MALIGNANT CUTANEOUS SQUAMOMELANOCYTIC TUMOR, DIFFERENTIAL DIAGNOSIS ISSUE AND PECULIAR PERITUMORAL IMMUNE RESPONSE-CASE REPORT

Pascalau Andrei, Mircea Sandor, Vilceanu Narcis , Ovidiu Pop

*Marghita City Hospital, Marghita, strada Eroilor, nr. 12-14, Romania, pascalau_andrei@yahoo.com
**University of Oradea- Faculty of Medicine and Pharmacy, Pta 1 Decembrie, nr 10, Oradea, Romania, drims75@yahoo.com, forensicanv@yahoo.com, drovipop@yahoo.com

Abstract

In the last decade there has been a real interest in the scientific community in understanding regarding the existence of mixed tumor cell populations what long had been and still are viewed with different points of embryological development.

In this sense, the study of this relationship provided by melanocytes and keratinocytes and neoplasia is intriguing and still raise many questions and many difficulties of histological diagnosis; meantime difficulties of treatment ad poor prognostic understanding .

In this paper we present the case rapport of 66-year-old patient, who had presented two synchronous tumors at the level of the left ear. These tumors were basal cell carcinoma and a special tumor type named squamo-malanocytic tumor.

Immunohistochemistry methods managed to got a precise diagnosis using reactions for citokeratine, S100 and HMB45. The case presents a particularity of peritumoral immune response by this many CD4 lymphocytes Treg expressing CD25. These are lymphocyte subpopulations involved in mechanism of carcinogenesis.

Key words*: skin cancer, HMB45, S100,Treg, CD25, CD4*

INTRODUCTION

Between keratinocyte and melanocyte there is normally a close anatomical and functional relationship. In an attempt to explain this relationship have mentioned several hypotheses. One of these is the theory of "collision tumor ". This theory refers to the presence of two malignant tumors, one with melanocytic origin (melanoma) and the other with keratinocytic origin (basal cell carcinoma or squamous cell) which are located very close and inevitably "collide".

Another theory is the theory that sad that basal cell carcinoma or squamous cell carcinoma are invaded by non-neoplastic melanocytes, containing abundant pigment (melanin), a phenomenon much more commonly encountered in the proliferation of skin benign lesion, such as Seborrheic keratoses.

A third theory refers to the metastasis of melanoma "in transit", when it reaches a squamous cell carcinoma or a basal cell carcinoma. Malignant cutaneous tumor basomelanocytic or squamoumelanocyic is a lesion that

has a double cell neoplastic composition; one melanocytic and a second consisting of basal cell or squamous carcinoma

Differences of perspective and understanding of these entities exist between the authors of well-known from literature, not all are recognizing the existence of all malignant neoplasms scuamomelanocitice or basomelanocitice. Some authors described few cases of tumors when the squamomelanocytic tumors had a malignant melanoma behavior with highly metastasing tendency. (1,2)

MATERIAL AND METHOD

We present a case 66 year-old male, who was admitted in a surgical service for two synchronous tumors; one of theme is localized left preauricular area and the second one is localized in left earlobe. Clinically both tumors have been diagnosis as basal cell carcinoma. The excision performed by surgeon was according with surgical and oncological protocol.

Biopsies material excised was processed within the Pathology Department, Clinical Municipal Hospital Oradea by paraffin embedding. Processing has been carried out through the automatic method. In the final sections obtained were stained with hematoxylin-eosin (HE). In the second stage immunohistochemistry analyze has been carried out through the automatic method using GLX and BenchMark device; 34ßE12 antibodies (4A4 clone), S100 (clone 4 c 3.0), HMB45 (HMB45 clone), CD 20 (clone L26), CD 3 (2GV6 clone), CD25 (clone 4C9) according to the protocol provided by manufacturer Ventana Medical Systems, Inc. (3)

RESULTS AND DISSCUSIONS

Microscopic study of the paraffin embedding tissue show on HE stain shows the basal cell carcinoma metatipic-type, on left earlobe. (fig. 1)

The sample comes from preauricular area show a tumoral proliferation composed by polygonal-shape tumor cells and spindle-shape tumor cells. The cell proliferation is high with many mitosis and also atypical mitosis

Part of the tumoral bed show the cell tendency to keratinization and achantolitic aspects. Part of the tumoral cells show intracytoplamic brown pigment. Peritumoral zone presents a dense infiltration by lymphocytes.

