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Case Report

Immunoglobulin Heavy Chain Gene Rearrangement Studies in the Diagnosis of a Paediatric Conjunctival Lesion

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Abstract
We present a case whereby standard immunohistochemistry and flow cytometry studies for a conjunctival biopsy were unable to reliably differentiate between the two distinct pathological processes of benign reactive lymphoid hyperplasia from conjunctival lymphoma. A tissue diagnosis was only able to be conclusively attained after the application of immunoglobulin heavy chain rearrangement studies to the specimen. This is unusual and to our knowledge has not been previously expressed in the literature. Hence, the use of these further molecular studies may have great potential clinical implications in helping resolve such diagnostic dilemmas.

Introduction

Immunohistochemistry and flow cytometry are standard investigations utilised when analysing conjunctival biopsies [1, 2]. However, when subsequent findings cannot definitively confirm a diagnosis, the role of further molecular analysis becomes increasingly important [1, 2]. We report a case whereby immunoglobulin heavy chain gene (IgH) rearrangement studies

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established the diagnosis of a conjunctival lesion from a paediatric patient as benign reactive lymphoid hyperplasia (BRLH).

Case Report

An otherwise healthy 12-year-old boy was referred to eye clinic for assessment of a right-sided conjunctival lesion. The lesion was noted 6 weeks prior, and steroid eye-drops were trialled for 2 weeks with minimal change in its characteristics. The patient was asymptomatic, denying any recent trauma, foreign body exposure or ophthalmic surgery. A salmon-coloured lesion was found within the right medial caruncle whilst a smaller lesion of similar appearance was incidentally noted in the left medial caruncle. The remainder of his ocular examination was normal.

An uncomplicated excision biopsy of the right conjunctival lesion was undertaken. From the recommended 1-month follow-up, the patient displayed no extra-ocular manifestations of lymphoma on physical examination [3]. A chest X-ray and serological investigations were also conducted with no abnormalities detected.

Flow cytometry of the specimen demonstrated an atypical lymphoid population of mostly mixed CD20-positive B cells and CD5-positive T cells, whilst histopathology displayed these atypical cells infiltrating germinal centres. Such features were suggestive of an extranodal marginal zone type lymphoma; however, a pattern of clonality supporting this diagnosis was not confirmed given the absence of both kappa and lambda light chain staining on immunohistochemistry. Further testing with IgH rearrangement studies demonstrated a polyclonal B-cell population which was consistent with BRLH.

Three months on, no additional visual or systemic symptoms had developed. The excision site was well healed; however, the left-sided lesion had increased in size. A left conjunctival excisional biopsy was conducted, undergoing the same immunohistochemistry and flow cytometry studies to confirm the presence of both kappa and lambda light chains and a subsequent diagnosis of BRLH.

Discussion

BRLH is characterised by highly concentrated lymphoid tissue with well-defined follicles and germinal centres [2–5]. Although uncommon in children, it is usually situated in the nasal fornix; such as this case [4]. The paediatric demographic has a higher incidence of mucosa-associated lymphoid tissue; thus, this patient might have developed eye-associated lymphoid tissue due to an antigenic hyper-stimulation reaction [1, 2]. The use of steroid eye drops could have potentially masked the characteristics of the lesion, hence further confounding diagnosis. [3] Contamination or incorrect processing of the biopsy during initial histopathology and flow cytometry can produce inaccurate findings [5]. Since the proper methodology was conducted correctly for this case, this is unlikely. Eventual diagnosis of BRLH is reassuring given the very low risk of malignant transformation in children [3].

Immunohistochemistry and flow cytometry could not determine between a reactive lymphoid proliferative process or lymphoma for this patient. Normally one of either kappa or lambda light chains are found in lymphoma, whilst both light chains are present in BRLH, as seen in the left conjunctival biopsy [1, 5]. Testing negative for both light chains from the initial

right conjunctival biopsy is unusual and has not been previously documented from our literature review. Thus, the use of IgH rearrangement studies was critically important for differentiating between a polyclonal lymphoid population consistent with BRLH compared to monoclonality associated with lymphoma [1, 2, 5].

Absence of light chain staining from routine immunohistochemistry and flow cytometry of a conjunctival biopsy is unusual and complicates diagnosis. We report a case whereby IgH rearrangement studies established the diagnosis of BRLH from a conjunctival lesion in a paediatric patient.

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Statement of Ethics

Consent for publication of this case report has been obtained from the patient's guardian.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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