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CASE REPORT

'Now you see it…now you don't.' Carmoisine vital dye facilitates complete removal of cutaneous neoplasia by intraoperative visual enhancement

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Summary Patients presenting for excision of squamous cell carcinomata, including Bowen's disease, in sun-damaged skin often present with poorly defined, morphoeic or multifocal neoplasms, the extent of which can be difficult to identify intraoperatively. Use of vital staining has been commonly used to aid identification and appropriate excision of squamous lesions of the oral cavity and upper aerodigestive tract but has not been readily adopted for cutaneous lesions. We report a case of a morphoeic squamous cell neoplasm of the web space and fingers to illustrate the merits of vital staining cutaneous squamous neoplasms with the simple dye Carmoisine E122. This assists with intraoperative tumour identification and facilitates adequate oncological resection and appropriately planned reconstruction. By comparison with other methods such as Mohs, it is a simple, cheap, and rapid aid that may be used by surgeons of all grades to improve identification of the extent of the neoplasm, without special equipment.

Case report

A 79-year-old right handed male presented with a 1-year history of an enlarging flat papilliform lesion on his right second web space. Clinically this was a squamous lesion resembling Bowen's disease with macroscopic involvement of the web space, but poorly defined involvement of the adjacent actinic-damaged skin. In order to aid intraoperative identification of the extent of the tumour, the whole area was prepared with a skin preparation consisting of initial application of a solution of chlorhexidine acetate 0.015% with cetrimide 0.15%. Then a solution of chlorhexidine gluconate in 70% industrial methylated spirits (IMS) was applied, containing the biological stain carmoisine (E122) 1.5% w/v in 20% IMS. The E122 ensured complete coverage of the operative field by an otherwise transparent skin preparation, by staining both the neoplasm and surrounding skin. As soon as anti-sepsis was achieved the skin prep was removed with gauze soaked in normal saline. This effectively removed the stain from the normal skin, while the deep pink stain remained on the areas involved by tumour (Fig. 1). It was immediately evident that the

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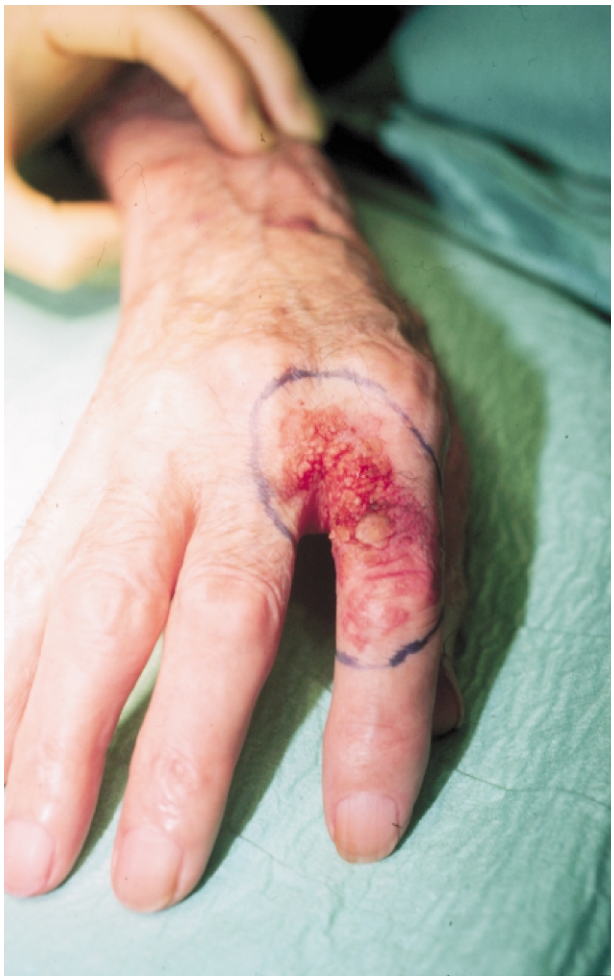

Fig. 1 Bowen's disease of the second right web space. The main focus is confined to the second web space. Carmoisine has been used to highlight the dysplastic skin extending over the index finger to the PIPJ. Histology subsequently showed that squamous cell carcinoma in situ extended to the region of the index finger PIPJ.

neoplasm was more extensive than previously suspected. It included not only the web-space, but also the contiguous sides of the index and middle fingers with several adjacent foci extending over the dorsum of the index finger to the proximal interphalangeal joint (PIPJ).

Vital staining allowed the margins to be identified with ease and excision of the tumour with considerable confidence of oncological clearance. The defect after excision measured approximately 6 cm × 5 cm and was reconstructed using a Quaba flap to resurface the web-space with primary closure of the donor. Full thickness skin grafts applied to the sides of the index and middle fingers with proflavine-impregnated wool tie-over dressings completed the reconstruction.

