clinically postulated, later confirmed during routine laboratory dissection of the breast tissue. Histology sections confirmed not only multiple SK lesions in the skin, but also revealed an associated breast cancer in the form of an infiltrative ductal carcinoma.

SIGNIFICANCE: The sign of Leser-Trélat is rare by itself and its association with breast cancer is even more uncommon. Once a clinician recognizes the multiple SK eruptions, the patient should be meticulously investigated for not only for an underlying GI malignancy, but also for other cancers like breast cancer. Additionally, a case report confirmed malignant melanoma that mimicked sign of Leser-Trélat, warranting the importance of further analyzing the pathology diagnosis when there is a proliferation of multiple seborrheic keratoses. Therefore, biopsy and histology diagnosis is crucial for ruling out both cutaneous as well as underlying malignancies and should be encouraged when patients present in clinic rather than assuming the typical benign characteristics of seborrheic keratosis..

Key Words: *Cadaver; Dermatology; Seborrheic keratoses; Leser-Trélat; Paraneoplastic syndrome*

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Seborrheic keratoses (SK) is considered the most common benign skin lesions encountered in clinic. Generally, these pigmented "stuck on" keratoses pose no harm to the individual, but acute proliferation of these lesions has been documented to be of concern due to a paraneoplastic syndrome known as "Leser-Trélat". Multiple SK lesions covering the face, abdomen, back, as well as both upper and lower extremities were observed in one of the cadavers in the gross anatomy laboratory at Philadelphia College of Medicine (PCOM), in Moultrie, Georgia. Due to the significant number of pigmented, verrucous lesions, the sign of Leser-Trélat was clinically postulated, and later confirmed during routine laboratory dissection of the breast tissue. Histology sections confirmed not only multiple SK lesions in the skin, but also revealed an associated breast cancer in the form of an infiltrative ductal carcinoma.

The sign of Leser-Trélat is rare by itself and its association with breast cancer is even more uncommon. Once a clinician recognizes multiple SK eruptions, the patient should be meticulously investigated for not only the onset of SK eruptions and for an underlying malignancy (most commonly gastrointestinal related), but also for other less common sites of dysplasia such as breast cancer that was seen in this individual. Therefore, biopsy and histology diagnosis are crucial for ruling out both cutaneous as well as underlying malignancies and should be encouraged when patients are present in clinic rather than assuming the typical benign characteristics of seborrheic keratosis.

Introduction

Seborrheic keratoses (SK) is considered the most common benign skin lesions found in individuals that are middle aged and older [1-7]. In dermatology practice, these lesions pose no threat to the individual but are most often dismissed as cosmetic concern. Treatment of these lesions involves removal via liquid nitrogen therapy, which is not covered under insurance, unless the SK lesion is determined to be irritated. Therefore, lack of reimbursement for this procedure leads to many cases being untreated. Additionally, one of the most important aspects that is commonly failed during regular skin examination, is asking the history of present illness regarding the appearance of numerous widespread SK's. It should be explored further by the clinician, since an acute appearance of widespread appearance of numerous SK lesions is seen in paraneoplastic syndrome known as Lesar-Trélat while chronic proliferation of these lesions supports a benign diagnosis [8-12].

Of specific concern is Leser-Trélat, is that it has been documented as a cutaneous harbinger of underlying malignancy associated with proliferation of the size and/or number seborrheic keratoses within a few years or less [1-6], [9-12]. This rare sign is usually caused by malignancies such as gastrointestinal (GI) adenocarcinoma and lung, kidney, liver, pancreatic cancer, or malignant melanoma [8-9]. Additionally, Leser-Trélat has been documented as having an incidence of 57% when discussing metastatic invasion [13-17]. Therefore, it is important to be aware of this paraneoplastic syndrome, as it is often underdiagnosed due to the common encounter of SK lesions in clinic [13].

This cadaveric study will describe the histopathology of the skin lesions that are determined to be highly likely indicative of Leser-Trélat within a cadaver as well as analyze the current literature regarding its associated with this syndrome. This study holds significance as the determined underlying malignancy was discovered to invasive ductal carcinoma of the breast, which is quite rare as most literature has cited most cases due to GI malignancy.

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Cadaveric Study

We report a 79-year-old African American female cadaver that was donated to Philadelphia College of Medicine, South Georgia Campus via the donor body program. The only medical records provided for review was the age of the patient and race. On examination, the cadaver had a significant number and size of verrucous, waxy brown plaques that were scattered diffusely across the body. Due to the impressive presentation of the skin findings, a medical student who is interested in Dermatology wanted to analyze the possible association between this skin finding with the neoplastic syndrome, named "Leser-Trélat sign".

