Letter to the Editor

Heterogeneity of cytokeratin 7 expression in pagetoid Bowen’s disease

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To the Editor,

Cytokeratin (CK) 7 has been found to be expressed in the secretory cells of the eccrine/apocrine glands,1–3 and has been used as a marker of extramammary Paget’s disease.4 CK7 has been reported to generally be absent in Bowen’s disease.5 However, several previous reports have called attention to the fact that CK7 (OV/TL 12/30) is sometimes expressed in pagetoid Bowen’s disease,6–10 which represents an important consideration in the differential diagnosis of extramammary Paget’s disease.

We recently evaluated a case of pagetoid Bowen’s disease (a 59-year-old male with an erythematous plaque on his right thigh close to the groin). In addition to the histopathologic findings (Fig. 1A), the expression of both CK1 and CK10 (Fig. 1B), which are markers for suprabasal cells in the epidermis and generally positive in Bowen’s disease,3 supported the diagnosis of pagetoid Bowen’s disease in this instance. None of the pagetoid cells contained mucin, as confirmed by negative staining for mucicarmine, Alcian blue at pH 2.5, and periodic acid-Schiff staining with diastase digestion, and there was a lack of expression of gross cystic disease fluid protein-15, thereby further excluding the diagnosis of extramammary Paget’s disease. At that time, we observed the expression of CK7 (OV/TL 12/30, Dako) (Fig. 1C) by immunohistochemical staining using an antibody that had been purchased in 1999 (abbreviated hereafter identified as 1999), using a standard avidin-biotin-peroxidase (ABC) complex system, thus confirming the results of previous reports indicating the presence of CK7 expression by pagetoid Bowen’s disease.6–10

Although the observation of CK7 expression in pagetoid Bowen’s disease has been hypothesized to be due to either adnexal (glandular) differentiation in epithelial stem cells8,10 or phenotypic changes of the neoplastic cells of squamous cell carcinoma (SCC) toward Toker’s cells,7 the exact reason for this type of CK7 expression remains unclear.6–10 We believe the finding of CK7 (OV/TL 12/30) expression in poorly differentiated cutaneous SCC, recently reported by Pulitzer et al.,11 represents a different phenomenon from the CK7 expression observed in pagetoid Bowen’s disease.

More recently, while conducting another investigation involving CK7, we again checked the expression of CK7 (OV/TL 12/30, Dako, Glostrup, Denmark), this time using an antibody purchased in 2010 (abbreviated hereafter as 2010), using both the ABC complex system and the newer Envision system in the same specimen that was used for the first examination. Surprisingly, a negative expression was revealed by both systems (Fig. 1D). This type of heterogeneity in the CK7 (OV/TL 12/30) expression has also been recently experienced in some cases of Bowen’s disease with clear cell change.

The heterogeneity in the expression of CK7 in normal cutaneous tissue depending on the clone of the antibody has also been found in previous reports; clone (OV/TL 12/30) reacted with normal sebaceous glands in addition to the eccrine/apocrine glands2,3 whereas clone (Ks7.18) did not react with normal sebaceous glands.1 We previously confirmed this type of difference between the two clones12 and found the fact that one clone (OV/TL 12/30) (1999) also reacted to the normal outer root sheath cells of hair follicles, while it reacted to the normal sebaceous glands in addition to the eccrine/apocrine glands.13,14

On the basis of the CK7 (OV/TL 12/30) expression in the outer root sheath cells, we previously
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reported a method that combined immunostaining for CK7 (OV/TL 12/30) and CK17 for the detection of tricholemmal differentiation.13,14 However, similar to the result observed herein, namely the loss of the CK7 (OV/TL 12/30) (2010) expression in pagetoid Bowen’s disease, our recent investigation revealed that CK7 (OV/TL 12/30, Dako) (2010) only reacted with the eccrine/apocrine glands, thereby losing its ability to detect CK7 in normal sebaceous glands and outer root sheath cells.

It was therefore surprising to discover that CK7 (OV/TL 12/30, Dako) (2011) reacted with the pagetoid Bowen’s disease, and that it reacted with the peripheral germinative cells of the sebaceous glands as well as with eccrine glands. The reason for the heterogeneity observed in the CK7 (OV/TL 12/30) staining pattern remains unclear. We therefore performed a side-by-side test of the CK7 expression in the same specimen (pagetoid Bowen’s disease), using the antibodies, i.e. OV/TL 12/30 (2010, lot number 00034196), OV/TL 12/30 (2011, lot number 00050559) and KS7.18 (Progen, Heidelberg, Germany), with the methods of both the ABC complex system and the newer Envision system. This side-by-side test revealed a positive expression by OV/TL 12/30 (2011) with the ABC complex system, only a partial expression by OV/TL 12/30 (2011) with the newer Envision complex, and a negative expression by the other antibodies with both systems. These results suggested that the date of manufacture or the lot numbers of the antibody, the type of clone (OV/TL 12/30 or KS7.18) and/or the conditions in the laboratory (such as the selected method, ABC complex system or the newer Envision system) may cause heterogeneity in CK7 expression.

We would like to call attention to this heterogeneity in CK7 expression when it is being used for the purposes of either making a diagnosis or for conducting research studies on the histogenesis of cutaneous neoplasms.

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