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## Synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in a cervical lymph node: Case report of an unusual event

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### Abstract

The synchronous occurrence of two different neoplasias is an uncommon event, which may arise between tumors originating in the same organ or in cancer-to-cancer metastasis. We report a rare case of chronic lymphocytic leukaemia / small lymphocytic lymphoma associated with a cutaneous metastatic squamous cell carcinoma in a cervical lymph node. In the affected lymph node, it was observed an effacement of the normal architecture by neoplastic lymphocytes and it was noted the presence of neoplastic invasive epithelial islands. Immunohistochemical analysis demonstrated that lymphocytic proliferation was positive for CD20, CD5, CD23 and Kappa, and negative for CD3, CD10, Cyclin D1 and Lambda. The morphological and immunohistochemical profile lead to a phenotype of B-cell chronic lymphocytic leukaemia / small lymphocytic lymphoma. The epithelial cells were positive for CK5, thus rendering the diagnosis of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma. Literature supports the poor prognosis in cases that present coexistence of squamous cell carcinoma and chronic lymphocytic leukaemia / small lymphocytic lymphoma. Thus, it is necessary to be aware about this unusual finding in order to provide specific treatment.

**Key words:** Chronic lymphocytic leukaemia, small lymphocytic lymphoma, squamous cell carcinoma, metastasis.

### Introduction

The coexistence of two different neoplasias is a rare event, which may arise between tumors originating in the same organ or in cancer-to-cancer metastasis (1,2). In regard to cancer-to-cancer metastasis, lymphoma seems to be strongly related to metastasis by a secondary

malignancy (3). In the head and neck region, lymphoma and squamous cell carcinoma (SCC) are common neoplasias, so simultaneous occurrence may be an eventual finding (4). In relation to chronic lymphocytic leukaemia (CLL) / small lymphocytic lymphoma (SLL), patients have susceptibility to develop second malignancies in

25% of the cases. To the best of our knowledge, only 12 cases of concomitant squamous cell carcinoma and CLL/SLL have been reported in the English-literature so far. These cases in general are more susceptible to recurrence, metastasis and death (5).

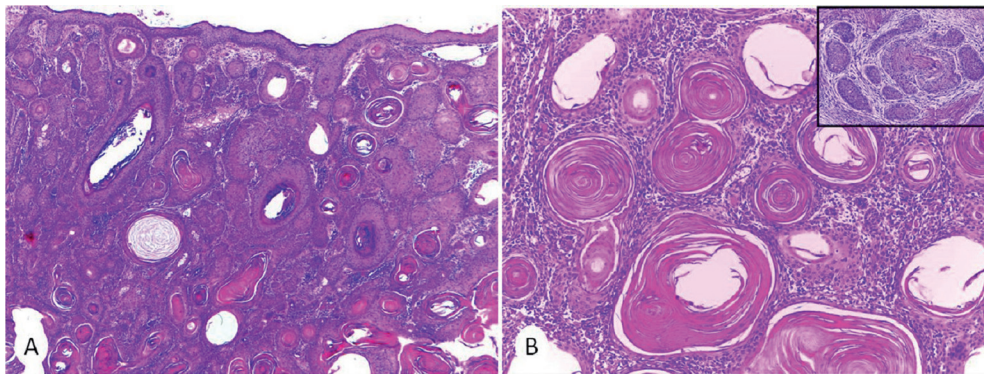
Herein, we report a rare case of CLL/SLL associated with an aggressive metastatic SCC. We also compared the characteristics of our case with previous reports of the literature.

### Case Report

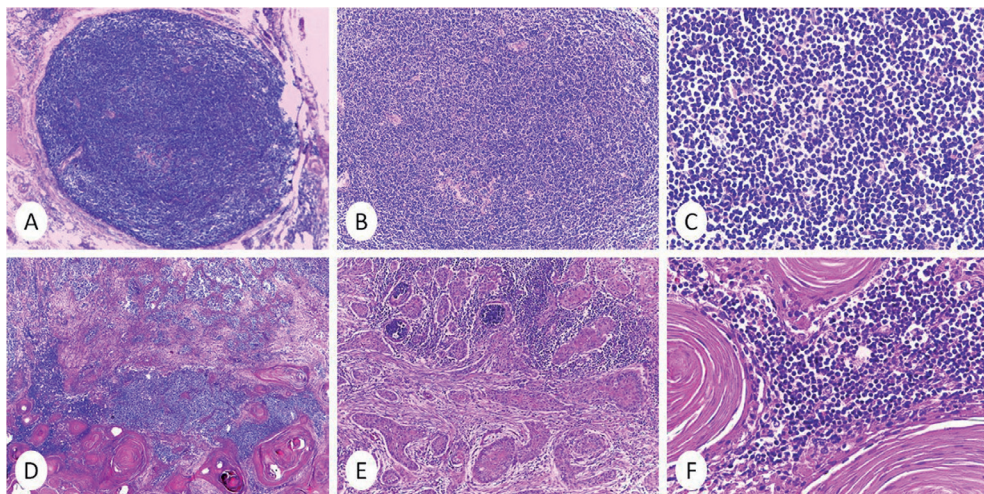
A 71 year-old male presented with a papular, invasive, hyperkeratotic, desquamative and erythematous lesion measuring 1 cm in greater diameter in the left malar region of the skin. Concerning his medical history, he was diagnosed with chronic lymphocytic leukaemia / small lymphocytic lymphoma (CLL/SLL) three years ago, and was submitted to a chemotherapy regimen with fludarabine and cyclophosphamide. The cutaneous lesions was biopsied and microscopic features were characterized by