For this case study, a cadaver from the body donor program at Philadelphia College of Osteopathic Medicine (PCOM), South Georgia, was studied. Gross clinical presentation involved lesions located on the face, scalp, abdomen, pelvis, upper & lower extremities which prompted further investigation (Figures 1 and 2). Shave biopsies were taken from the right mid flank (Figure 2), left superior inguinal crease (Figure 3), and right breast (Figures 4 and 5). Skin samples were sent to Colquitt Regional Center for processing, where sections were embedded in paraffin and were stained with hematoxylin and eosin (H&E) stain [16]. A pathologist reported histopathological findings of the skin lesions and the breast tissue samples.

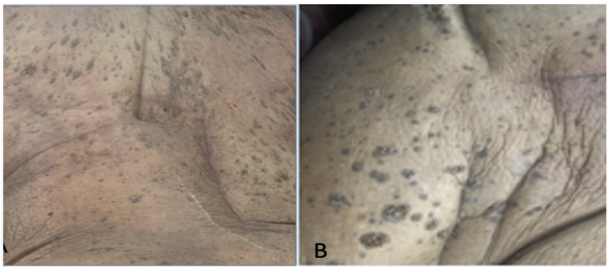

Figure 1) *To the left* ***(Figure, 1A)*** *is a dorsal view of the back/superior buttocks and lateral view of the left flank/stomach* ***(Figure, 1B)*** *that both demonstrate the gross proliferation of scattered pigmented, brown waxy "stuck on" plaques that are common characteristics of seborrheic keratoses.*

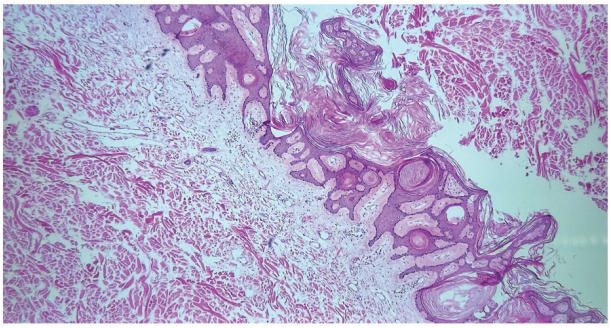

Figure 2) *A shave biopsy was performed of the right mid flank that revealed hyperkeratosis, horn cysts and pseudohorn cysts filled with keratin, common findings in SK lesions (Magnification: 40x, H&E staining).*

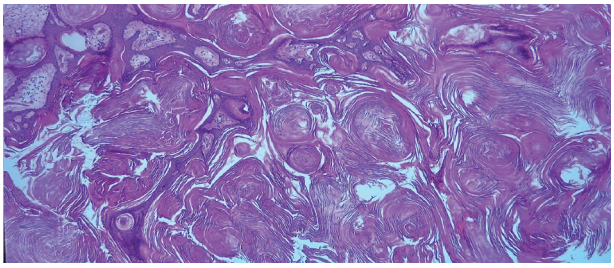

Figure 3) *A shave biopsy was performed at the left superior inguinal crease that confirmed the gross diagnosis of seborrheic keratosis with marked hyperkeratosis (Magnification: 100x, H&E staining).*

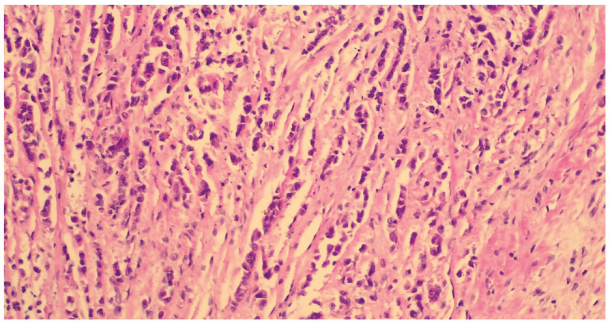

Figure 4) *Shave biopsy from the right breast mass revealed infiltrating cords of malignant tumor cells diagnostic of invasive ductal carcinoma of the breast, NOS type (Magnification: 40x, H&E staining).*

