**Comment to “Conjunctival Primary Acquired Melanosis: Is It Time for a New Terminology?”**

By Jakobiec FA.

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We are delighted that Dr Jakobiec in his recently published review on conjunctival melanocytic lesions endorses our criticism of the term ‘primary acquired melanosis (PAM)’ when describing histologic findings (1). In 2008, we suggested that it would be more precise for histopathologists to differentiate between ‘conjunctival melanocytic intra-epithelial neoplasia (C-MIN)’ and ‘hypermelanosis’ (i.e., melanin over-production) (2). We proposed that ‘PAM’ should be used only as a clinical term, when the pathology of the conjunctival pigmentation is not known. We are also glad that Jakobiec supports our grading system for C-MIN, which scores objectively melanocytic pattern, atypia and vertical spread in an attempt to avoid the subjective terms ‘mild’, ‘moderate’ and ‘severe’.

It is unfortunate that Dr Jakobiec was not aware of our proposal or nomenclature prior to writing his recent review. He suggests our 2008 paper ‘has received less attention in the United States than it ought to have, owing to its publication in the Australian ophthalmic literature.’ However, despite being written 8 years ago, our article has been cited nearly 60x by authors, including those from the USA, and indeed by Dr Jakobiec himself in 2009 and 2010 (3, 4)! We repeated our nomenclature proposal and C-MIN scoring system in subsequent review papers (5, 6), and presented them at numerous international conferences. C-MIN scoring is currently undergoing a multicentre collaborative validation, to better define ‘conjunctival melanoma in situ’ potentially for future TNM staging systems. Hence, our proposal received/s wide attention.

Interestingly, Dr. Jakobiec prefers the noun ‘proliferation’ instead of ‘neoplasia’, because he suggests that some cases can be hyperplastic. To our knowledge, there is no convincing evidence that the histopathologic features of ‘PAM’ are ever caused by hyperplasia. As a pathologist, Dr Jakobiec will know that ‘hyperplasia’ is caused by an external stimulus and that the changes are potentially reversible should the stimulus be removed. With respect, Dr. Jakobiec is basing his argument on speculation, and in the quest for precision is making a retrograde step in proposing ‘proliferation’ instead of ‘neoplasia’. We use the term ‘neoplasia’ in its true sense – a ‘new growth’ of benign or malignant cells, which may or may not be associated chromosomal alterations. Dr. Jakobiec is concerned about the insurance implications of the word ‘neoplasia’; however, we believe that one should ‘call a spade a spade’ as one does with any other disease entity, avoiding misleading patients and insurance companies about the true pathology of a lesion. The same argument can be used for the term ‘conjunctival melanoma in situ’, which has been controversial for years, but really should be recognized and treated as such.

Dr. Jakobiec takes issue with our term ‘hyper-melanosis’, maintaining that ‘melanosis’ should suffice, since the conjunctiva is normally non-pigmented.  Clinically, the conjunctiva is indeed non-pigmented, which is why we retain the clinical terms ‘congenital melanosis’, ‘primary acquired melanosis’ and ‘secondary acquired melanosis’, according to the patient’s history. With high-power microscopy, however, an overproduction of melanin granules is visible, which is why we proposed the term ‘hyper-melanosis’. In any case, Dr. Jakobiec would also know that the addition of “hyper” to other pathology terms – e.g. ‘somatic mutation’ and ‘somatic hypermutation’– are essentially interchangeable. Besides being unnecessarily wordy, Jakobiec’s term ‘intraepithelial nonproliferative melanocytic pigmentation’ is inaccurate, because many melanin granules are also located in the epithelial cells, having been transferred there through melanocytic dendrites.

In summary, we are pleased that an eye pathologist of such prominence as Dr Jakobiec has joined us in ‘taking up the cause’ to rename conjunctival melanoma precursors more precisely. Further work is required to demonstrate the underlying genomic alterations differentiating benign and malignant conjunctival melanocytic intra-epithelial neoplasia.

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