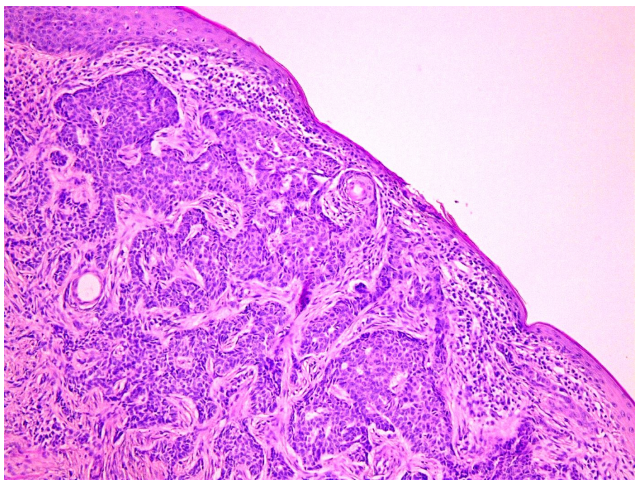

Fig. 1 Skin; basal cell carcinoma; HE 40X

The existence of actinic kerathosis meantime with epidermal connecting bridges with tumor, the tumor architecture, it concludes that the diagnosis of squamous cell carcinoma (G2) (fig. 2)

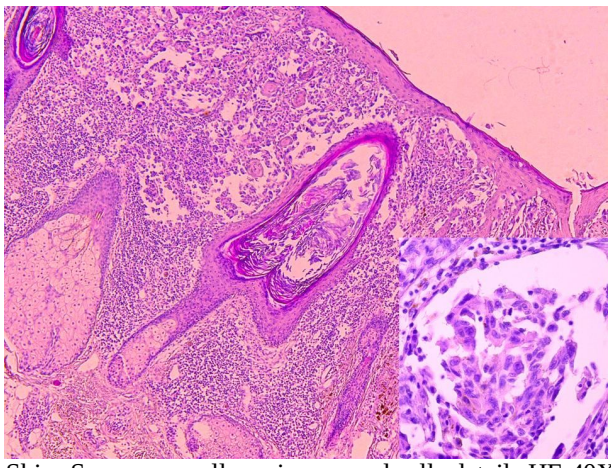

Fig. 2; Skin- Squamous cell carcinoma and cells details HE 40X/400X

The tissue examination show also some overlapping aspect with melanoma; brown pigment, few nuclear inclusions. The additional imunohistochemistry tests are need it for this reason to exclude a malignant melanoma.

In the next image can be seen the imunoprofile tumor. Cells were: citokeratina negative, positive S100 and HMB45 positive. (fig. 3). The citokeratin marker is a negligible percentage positive cells (5%), and leading to exclude carcinoma diagnosis. Immunostain guide us to malignant melanoma.

