JHGD
Journal of Human Growth and Development
www. jhgd.com.br

ORIGINAL ARTICLE

Malignant adnexal cutaneous tumor of the scalp: a case report of difficult differential diagnosis between metastatic breast cancer and primary sweat gland tumor.

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Manuscript received: December 2020
Manuscript accepted: February 2021
Version of record online: March 2021

Abstract

This paper describes a case of a 71-year-old female who initially went to a dermatologist to assess a scalp skin tumor, which performed an incisional biopsy. Anatomopathological and immunohistochemical study revealed a preliminary diagnosis of breast carcinoma metastasis. Although the patient had no medical history of breast cancer, due to this result, she was referred to a mastologist, who investigated her breast nodules for the possible primary focus of the carcinoma. Despite an active investigation through imaging tests, biopsies, and mammotomy, without finding any possible primary focus on the breasts. Finally, the lesion on the scalp was entirely removed by a plastic surgeon. New anatomopathological and immunohistochemical exams confirmed the diagnosis of breast carcinoma metastasis. Given these results, the authors discuss the difficulty in diagnosing differentiation from a primary or metastatic neoplasm of the scalp, with the resources currently available, until the conclusion that it was a primary carcinoma of the sweat gland.

Keywords: breast carcinoma, sweat gland carcinoma, skin cancer.

Suggested citation: Martins MA, Moreira CA, Queiroz MCGAA, Martins WH, Pereira GV, Abreu LC. Malignant adnexal cutaneous tumor of the scalp: a case report of difficult differential diagnosis between metastatic breast cancer and primary sweat gland tumor. *J Hum Growth Dev. 2021; 31(1):177-183.*
DOI: 10.36311/jhgd.v31.10361

Authors summary

Why was this study done?
This study aimed to report and discuss the challenging differential diagnosis between a primary tumor of sweat glands and cutaneous metastasis of mammary carcinoma using anatomopathological and imaging diagnostic resources available today.

What did the researchers do and find?
The researchers examined the patient through clinical, imaging, and laboratory analysis tests. They performed comparative studies of the cutaneous malignancy and breast nodules, especially with immunohistochemical examinations.

What do these findings mean?
The findings show the challenge in differentiating a primary tumor of the sweat gland from a metastatic cutaneous tumor of mammary carcinoma, even with the immunohistochemical resources currently available. It also evidenced the importance of the clinical history, the correct propaedeutics, and a detailed study of the breasts to arrive at the proper diagnosis, ruling out others possibilities.

INTRODUCTION

Primary malignant neoplasms of the sweat glands are rare, constituting less than 1% of all primary malignant skin lesions[1]. Apocrine skin carcinoma has characteristics similar to those of cutaneous breast carcinoma metastases when it presents a tubule-lobular, or cordonal differentiation. This is a unique case due to the low frequency[2], the atypical clinical history, but mainly the difficult histopathological differential diagnosis and immunohistochemical evaluation among these neoplasms.

CASE REPORT

A Brazilian female, 71 years old, presented to a dermatologist with a scalp lesion in her right temporal region. After an incisional biopsy, her sample was firstly sent for anatomopathological study in a first pathology laboratory, chosen by the dermatologist, with the diagnostic hypothesis of basal cell carcinoma.

The pathology laboratory received a 0.3 cm surgical skin sample, which was microscopically described as a dermis fragment infiltrated by neoplasia consisting of small cells, hyperchromatic nuclei, grouped into small nodules, cords or outlining structures ring, dissecting the entire dermis and with preserved epidermis. There is no description of margin commitment. The anatomopathological report indicated breast carcinoma metastasis and the pathologist recommended a further immunohistochemical investigation to determine the neoplastic site of origin.