an invasive growth downward the dermis. Cytologically, it was observed epithelial neoplastic cells with glassy eosinophilic cytoplasm, intercellular bridges, sometimes arranged in a concentric fashion with keratin pearls. The stroma was desmoplastic with chronic inflammatory infiltrate, and perineural invasion was identified (Fig. 1). These features lead to the diagnosis of cutaneous squamous cell carcinoma (SCC). After the diagnosis, he had the rest of the cutaneous lesion removed.

Eight months later, the patient returned and it was observed a clinical involvement of the cervical lymph nodes, which had a hard consistency, adherence to deep tissues and measured up to 2.5 cm. A neck dissection was performed. Eight out of the 79 examined lymph nodes presented an effacement of the normal architecture by mature, small and uniform lymphocytes with a narrow border of cytoplasm and a densely-stained nucleus. Additionally, it was identified the presence of neoplastic invasive epithelial islands, with significant keratin pearls production. Besides, the epithelial clusters were infiltrating the connective tissue (Fig. 2).



**Fig. 1.** Histopathological features of primary cutaneous squamous cell carcinoma. **A,B)** Well differentiated squamous cell carcinoma with significant number of keratin pearls. Perineural invasion was found [inset] (H&E, A x40, B x100, inset x40).



**Fig. 2.** Histopathological features of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in lymph nodes. **A)** Diffuse effacement of lymph node by a proliferation of small lymphocytes. **B,C)** Monotonous population of small lymphocytes with round nuclei. **D-F)** Coexistence of well differentiated squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma. (H&E, A-B x40, C x400, D-F x 40, F- x400).



An immunohistochemical assessment was performed with the antibodies listed in table 1. The epithelial cells were positive for CK5. In relation to neoplastic lymphoid cells it was observed positivity for CD20, CD5, CD23 and Kappa. CD3, CD10, Cyclin D1 and Lambda were negative. CD3 was only identified in reactive T lymphocytes (Fig. 3). The proliferative index with Ki-67 was 10%. The morphological and immunohistochemical profile were sufficient to render a diagnosis of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in a cervical lymph node.

The patient was submitted to radiotherapy and chemotherapy. In the last evaluation it was noticed absence of skin lesion as well as negative palpable lymph nodes. The patient is still under follow-up.

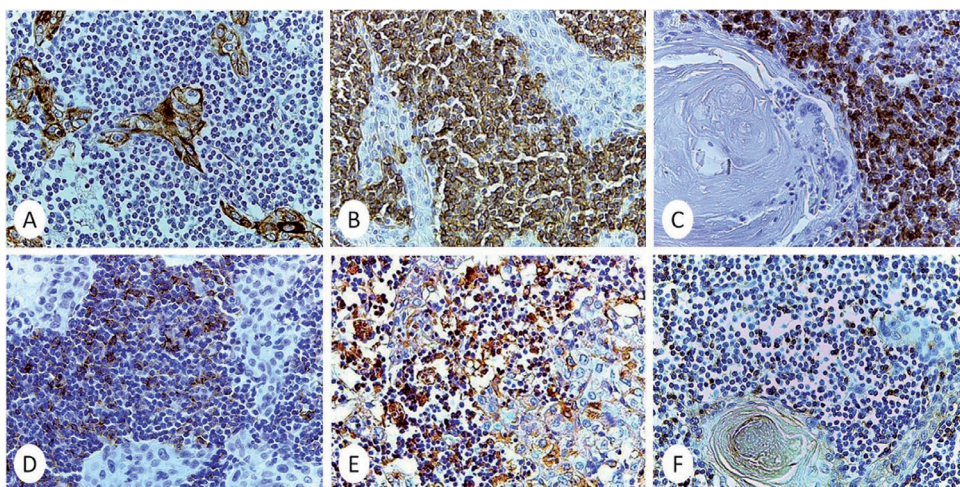
**Table 1.** Antibodies used for immunohistochemistry in the case of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in lymph nodes.