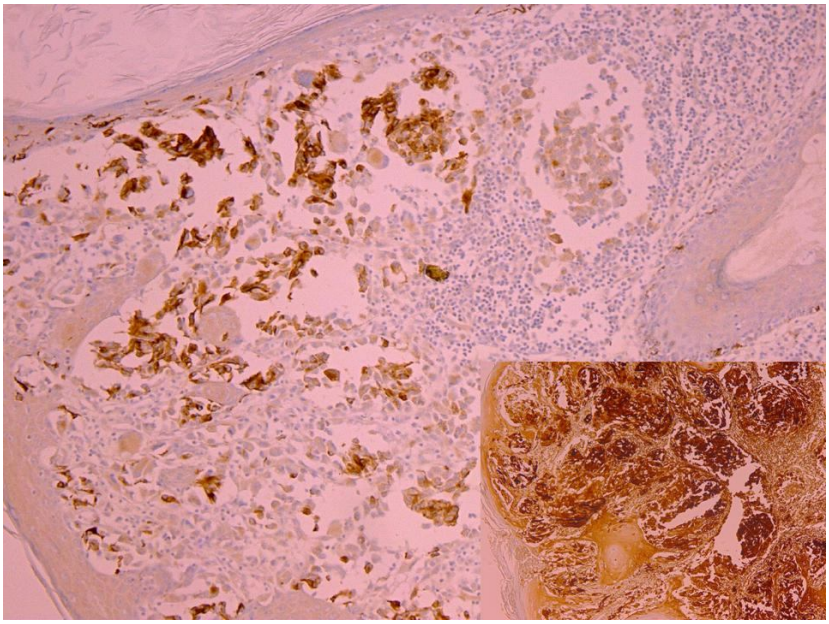

Fig. 3 Positive expression for HMB45 and S100 (100%)

Immune response in peritumoral area had a high intensities. For this reason we tried to clarify which lymphocytes populations are involved. Most peritumoral lymphocytes were of type T (CD4) ,compared to lymphocytes type B (CD20). (fig 4)

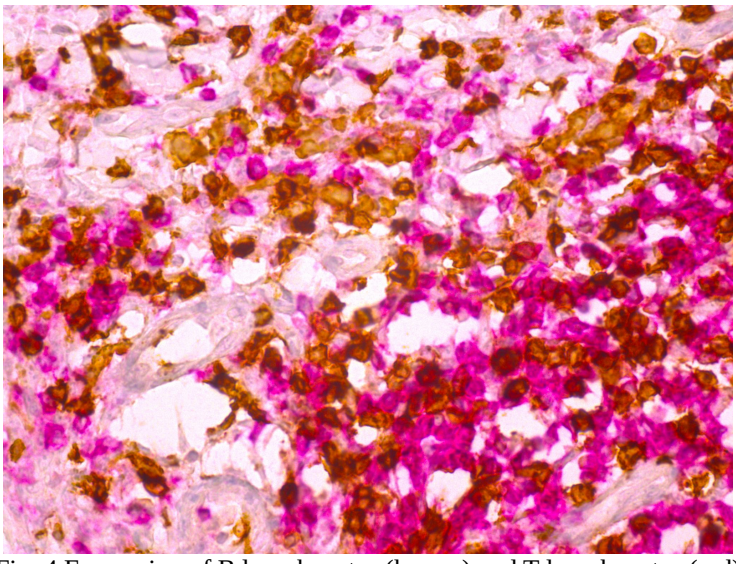

Fig. 4 Expression of B lymphocytes (brown) and T lymphocytes (red)

In an attempt to identify the presence of FOXp3 gene expression I marked T lymphocytes with CD4+CD25+ lymphocyte expression. When we analyzed the Treg expression a higher number of CD4+CD25+ lymphocytes can be seen. (fig.5)

It is known as lymphocytes expressing transcription factor Foxp3 (CD4 and CD25) named and Treg are involved in tumor growth and progression through a mechanism of immune suppression. (4,5,6)