The immunohistochemical analysis was performed by the same pathologist and revealed positive markers for Estrogen Receptor (ER), Cytokeratin 7 (CK7), and BRST2 Monoclonal Antibody (BRST2) (focally positive); and negative for Progesterone Receptor (PR), Anti-c-erbB-2 (c-erbB-2) antibody, Cytokeratin 20 (CK20), Thyroid Transcription Factor-1 (TTF1), and Monoclonal antibody CDX-2 (CDX2). According to the report, the pathologist indicates that this immunohistochemical profile favors the diagnosis of metastasis of ER-positive mammary carcinoma origin.

Although the absence of breast cancer history, metastasis of mammary carcinoma origin was the major diagnostic hypothesis of the patient. The patient was referred to a mastologist, where she underwent consultation and screening tests for possible breast carcinoma.

Initially, the mastologist requested digital mammography, which revealed benign findings that remained stable since her two-year earlier examination. The current mammography reported dense heterogeneous breasts, which reduces the sensitivity of the method; absence of nodules; Bilateral, sparse calcifications, benign in appearance, including coarse in the right breast; usual-looking lymph nodes; BI-RADS 2.

The ultrasonographic (USG) results indicated skin and subcutaneous tissue without abnormalities; breast parenchyma with preserved echotexture; preserved axillary areas and three hypoechogenic nodules, oval and circumscribed, with intermingled hypoechogenic foci (calcifications) at the of the lateral quadrant union of the right breast (BI-RADS 3), recommending a three-month follow-up for cancer surveillance.

Given these results, a further magnetic resonance imaging (MRI) scan of the breast revealed a moderate amount of heterogeneous fibrous-glandular tissue, which presented a slight enhancement in the parenchymal background. The oval nodule with irregular margins was described as a heterogeneous and rapidly progressive post-contrast enhancement. It was located in the middle compartment of the junction of the lateral quadrant of the right breast, measuring 1.4 x 0.9 x 0.8 cm, 3.4 cm away from the papilla, and 3.2 cm of the skin (N1), which may correspond to the nodule with calcifications described in the mammography. Three oval nodules, with irregular margin and rapidly progressive post-contrast enhancement, located at the junction of the lateral quadrant of the right breast: N2, situated in the middle third (anterior to N1), measuring 0.8 x 0.7 x 0.6 cm, approximately 3.5 cm from the papilla, and 1.5 cm from the lateral skin; N3, located in the anterior third, measuring 0.7 x 0.6 x 0.5 cm, about 3.5 cm from the papilla, and superficial; N4, found in the middle third, measuring 0.7 x 0.6 x 0.4 cm, about 1.5 cm from the papilla, and 1.0 cm from the lateral skin.

Besides, the MRI described nonspecific bilateral sparse enhancement spots, with less than 0.5 cm, and absence of cystic images as well as axillary, intercostal, or infraclavicular lymph node enlargement. Thus, these results suggested that one of the nodules with heterogeneous enhancement may correspond to the mammography's calcifications and was categorized as BI-RADS category 4.

A second look USG was performed to confirm previous findings and showed four solid nodules at the junction of the right breast's lateral quadrant, the largest heterogeneous and the deepest measuring 1.3 x 0.9 x 0.7 cm (N1), associated with calcifications in between. The other solids and angled margins nodules are described as: N2, measuring 0.7 x 0.6 x 0.4 cm (middle third), N3 measuring 0.5 x 0.4 x 0.3 cm (anterior third), and N4, measuring 0.3 x 0.3 x 0.3 cm, corresponding to those of the MRI described above. USG-guided biopsies of the two largest nodules were recommended.

Before the mammotomy was performed, the clinical oncologist requested a positron emission tomography scan associated with computed tomography (oncology PET/CT), which did not demonstrate any abnormality of significant radiopharmaceutical for this case.

USG-guided mammotomy of two right breast nodules was performed. The anatomopathological study, that was performed by another patologist, chosen by the mastologist, indicated fragments of intraductal papilloma with sclerosis areas, foci of sclerosing adenosis, and dystrophic calcification. Adjacent breast tissue with alteration of columnar cells, usual ductal hyperplasia, rare intraluminal microcalcifications, apocrine metaplasia, fibrosis, and interstitial adipose infiltration was also detected. Thus, the pathologist suggested an excisional biopsy of the lesion for a comprehensive histopathological study.

