Case Report

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Progression of Follicular Lymphoma Observed in Collision with Basal Cell Carcinoma During Mohs Surgery

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The collision of basal cell carcinoma (BCC) and systemic lymphoproliferative disorders (LD) is well-documented[1-6]. Follicular lymphoma (FL) has previously been described in collision with squamous cell carcinoma; however, the collision of FL and BCC is not well documented [7]. Here we report a case in which FL was detected during Mohs micrographic surgery (MMS) for BCC.

A 71-year-old male with stage IVA, grade 1 to 2 systemic FL involving the spleen and bone marrow presented to the clinic to undergo MMS of a superficial and micronodular BCC on the right frontal scalp. Physical examination showed a 1x1.3-cm erythematous and depressed biopsy site with scattered ill-defined erythematous macules and patches on the superior forehead and scalp (Figure 1). The patient underwent two stages of MMS (Figures 2 and 3).

Figure 1: Surgical site. On the right frontal scalp there was a 1x1.3-cm erythematous and depressed biopsy site surrounded by ill-defined erythematous macules and patches

Figure 2: First Mohs stage. Microscopic examination of the first stage revealed small nodular and angulated aggregates of basaloid cells with fibromyxoid stroma and epithelial-stroma clefts in the superficial and deep dermis. There were scattered nodular lymphoid infiltrates. H&E original magnification x20.

Figure 3: Second Mohs stage. Microscopic examination of the second stage revealed moderately dense, nodular lymphoid infiltrates in the dermis and subcutaneous fat. H&E original magnification x40.

There was obvious BCC on the first Mohs stage. The second stage revealed a nodular lymphoid infiltrate concerning for FL. The density of the infiltrate made it difficult to definitively exclude residual BCC. An additional layer was excised and submitted for permanent section examination, with the repair delayed pending the results. Cytokeratin 5/6 immunostaining failed to show residual BCC in the second or third stages. An atypical lymphoid infiltrate consisting of CD20 positive B-cells co-expressing BCL6 and BCL2 (Figure 4), and smaller CD3 and CD5 positive T-cells consistent with FL was observed in all specimens. The patient returned to clinic one week later for repair.

Figure 4: Third stage submitted for permanent section examination. Microscopic examination revealed dense dermal nodular infiltrates consisting of CD20 positive B-cells co-expressing BCL6 and BCL2 A. CD20, original magnification x20. B. BCL6, original magnification x20. C. BCL2, original magnification x20

BCC has been reported to be more common in patients with non-Hodgkin lymphoid neoplasms, particularly chronic lymphocytic leukemia [1-6]. Parnes et al reported that the diagnosis of lymphoma preceded that of BCC in 79% of patients, with a shift in the distribution of BCC to less sun exposed areas in those who had a diagnosis of lymphoma first. While our patient was known to have systemic lymphoma, occasionally dense lymphocytic infiltrates seen on Mohs sections may herald an underlying LD [3].

Immune dysfunction likely plays a role in BCC development in patients with underlying LD. In chronic lymphocytic leukemia, neoplastic B-cells comprise a large percentage of circulating immune cells which, when recruited by tumor specific antigens, do not adequately stimulate the T-cell mediated response, thus facilitating tumor growth [3,4]. In lymphomas in which the circulating immune function may not be altered, abnormal B-cells present in the skin may disrupt the cell mediated response [6].

BCL2 is a proto-oncogene that inhibits programmed cell death increasing cell survival, and regulates the tumor microenvironment promoting tumor development [8,9]. While BCL2 expression is uncommon in primary cutaneous follicle center lymphoma, it is often seen in nodal FL [8]. In a study by Verhaegh et al, all BCCs were BCL2 positive with prominent staining throughout the tumor [10]. Perhaps this common pathway plays a role in the coexistence of BCC and FL.

Peritumoral inflammation is common, even in patients without underlying LD. Dense lymphocytic infiltrates make interpretation of Mohs sections difficult as they may obscure residual tumor [4,11]. When the infiltrate is directly associated with tumor, further resection is indicated; however, if the infiltrate is a coexistent LD without residual tumor, additional stages lead to an unnecessarily larger surgical defect [4]. Unfortunately, making this distinction may be impossible without the assistance of immunohistochemical stains. Therefore, when a dense infiltrate is present in patients with an underlying LD, it is prudent to take an additional stage for permanent section examination to confirm clear margins and the presence of a LD [6]. Alternatively, rapid cytokeratin stains, if available, can be performed on frozen sections preventing the delay of further excision or repair.

Notably, BCC recurrence and metastasis rates are increased in patients with LD, likely secondary to an inadequate immune response [2,5]. These patients should be treated aggressively, with MMS the preferred treatment [2,5]. Close clinical follow-up with, and communication between, both dermatology and hematology is imperative.

Our patient's hematologist was informed of the cutaneous involvement seen in the Mohs sections, and shortly after undergoing MMS a positron emission tomography scan revealed hyper metabolic adenopathy in the neck, chest, abdomen, and pelvis. Due to disease progression, the patient was started on bendamustine and rituximab which was discontinued after four cycles due to pancytopenia. He is doing well with no evidence of recurrence of the BCC, improving pancytopenia, and complete response of his FL 14 months after undergoing MMS.

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