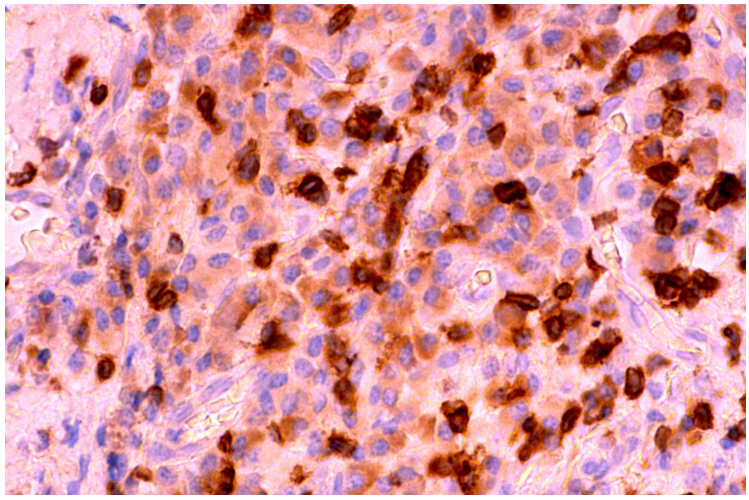

Fig. 5 Treg lymphocytes with CD4+CD25+ expression

CONCLUSIONS

Differential diagnosis between tumor entities presented remains sometimes difficult, and the ancillary technique playing a very important role in final diagnosis. Finding some clear evidence that sustains the existence of scuamomelanocitare tumors would change not only the way of interpretation and diagnosis, but would imply rethinking the origin of this tumors, as well as therapeutic protocols.

Lymphocytes Treg type involvement in the mechanism of carcinogenesis is not very well understood. Studies from the literature reveal their involvement in growing and tumor progression by inhibiting antitumor immune mechanism.

Data obtained from a case are not relevant to draw a conclusion in this way, but are founded in a premise for further study in the pathology of malignant tumors. Studies on mice proved defense capacity loss to antitumor induced Treg Foxp3-level changes. (7,8,9)

REFERENCES

1. Bennett CL, Christie J, Ramsdell F, Brunkow ME, Ferguson PJ, Whitesell L, Kelly TE, Saulsbury FT, Chance PF, Ochs HD, 2001, *The immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) is caused by mutations of Foxp3. Nat Genet.* 27(1):20-1.[PubMed].
2. Brunkow ME, Jeffry MW, Hjerrild KA, Paeper B, Clark LB, Yasaiko S-A, Wilkinson JE, Galas D, Ziegler SF, Ramsdell F., 2001, *Disruption of a new forkhead/winged-helix protein, scurfin, results in the fatal lymphoproliferative disorder of scurfy mouse*. Nat Genet. 27(1):68-73[PubMed].
3. Chen W, Jin W, Hardegen N, Lei KJ, Li L, Marinos N, McGrady G, Wahl SM., 2003, *Conersion of peripheral CD4+CD25 - naive T cells to CD4+CD25+ regullatory T cells by TGF - beta induction of transcription factor Foxp3. J Exp Med*; 198(12): 1875-86 [PMC free article][PubMed].
4. Curiel TJ, Coukos G, Zou L, Alvares X, Cheng P, Mottram P, Evdemon-Hogan M, Conejo-Garcia JR, Zhang L, Burow M, Zhu Y, Wei S, Kryczek I, Daniel B, Gordon A, Mayers L, Lakner A, Disis ML, Knutson KL, Chen L, Zou W., 2004, *Specific recruitment of regulatory T cells in ovarian carcinoma fosters immune privilege and predicts reduced survival*. Nat Med.;10(9):942-9[PMC free article][PubMed].
5. Kim JM, Rasmussen JP, Rudensky AY., 2007, *Regulatory T cells prevent catastrophic autoimmunity throughout the lifespan of mice*. Nat Immunol.;8(2):191-7[PubMed].
6. Miteva M, Herschthal D, Ricotti C, Kerl H, Romanelli P., 2009, *A rare case of a cutaneous squamomelanocytic tumor: revisiting the histogenesis of combined neoplasms. Am J Dermatopathol* ; 31:599-603.
7. Pouryazdanparast P, Yu L, Johnson T, Fullen D., 2009, *An unusual squamo-melanocytic tumor of uncertain biologic behavior: a variant of melanoma?. Am J Dermatopathol* ; 31:457-461.
8. Wei S, Kryzek I, Zou W - Regulatory T-cell compartmentalization and trafficking. Blood. 2006, 108(2):426-31[PMC free article][PubMed].
9. www.ventana.com.