Given this situation, not finding the possible primary focus of breast carcinoma, a review of the anatomopathological and immunohistochemical studies of the primarily biopsied sample on the scalp was requested. To avoid conflicts of interest, the sample was analyzed by a third pathology laboratory, different from the two laboratories involved in the previous examinations of the scalp and the breast. The novel immunohistochemical results revealed ER Protein (ID5) a 100% positive (+++/+++) (Fig. 1), PR Protein (PgR636) negative (Fig. 2), Oncoprotein c-erbB-2 negative (score 0), Ki-67 (MIB1) <1% positive, and Mammaglobin positive (Fig. 3) in neoplastic cells. Thus, a diagnosis of ER-positive breast carcinoma infiltration was reiterated.

With this information, it was decided, in a multidisciplinary team discussion, that surgery should be performed to remove the right breast sector, with the removal of nodules to rule out or confirm the breast pathology and the reopening of the scalp lesion site, for the removal in its entirety and expansion of margins.

The mastologist performed the surgery to remove the right breast sector, together with the plastic surgeon, who resected and enlarged the scalp lesion margins and the final anatomopathological in the right breast sector feported a multiple peripheral sclerosing intraductal papilloma and associated with dystrophic calcification; fibrocystic changes with apocrine metaplasia. At the same time, in immunohistochemical examination it presented ER protein (ID5) 80% positive (+++/+++), PR Protein (PgR636) positive (+++/+++), Oncoprotein c-erbB-2 negative (score 0), and Ki-67 (MIB1) <1% positive in proliferated cells as well as p63 positive in myoepithelial cells, concluding: intraductal and sclerosing papilloma.

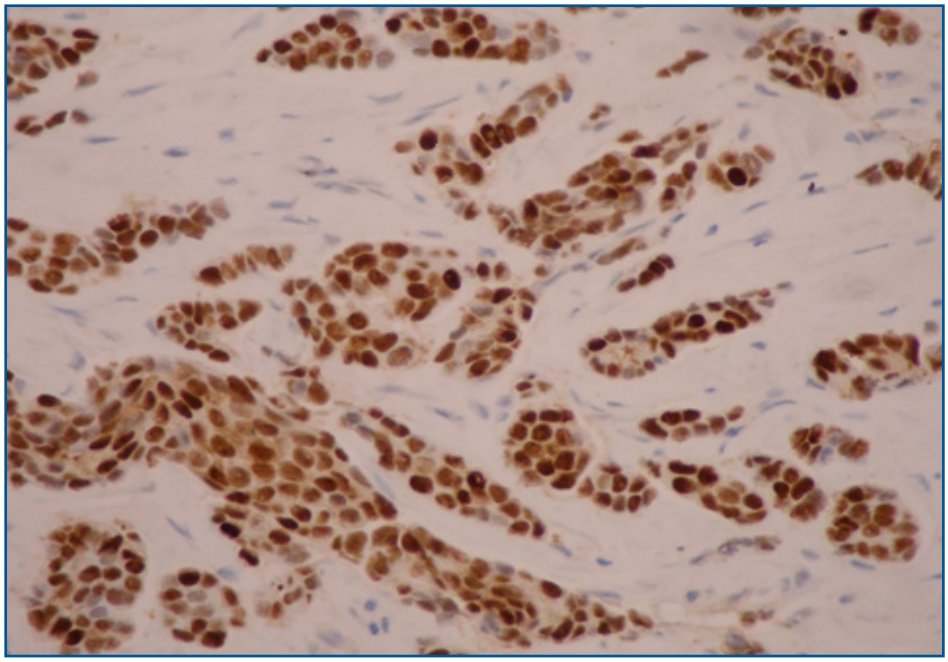

Figure 1: Immunohistochemical detail of the primary scalp tumor, demonstrating positive Estrogen Receptor (ID5 +). Positivity visible in nuclei of the neoplastic cells