Antigen	Clone	Source	Dilution
CK5	SP27	Abcam	1:200
CD20	PANB	Dako	1:300
CD5	CD5/54/F6	Dako	1:50
CD23	MHM6	Dako	1:25
CD3	PC3/188-A	Dako	1:1000
CD10	56C6	Dako	1:60
Cyclin D1	Bcl-1	Biosb	1:50
Kappa	A8b5	Dako	1:100
Lambda	N10/2	Dakp	1:100

**Discussion**

We described a case of a patient previously diagnosed with CLL/SLL who developed cutaneous SCC, which metastasized to lymph nodes affected by CLL/SLL. In Western countries, CLL/SLL is the most common adult leukemia and affects mainly males (6,7). Although its etiology remains unclear, genetic factors have been proposed as carcinogenic agents (6,8). CLL/SLL is featured by a clonal proliferation of mature and frequently CD5+ B- cells within bone marrow, blood, spleen and lymph nodes (6). Microscopically, the cells express CD5, CD19, CD23, and CD20 (9). The differential diagnosis included mantle cell lymphoma, follicular lymphoma and marginal-zone lymphoma (10). The immunohistochemical profile of the lymphoproliferative disorder in the present case was in accordance with the diagnosis of CLL/SLL.

The pathogenesis of secondary tumors associated with CLL/SLL patients is unknown, but some theories have been proposed such as immune dysfunction related to CLL/SLL (11), genetic susceptibility, age, exposure to common carcinogenic agents (12), mutagenic effects of chemotherapy and radiotherapy (13). Although the exactly mechanism underlying lymphoma-associated tumor is still unclear, we believe that our patient developed a metastatic cutaneous SCC as a secondary tumor related to the previously diagnosed lymphoproliferative disorder. The development of SCC in our patient is in accordance with a study that documented a spectrum of cutaneous conditions in patients with CLL/SLL, which included SCC as one of the most common lesions (14). In addition, the coexistence of SCC with CLL/SLL in the same lymph node is a rare event based on studies which concluded that 5% of patients with head and neck cancer presented unexpected findings in neck dissection, such as malignant tumors (15).



**Fig. 3.** Immunohistochemical features of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in lymph nodes. **A)** Epithelial islands of SCC express CK5. **B-E)** The neoplastic lymphocytes express CD20 **B)**, CD5 **C)**, CD23 **D)** and Kappa **E)**. Only scattered T lymphocytes are positive for CD3 **F)**. (Immunoperoxidase, A-F x400).

Table 2 presents the clinical characteristic of previously reported cases of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in lymph nodes. In regard to age, the range was 44 to 82 years (mean, 72 years). All patients were male. Most of the sites affected by SCC were the skin of the head. From the available data, the interval between the diagnosis of CLL/SLL and

first SCC was 6 years. According to the diagnosis of the simultaneous occurrence of SCC and CLL/SLL, it was mainly based on neck dissection (3,5,12,16-20). Hence, the clinical characteristics of our case corresponded to previously reported features in the literature.

According to the literature, patients with CLL/SLL are prone to develop SCC with an aggressive biological behavior, featured by recurrence and extensive metastasis (18,21). The clinical behavior of SCC in our patient corresponds to those observations reported in the literature. In addition, the information about the outcome of Table 2, showed that most of the patients died of SCC and/or CLL (3,5,12,16-20). Nevertheless, our patient stills alive without evidence of recurrence or metastasis.

In conclusion, the occurrence of CLL/SLL may be related to second malignancies, such as cutaneous SCC. The coexistence of metastatic cutaneous SCC and CLL/SLL in a lymph node is a rare event, which generally results in a poor prognosis. Therefore, it is necessary to be aware about this unusual finding as SCC and CLL/SLL require specific treatment.

**Table 2.** Clinical characteristic of previously reported cases of synchronous metastatic cutaneous squamous cell carcinoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma in lymph nodes.

Reference	Age (years)	Sex	SCC site(s)	Interval between CLL/SLL and first SCC (years)	Diagnosis of cancer-to-cancer metastasis	Outcome
Villet <i>et al.</i> (1977)	73	M	Nose	6	Neck Dissection	Not Reported
Mora (1985)	61	M	Left and Right ear, nose, Left hand, supraasternal notch	8	Biopsy	Died of SCC
Bridges and Steinberg (1986)	44	M	Left parotid area	8	Autopsy	Died of SCC and CLL
Perez-Reyes and Farhi (1987)	77	M	Nose	Several	Neck Dissection	Not Reported
	68	M	Face	Not Reported	Not Reported	Died of SCC and CLL
	76	M	Scalp	Not Reported	Not Reported	Died of SCC and CLL
Soares <i>et al.</i> (1992)	75	M	Left neck	0	FNAC	Lost to follow-up
Gray <i>et al.</i> (2001)	73	M	Right preauricular area	Not Reported	Nodectomy	Not Reported
Pandey <i>et al.</i> (2003)	83	M	Right ear	0	Neck Dissection	Died of SCC
Strojan <i>et al.</i> (2005)	78	M	Right forehead	6	FNAC	Died of CLL
	75	M	Right forehead, nose	4	FNAC	Died of SCC
Sheahan <i>et al.</i> (2005)	82	M	Skin	Not Reported	Neck Dissection	Died of SCC
Present case	71	M	Left malar region, Left epicanthus, forehead	4	Neck Dissection	Still under follow-up

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