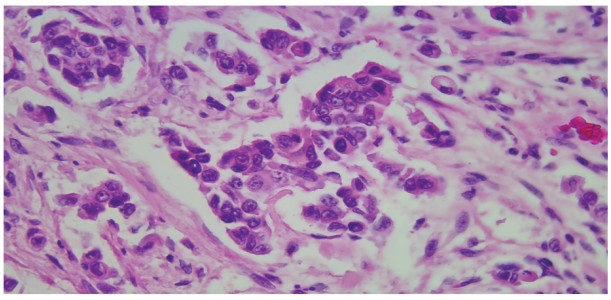

Figure 5) *Higher magnification of the breast tumor showing the malignant cell proliferation of the invasive ductal carcinoma of the right breast (Magnification: 200x, H&E staining).*

Diagnosis was confirmed by histopathology of H&E staining of the plaques that were taken from various locations. Provided for this article, is an example of histopathological confirmation of seborrheic keratoses located in right mid flank and left superior inguinal crease (Figures 3 and 4). During routine anatomy dissection performed by 1st year medical students, a mass was found within the right breast. This lesion was excised by a shave biopsy that was sent for analysis. This was determined to be the hypothesized malignancy that was the cause of the cutaneous eruption of Leser-Trélat. It should be noted that during the final anatomy lab dissections, no other masses or metastasis was seen through dissection.

H&E sections from the right breast revealed an invasive ductal carcinoma of the breast, not otherwise specified (NOS) type (Figures 5 and 6). Once breast malignancy was confirmed, diagnosis of Leser-Trélat was deemed very likely as a cutaneous sign of the underlying malignancy.

Discussion

Multiple SK lesions covering the face, abdomen, back, as well as both upper and lower extremities were observed in one of the cadavers in the gross anatomy laboratory. Due to the significant number of pigmented, verrucous lesions, the sign of Leser-Trélat was clinically postulated, later confirmed during routine laboratory dissection of the breast tissue. Histology sections confirmed not only multiple SK lesions in the skin, but also revealed an associated breast cancer in the form of an infiltrative ductal carcinoma.

Limitations to the study included unknown medical records that failed to acknowledge an acute versus chronic presentation of multiple eruptions of seborrheic keratosis, that is characteristic of this paraneoplastic syndrome [9-12]. Another major limitation to this study is the lack of criteria fulfilled by Curth's postulates which helps to determine the likelihood of the association between underlying malignancy and cutaneous proliferation of lesions. One of the major criteria of Curth's postulates focuses on whether treating the underlying malignancy causes a resolution of widespread SK lesions, which is seen in 50% of patients with Leser-Trélat [2,14,15]. This postulate was unable to be investigated as the patient was analyzed post-mortem.

Additionally, future studies should investigate the correlation between this syndrome and influence by genetic predisposition, tumor suppressor genes and more that could have an effect. Some researchers have hypothesized the roles of epidermal growth factor and transforming growth factor-alpha but further studies are required to determine this relationship [16-18]. Genetic correlation has been shown in previous case reports that have cited a mother and daughter that presented with rapid onset of widespread hyperkeratotic, wax plaques and were diagnosed invasive ductal carcinoma (74-year-old Mother) and infiltrating ductal carcinoma (41-year-old Daughter).

Lastly, the incidence of Leser-Trélat was unable to be determined as multiple studies have cited that the determination of "true Leser-Trélat" is difficult to calculate with current research due to the confounding factors: association with benign conditions (i.e. pregnancy, HIV, acromegaly, etc.) as well its common presentation in elderly that is often not further explored by clinicians [17]. Interestingly, an article stated that neither sex nor race of the individual puts them at increased risk of obtaining this paraneoplastic syndrome, which further adds to the importance of more detailed screening in patients with an acute widespread proliferation of cutaneous lesions [2]. Future studies need to determine the

incidence, prevalence and patient population that is at most risk (i.e. occupational exposure, type of malignancy, etc).

Conclusion

The sign of Leser-Trélat is rare by itself and its association with breast cancer is even more uncommon. Once a clinician recognizes the multiple SK eruptions, the patient should be meticulously screened, primarily with a thorough investigation regarding the timing on the appearance & number of the lesions, as this condition has been associated with an acute sudden proliferation presentation. If deemed likely due to history of present illness, then clinicians should pursue further testing should not focus solely on underlying GI malignancy, but also other cancers, due to ruling out unlikely malignancies, such as breast cancer that was found in this report. Shave biopsy and histology diagnosis as well as using imaging screening such as CT Chest with contrast is crucial for ruling out both cutaneous as well as underlying visceral malignancies; and should be encouraged when patients present in clinic rather than assuming the seborrheic keratosis is benign.

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