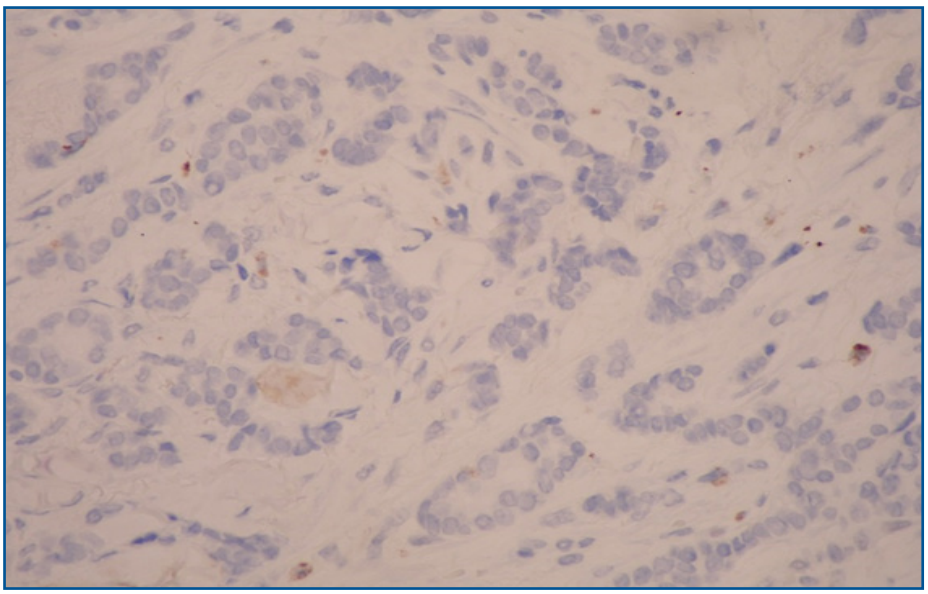

Figure 2: Immunohistochemical detail of the primary scalp tumor, showing a negative Progesterone Receptor (PgR636 negative).

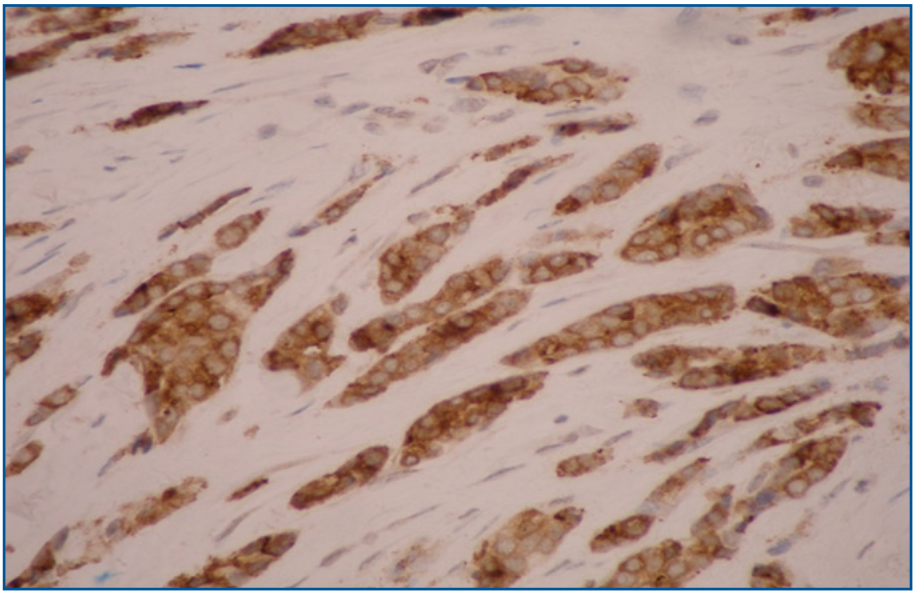

Figure 3: Immunohistochemical detail of the primary scalp tumor, showing positivity for Mammaglobin.

