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Regulatory T cells are present in Kaposi's sarcoma and increasingly frequent in advanced disease

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Background

Regulatory T cells (Tregs) are thought to play a crucial role in preventing and controlling hyperactive immune responses in malignancies and inflammatory disease. The role of Tregs in Kaposi's sarcoma (KS) has not been explored and is of particular interest in that this disease demonstrates characteristics of both inflammation and malignancy. We examined the presence and frequency of Tregs in KS tissue samples compared to normal skin. In addition, we compared presence and frequency of Tregs across three distinct histopathologic stages of KS. The histopathologic comparisons included the earlier patch and plaque stages, and the most advanced, nodular stage of KS.

Methods

Regulatory T cells are characterized by the expression of FOXP3, CD4 and CD25. A total of 15 cutaneous KS samples were obtained from different patients. Of the total 15 KS samples, breakdown of histopathologic subtypes included 6 samples from patches, 4 samples from plaques, and 5 samples from nodules. Eight samples from normal skin served as controls. Immunohistochemical and immunofluorescent assays and image analysis were performed on all samples.

Results

The frequency of FOXP3+ cells in all stages of KS was significantly higher compared to normal skin with means ± standard deviation of 43.4 ± 47.8 FOXP3+ cells/mm^2 in KS versus 4.56 ± 12.5 FOXP3+ cells/mm^2 ($p < 0.001$). This difference remained significant when comparing each individual stage to normal skin ($p < 0.001$ for nodular and plaque stages versus normal skin, $p = 0.002$ for patch stage versus normal skin). The number of FOXP3+ cells was highest in the nodular stage 70.3 ± 47.8 FOXP3+ cells/mm^2 compared to both patch 29.3 ± 50.8 $p = 0.001$ and plaque 27.8 ± 33.2 $p < 0.001$ stages. The frequency of FOXP3+ cells in patch and plaque stages was not significantly different.

Conclusion

Tregs are present in KS and are increasingly frequent in advanced disease. This finding of increased Tregs in the most advanced stage of KS is a phenomenon that has also been demonstrated in other malignancies including melanoma, ovarian cancer, and hepatocellular carcinoma. Tregs might play a critical role in suppressing the KS-specific immune response and contributing to the unchecked proliferation that is characteristic of KS. In addition, our finding that Tregs were markedly increased in the most advanced stage of KS suggests that regulatory T cells may also play a key role in KS progression. Ultimately, targeted regulatory T cell immunotherapy may lead to improved treatment response and prognosis.