A 48-year-old man with a history of birdshot chorioretinitis presented with blurry vision, retrobulbar pain and sinusitis. Though visual acuity was unaffected, he had left optic disc oedema and mild restriction of left eye abduction. His symptoms progressed quickly, with diplopia in primary gaze, epistaxis from his left nostril, and a left relative afferent pupillary defect (RAPD). On computed tomography, there was a mass in the nasal cavity that extended through the left cribiform plate and lamina papyracea and posteriorly into the optic canal.

Pathological examination of biopsy specimens revealed sheets of undifferentiated cells with extensive areas of necrosis and islands of squamous differentiation. The tumour cells expressed monokeratin, p63, CD34, and p16. Molecular testing indicated rearrangement of the NUTM1 (15q14) locus and fusion of the NUTM1 and BRD4 (19p13.12) loci, confirming the diagnosis of NUT carcinoma of the sinonasal tract.

This is the first reported case of NUT carcinoma in a patient with birdshot chorioretinitis. The onset of chorioretinitis may have been the earliest sign of the effects of the BRD4-NUTM1 fusion protein, resulting in expression of HLA-A29. There is evidence that bromodomain and extra terminal (BET) family proteins play a role in inflammatory marker expression.

Keywords: NUT carcinoma, Orbit, Birdshot chorioretinitis, Epigenetics, Bromodomain and Extra Terminal (BET) proteins

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Introduction

Birdshot chorioretinitis is a chronic choroidopathy and vasculopathy that typically occurs in healthy, middle-aged women who are HLA-A29 – positive. NUT carcinoma is a rare, aggressive variant of squamous cell carcinoma characterised by a NUTM1 (nuclear protein in testis) gene rearrangement. We present the case of a man who developed birdshot chorioretinitis at the age of 38 years and ten years later developed a NUT carcinoma of the sinonasal tract that infiltrated the orbit. A possible genetic linkage between these two uncommon diseases is discussed.

Case report

A 48-year-old man with a 2-month history of sinusitis presented to an optometrist with blurry vision and retro-bulbar pain. On examination, his best corrected visual acuity was 6/6 OU, his intraocular pressures were 18 mm Hg OD and 16 mm Hg OS and his anterior segments were unremarkable.
He had left optic disc oedema and mild restriction of left eye abduction causing diplopia on left gaze. The patient had a history of birdshot chorioretinitis treated with intravitreal triamcinolone ten years previously and was HLA A29 – positive. His father had glaucoma but there was no other relevant family history. He was immediately referred to an ophthalmologist. On further examination his visual fields by confrontation were full. There was no proptosis and no alteration in colour vision. Fundus examination showed evidence of healed chorioretinitis and left optic disc oedema (Fig. 1). He was sent for an urgent computed tomography (CT) scan of his head.

Two days later, his retrobulbar pain had worsened and he had diplopia in primary gaze. A left relative afferent pupillary defect was accompanied by reduced colour vision on the left side. Hertel exophthalmometry revealed 2.5 mm of left proptosis. He had developed a continuous slow trickle of blood from the left nostril. The CT scan showed a destructive mass in the nasal cavity that extended through the cribriform plate and the lamina papyracea on the left side, pushing on the left medial rectus (Fig. 2). Posteriorly, there was extension into the optic canal. The radiological differential diagnosis included nasopharyngeal carcinoma, sinonasal undifferentiated carcinoma, lymphoma and esthesioneuroblastoma. He was admitted for endoscopic debulking and evaluated by both radiation and medical oncology.

The pathological specimen consisted of numerous fragments of grey-brown, friable tissue. Microscopic examination revealed sheets of undifferentiated cells with nests of squamous epithelium and extensive areas of necrosis (Fig. 3). The sheets were infiltrated by neutrophils and in one small focus the surface epithelium was involved by tumour cells. The tumour cells had oval-round nuclei with vesicular chromatin and small but distinct nucleoli. Mitotic figures were readily recognizable and the cells had a moderate amount of cytoplasm. The tumour cells expressed monokeratin, p63 (strong, nuclear), CD34 (strong, membranous) and p16 (moderate, cytoplasmic, patchy), but there was no expression of S100 protein, HMB45, leukocyte common antigen, chromogranin, or synaptophysin. In-situ hybridisation for...
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