The anatomopathological analysis of the scalp lesion surgical reintervention confirmed the presence of residual invasive carcinoma (Fig. 4) with a tubule-lobular pattern (Fig. 5 and 6), chronic inflammatory process with scarring fibrosis, and giant cells' foreign body reaction, and free surgical margins. It was not necessary to repeat the immunohistochemical study of this sample.

Up to twelve-months follow-up at the outpatient clinic, the patient remained recurrence-free of either breast or cutaneous tumors.

DISCUSSION

The breast can be considered an apocrine gland, as well as the sweat gland, but modified [3]. A primary adnexal cutaneous tumor is rare and may share characteristics with mammary ductal carcinoma since the mammary ducts are modified sweat glands[4]. The major difficulty is that there may be no histopathological distinction between cutaneous metastatic breast carcinoma and a primary carcinoma of sweat glands.

Skin metastases are detected in about 0.6 - 10.4% of patients with internal malignancy. After melanoma, breast and lung carcinomas are the primary sources of skin metastasis in women and men, respectively[5].

From the anatomopathological point of view, the present case is quite interesting because it presents some peculiarities. The first of these is the histological aspect itself, since the neoplastic cells form, in addition to tubules (Fig. 5), a cordonal disposition (Fig. 6), an aspect that is widely found in breast neoplasms (lobular carcinoma with a classic aspect or tubule-lobular). Sweat gland carcinomas can present this histological aspect. However, it is a rarer

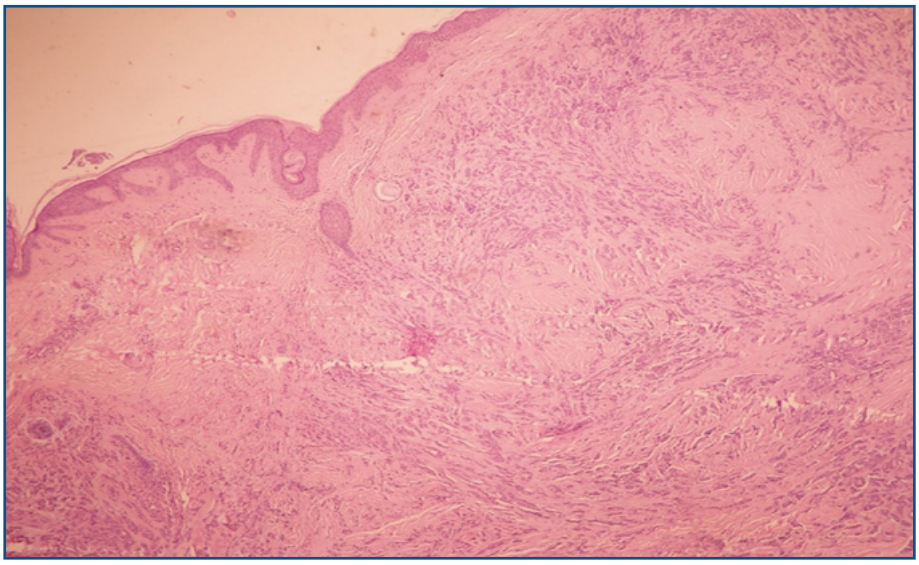

Figure 4: Primary scalp tumor showing neoplastic infiltration. HE 10x.

