
Footnotes and Disclosure
The authors have no proprietary or commercial interest in any materials discussed in this article.

A case of complete spontaneous regression of extensive Merkel cell carcinoma involving the orbit

Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine cutaneous carcinoma with an annual incidence of 0.18–0.42 cases per 100 000.1 MCC has a propensity for local recurrence, lymphatic, and distant metastasis, and most commonly presents in the head and neck region of elderly and immunocompromised patients.1,2 Despite its aggressive nature and poor 5-year survival rate (60%), complete spontaneous regression (CSR) has been documented in approximately 1.67% of cases.3 In all reported cases of CSR, resolution occurred within 18 months of diagnosis of the primary tumour, and the regression was rapid, occurring over 1–3 months.3 In most cases, CSR followed diagnostic biopsy or incomplete excision of a primary cutaneous lesion.3 In a few, CSR occurred in locally recurrent disease or nodal metastasis without prior intervention.3

To our knowledge, there has not been a previously documented case of spontaneous regression of MCC invading the orbit. Herein, we report a case of CSR following diagnostic incisional biopsy of an extensive MCC involving the left lower eyelid, cheek, and anterior orbit.

A 71-year-old woman presented to an outside institution in March 2016 with a 4-month history of a fast-growing, protruding mass on the left lower eyelid and cheek (Fig. 1). Computed tomography revealed a 4 cm × 3 cm × 3 cm rounded isodense homogenous cutaneous/subcutaneous mass at the level of the left lower eyelid and inferior orbital rim with invasion into the intraorbital fat. There was abutment of the globe with no globe deformation, extraocular muscle involvement, or lymphadenopathy. An incisional biopsy was performed, and histology showed small blue cells with sparse cytoplasm and irregular hyperchromatic nuclei (Fig. 2A). Tumour cells stained positively for

![Fig. 1—Clinical photograph of a large, nodular, exophytic solid and reddish mass with rapid growth over 4 months at the left lower eyelid–cheek junction. Histopathological studies revealed a diagnosis of Merkel cell carcinoma.](image)

![Fig. 2—(A) Initial biopsy. Hematoxylin & eosin stain demonstrating small, round malignant cells with little cytoplasm and irregular hyperchromatic nuclei (black arrows) with associated lymphocytic infiltration (white arrows). Immunohistochemical staining was diagnostic of Merkel cell carcinoma. (B) Repeat biopsy after clinical signs of regression. Hematoxylin & eosin stain demonstrating granulomatous inflammation consisting of many histiocytes and lymphocytes, but the absence of malignant cells.](image)
immunity and apoptosis of neoplastic cells, which may result from an immune response triggered by a biopsy.\textsuperscript{3,4} As was the case in our patient, approximately half of previous reports of CSR in MCC have documented the presence of lymphocytic infiltration among MCC tumour cells.\textsuperscript{1} The presence of tumour-infiltrating lymphocytes, and CD8+ lymphocytes in particular, may reflect an anti-tumoural immune response and serve as independent predictors of improved prognosis.\textsuperscript{3} Our patient’s initial biopsy was performed at another institution. Attempts to conduct delayed immunostains to better characterize T-cell subsets within the lymphocytic infiltrate were unfortunately limited by the amount of tissue available from the initial biopsy.

Another marker of improved prognosis is Merkel cell polyoma virus positivity (MCPyV).\textsuperscript{2,3,5} Rare mutational events and immune senescence may enable MCPyV clonal integration into the host genome, contributing to MCC oncogenesis.\textsuperscript{6} MCPyV-negative MCC may be attributed to UV mutations related to prolonged UV exposure.\textsuperscript{6} The presence of MCPyV within tumour cells may provide an immunostimulatory signal that generates a systemic response targeting MCPyV-positive tumour cells.\textsuperscript{2,3,5} Merkel cell polyoma virus testing was not available at our institution, but could have served as an additional predictor of the favourable outcome seen in our patient.

Seroprevalence studies suggest that MCPyV is widespread among healthy individuals, colonizing the skin of 50%–95% of adults.\textsuperscript{6} In contrast, MCC incidence is estimated between 0.18 and 0.41 per 100 000 persons,\textsuperscript{1} of which approximately 80% of cases are MCPyV positive.\textsuperscript{6} There are current efforts underway to develop a therapeutic vaccine to augment existing T-cell responses and promote de novo immune responses to clear MCC after viral integration has occurred.\textsuperscript{6} Vaccine targets include MCPyV oncoproteins, tumour-associated antigens, or mutated self-antigens.\textsuperscript{6} For the majority of cases of MCC that do not undergo CSR, a therapeutic vaccine could be employed in 2 ways. By inducing an enhanced T-cell response that could target micrometastases, a therapeutic vaccine could help to reduce recurrences, which occur in up to 70% of cases, when used as an adjuvant to surgical excision and radiotherapy.\textsuperscript{6} Alternatively, a therapeutic vaccine could be tried in combination with immunotherapy in advanced MCC when there has been a suboptimal clinical response.\textsuperscript{6}

Among previously reported cases of CSR in MCC, 87% occurred in the head and neck.\textsuperscript{2} The most common site of CSR involved the cheek, but CSR has also been described in MCC of the eyelid, nose, and forehead.\textsuperscript{2} To our knowledge, we report the first case of CSR following biopsy of a primary cutaneous MCC of the eyelid and cheek that also demonstrated orbital invasion. This suggests that CSR can occur in invasive MCC. No previous case of CSR has described recurrence or metastasis during follow-up. Accordingly, our patient has remained disease-free during 3.5 years of follow-up. This case reaffirms that CSR appears to carry a positive prognosis for an otherwise aggressive
cancer that is associated with high rates of recurrence, metastasis, and mortality.

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From trenches to trailblazers: the First World War and its influence on ophthalmology in Canada

When the First World War erupted in 1914, thousands of Canadians rushed to enlist out of patriotic fervour. Hundreds of doctors and nurses sailed overseas to attend to the masses of wounded in this war of unprecedented scale and destruction. Among these practitioners was a group of Canadian ophthalmologists.

We highlight the stories of 2 pioneering Canadian ophthalmologists (Fig. 1): Walter Walker Wright (1882–1967) and Alexander Edward MacDonald (1892–1976). Both were deeply affected by their war service. What makes their stories unique is how they called upon their military

Fig. 1—Dr. Walter W. Wright (left) and Dr. Alexander E. MacDonald (right) at the Toronto General Hospital, circa 1960. Courtesy: The Wright Family.