INTRODUCTION
Progressive transformation of germinal centers (PTGC) was first described by Lennert and Muller-Hermelink in 1975 as enlargement of secondary follicles with blurring of the germinal center-mantle zone junction [1-3]. PTGC is a clinically asymptomatic condition characterized by persistent lymphadenopathy. PTGC is more common in males compared to females, with an approximate 3:1 ratio [4]. The etiology of PTGC is unknown, but is proposed to be a result of abnormal follicle hyperplasia following antigenic stimulation [1]. PTGC has been proposed to be part of a sequential spectrum of hyperplastic follicles, follicular lysis, and PTGC, with progressive ingression of mantle B cells [5]. The germinal center architecture consisting of centroblasts, centrocytes, plasma cells, and dendritic reticulocytes are largely replaced with small lymphocytes [1-3].

PTGC may present in the head and neck in a manner similar to that of nodular lymphocyte predominant Hodgkin’s disease (NLPHD) and must be differentiated based on histologic, immunologic, and in situ hybridization analysis. An association between PTGC and the development of NLPHD has been described in the past, but evidence supporting a causal role is lacking (Table 1)[1, 4, 6-10]. This case study and literature review will describe a presentation of PTGC in the head and neck, as well as the necessary diagnostic studies used to differentiate it from more serious conditions, such as NLPHD.

METHODS
Retrospective chart review was performed. Computed tomography (CT) scans were reviewed. Pathologic specimen images were provided by the diagnosing pathologist (KMG). Immunohistochemical analysis was performed for the following antibodies: CD3, CD20, CD21, bcl-2, bcl-6, Ki-67. Flow cytometry was performed evaluating the following antigens: CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD19, CD20, CD22, CD23, CD25, CD34, CD38, CD45, CD56, CD103, skappa, and slambda. A Medline search for key words “progressive transformation of germinal centers” and “PTGC” was used.

RESULTS
Our patient is a 75 year old man with a past medical history significant for reactive lymphoid hyperplasia of the right orbit diagnosed with an orbitotomy and biopsy performed by Ophthalmology. Representative CT images obtained at that time demonstrate a right supraorbital soft tissue mass (Figure 1). He was then treated with radiation to 2000 cGy. He subsequently presented to the Head and Neck Surgery clinic approximately 14 months after completion of radiation with a one month history asymptomatic right cervical lymphadenopathy. He has a surgical history significant for a right superficial parotidectomy in the 1970s for a reportedly benign parotidectomy in the 1970s for a reportedly benign parotid mass. He has a past medical history significant for prostate cancer treated with radiation to 2000 cGy. He subsequently presented with a 3 cm right parotid mass in his right parotid bed. The residual right parotid mass was also present. An axial CT image from superior to inferior, demonstrating the position of the soft tissue mass.

Figure 2. (A) Axial CT image at the level of the orbits obtained two years prior to presentation demonstrating a soft tissue mass (black arrow) within the superolateral aspect of the orbit. (C-F) Axial CT images from superior to inferior, demonstrating the position of the soft tissue mass.

Figure 3. (A) A PTGC demonstrated as a large nodule (white arrow) 2-3 times the diameter of the surrounding reactive follicles (white arrowheads). (B) A magnified image demonstrates infiltration of small lymphocytes within the germinal center. (C) Bcl2 staining of a normal specimen demonstrates paucity of staining within the germinal center (black arrow). (D) Immunolabeling of the PTGC specimen shows scattered labeling within the germinal center indicative of mantle zone center migration (black arrowheads). (E) Bcl6 expression in a normal specimen. (F) Bcl6 labeling in a PTGC specimen with evidence of non-labeled cells in the germinal center.

Figure 1. (A, B) Coronal CT images at the level of the orbits obtained two years prior to presentation demonstrating a soft tissue mass (black arrow) within the superolateral aspect of the orbit. (C-F) Axial CT images from superior to inferior, demonstrating the position of the soft tissue mass.

An association between PTGC and the development of NLPHD has been described in the past, but evidence supporting a causal role is lacking [1, 4, 6-10]. In one study, only 2/206 patients with NLPHD had pathologic evidence of PTGC up to 3 years prior to diagnosis [17]. Two additional patients with PTGC had a previous diagnosis of NLPHD and another had concurrent diagnoses. Another study involving 50 patients showed no patients with PTGC prior to Hodgkin’s disease, but 15 patients with PTGC diagnosed subsequent to Hodgkin’s disease [1]. A large percentage of the patients (12/50; 24%) had been previously misdiagnosed, of which, six were diagnosed with NLPHD and three received therapy. In a study of 42 Japanese patients with PTGC, a chronic localized inflammatory process in the head and neck region was present in 13 patients (31%). The majority of patients presented with a solitary enlarged, cervical lymph node [4].

Persistent lymphadenopathy of the head and neck requires imaging and tissue diagnosis to exclude malignant etiologies. Immunologic and histologic studies are required to exclude lymphomatous processes. Following the diagnosis of PTGC, management is expectant with close follow-up and additional investigation warranted should new symptoms or lymphomatous develop.

REFERENCES

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