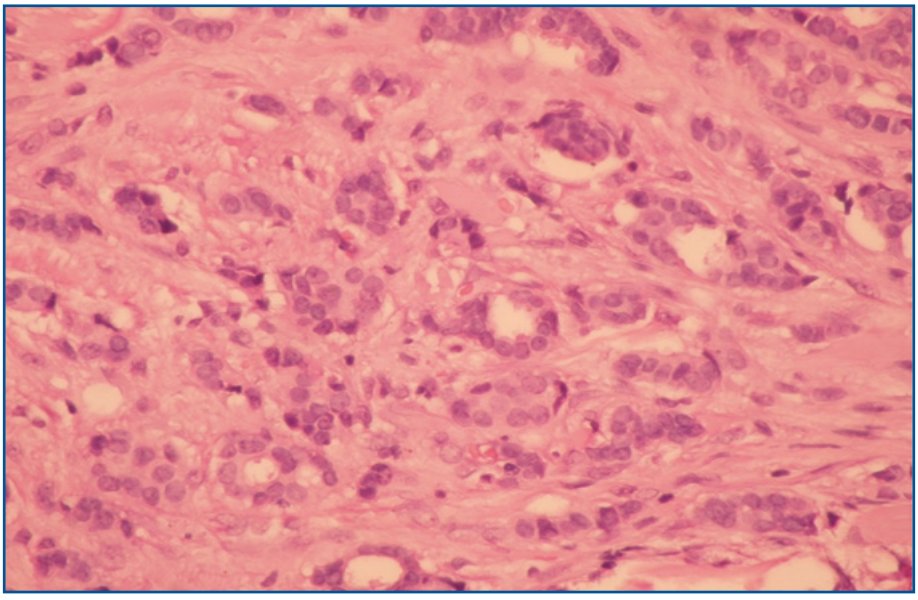

Figure 5: Histological detail of the primary scalp tumor, showing a tubular arrangement. HE 20x.

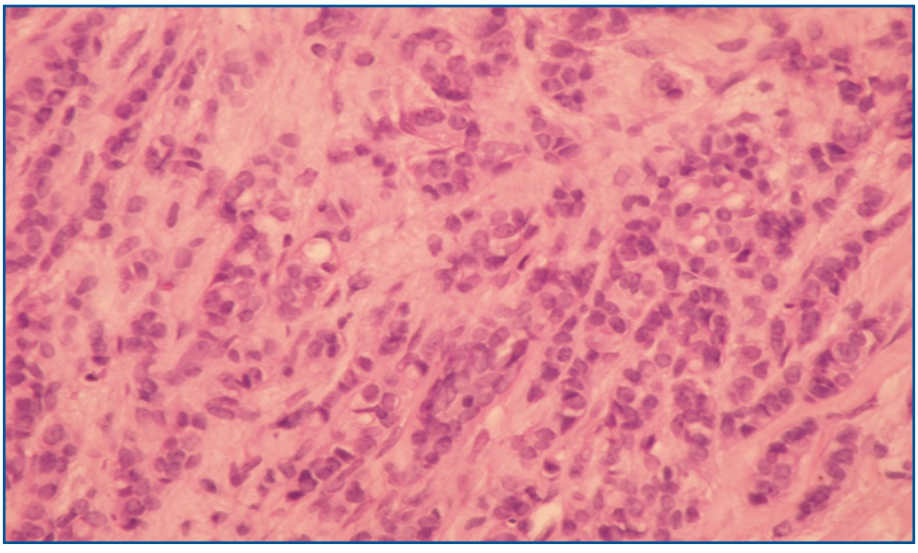

Figure 6: Histological detail of the primary scalp tumor, showing cordonal arrangement. HE 20x.

presentation, misleading the pathologist to think first about metastatic breast disease, the most frequent clinical condition. Sweat gland carcinoma is very rare[6].

The differential diagnosis between metastasis of breast carcinoma and a primary cutaneous adnexal tumor is also one of the most challenging immunohistochemistry tasks[7] since most of the markers are the same. In the literature, Piris *et al.,* compared profiles of the two tumors, and although there was no significant difference in the frequency of expression of Cytokeratin 5 (CK5) and Cytokeratin 6 (CK6), of protein p63 (p63), of protein HER2 (HER2), of protein GATA3 (GATA3) and Mammaglobin in apocrine cutaneous carcinoma versus apocrine mammary carcinoma, the expression of strong and diffuse CK5 and CK6 and/or the expression of Mammaglobin were observed only in cutaneous apocrine carcinoma[8].

Although the first pathologist stated in its report that the favor for the diagnosis of metastasis of carcinoma of mammary origin was due to the positivity of the ER, we can add that the BRST2 positivity also favored the suspicion of primary breast cancer. ER is very nonspecific, and BRST2 is positive for tumors of the breast, salivary and sebaceous glands[9].

Therefore, apocrine cutaneous carcinoma is probably Adipophilin negative, ER positive, PR can be negative or positive, HER2 negative and can exhibit strong and diffuse CK5 and CK6 and/or positive Mammaglobin expression. While an apocrine mammary carcinoma is probably Adipophilin positive, PR positive, ER negative and often exhibits HER2 positive (+++/+++), with the corresponding HER2 gene amplification. A panel of Adipophilin, ER, PR, HER2, CK5 and CK6, and Mammaglobin can be useful to distinguish apocrine cutaneous carcinoma from apocrine mammary carcinoma[8]. Anamnesis, clinical data of the patient, and imaging tests are essential to differentiate them, especially if the patient has a previous history of breast carcinoma or confirmation of a primary breast lesion[10,11].

Nowadays, immunohistochemical evaluation has been of great value in studying neoplasms for their diagnosis, identification of primary sites, prognostic and predictive factors of therapeutic response. Unfortunately, this reaction has limitations, and the present case demonstrates this since there is an overlap of positivity between tumors originating in cutaneous attachments and the mammary gland. The following markers can be positive in the breast and the glands of cutaneous annexes with varying intensities: ER, Mammaglobin, BRST2, and others. For this reason, it was essential to rule out the possibility of primary breast cancer.

As the patient had breast nodules, these were investigated, and their benignity was confirmed both by anatomopathological examination and by immunohistochemical study, which resulted in sclerosing intraductal papilloma.

CONCLUSION

The final diagnosis of primary sweat gland neoplasia was a diagnosis of exclusion, which means that after ruling out all possible origins of breast tumor, it was concluded that the scalp lesion was a primary sweat gland carcinoma.

Acknowledgments

We are grateful to the Samaritano Hospital of São Paulo, for supporting this research. We thank Dr. Isabella Batista Martins Portugal, for the technical review of the translation.

Research was carried out at the Centro Universitario Saúde ABC Plastic Surgery Discipline, Santo André, SP, Brazil and at the Samaritano Hospital of São Paulo, São Paulo, SP, Brazil.

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Resumo

Este artigo descreve o caso de uma mulher de 71 anos que inicialmente foi ao dermatologista para avaliação de tumor de pele no couro cabeludo, e que realizou biópsia incisional desta lesão. O estudo anatomopatológico e imuno-histoquímico revelou um diagnóstico preliminar de metástase de carcinoma de mama. Embora a paciente não tivesse história clínica de câncer de mama, devido a esse resultado, foi encaminhada à mastologista, que investigou seus nódulos mamários para localizar o possível foco primário do carcinoma. Apesar de uma investigação ativa por meio de exames de imagem, biópsias e mamotomia, não foi encontrado nenhum possível foco primário nas mamas. Por fim, a lesão no couro cabeludo também foi totalmente removida por um cirurgião plástico. Novos exames anatomopatológicos e imuno-histoquímicos confirmaram o diagnóstico de metástase de carcinoma de mama. Diante desses resultados, os autores discutem a dificuldade em diagnosticar a diferenciação de uma neoplasia primária ou metastática do couro cabeludo, com os recursos disponíveis atualmente, até a conclusão de que se tratava de um carcinoma primário da glândula sudorípara.

Palavras-chave: carcinoma mamário, carcinoma de glândulas sudoríparas, câncer de pele.