At follow-up 3 months post-operatively the patient was disease free, with a full range of movement in the hand and fingers. There is no evidence of scar contracture and abduction of the fingers of the second web is full. Histology confirmed the diagnosis of a large area of multifocal squamous cell carcinoma in situ, excision of which was complete.

Discussion

The skin preparation used to improve intraoperative identification of Bowen's disease in this case, has been used by our department as our standard skin preparation for many years. Exceptions may occur where perfusion at the operative site is compromised or requires monitoring, or where alcohol based preparations should be avoided, such as the peri-ocular areas. Historically, two skin preparations, one aqueous-based and one spirit-based, were used to facilitate thorough skin cleansing and antisepsis. Initially, these were clear solutions and once poured from their respective containers were difficult to identify from one another; hence the addition of the stain to the spirit-based skin preparation. An additional advantage was that the operative field was stained as it was prepared, thereby avoiding accidental incomplete coverage of the operative field, particularly in the extremities. It was noted that there was a differential affinity for the stain to adhere to normal skin and dysplastic lesions, which is exaggerated by the ease with which the stain may be removed from the former.

Vital staining has been used as an adjunct to facilitate adequate intraoperative identification of squamous cell carcinomata of the upper aerodigestive tract. Lugol's iodine has been used to facilitate endoscopic examination of the oesophagus by visual enhancement of the epithelium. Normal mucosa stains an orange–brown colour but dysplastic and carcinomatous cells do not stain. Toluidine blue has also been used to improve rates of oncological control of squamous neoplasms of the aerodigestive tract by facilitating complete resection of the tumour. The technique of staining tissue beds directly to identify residual squamous carcinoma has been established in principle, using UV light to visually enhance acridine orange in squamous carcinoma xenografts in nude mice.[1] Vital staining has not been readily adopted for resection of squamous cell tumours of cutaneous origin. We are not aware of any reports in the literature of the use of a topically applied vital stain to visually

enhance dysplastic/carcinomatous lesions, and appropriate stains appear to be deficient.

Kerawala et al. have suggested that while toluidine blue sensitively and reliably assists in identification of squamous cell carcinomata of the oral cavity, it is less specific in identifying squamous cell carcinoma in situ and severe dysplasia of the oesophagus.[2] They have also suggested that the false positive rate for toluidine blue staining normal tissues is so high as to restrict its use as a diagnostic adjunct to selective cases only.[3] Nonetheless, many surgeons and endoscopists worldwide frequently use these stains to assist clinical practice.

The false positive rate for staining of normal skin with carmoisine is not known, but based on our experience it is low. Its specificity in differentiating between premalignant/neoplasic lesions and benign skin conditions such as psoriasis may be limited. Despite this, it does confer significant visual enhancement of a suspicious lesion, which requires removal on clinical grounds. It also assists with identification of morphoeic lesions, particularly in obscure locations such as the interdigital spaces. Peripheral centres of multifocal tumour, which do not abut the main focus directly, may be visualised. These may not be recognised using methods such as Mohs. Healthy tissues are better preserved with improved cosmetic outcomes, while good control is achieved. Lastly, it is a useful tool for demonstration to junior trainees, which helps improve tumour clearance rates for surgeons in training.

More sophisticated methods are available to improve local tumour control. Mohs micrographic surgery (MMS) has been suggested as an alternative means of minimising loss of normal tissue while ensuring oncological clearance, but the technique is time-consuming. Cure rates for MMS range from 98% for uncomplicated lesions[4] to 71% for more complex/aggressive tumours such as Bowen's disease of the nail-bed.[5] Jimenez et al. have suggested the use of immunohistochemical staining of Mohs specimens, and although this has some merit in selected cases it necessitates additional operating time and expense for uncomplicated cases.[6] MMS should be reserved for recurrent, incompletely excised,[7] or aggressive tumours, such as Merkel Cell carcinomata[8] or Bowen's disease of the nail matrix.[9] MMS may also be appropriate for facial tumours when the deep margin of the tumour is poorly defined.[10]

Carmoisine is a commonly used food additive and while certain food additives have been associated with behavioural problems in children after ingestion, we are unaware of any problems associated with the topical application of carmoisine. We have not experienced any problems consequent upon its application topically in thousands of cases. We were unable to ascertain whether staining was attributable to binding to a skin component, even after extensive discussion with the manufacturers (Adams Healthcare, Leeds, UK). As it is possible that the method of staining may be purely a physical phenomenon, care should be exercised where there is a background of eczema, psoriasis or other skin disorders. Nevertheless, we recommend the use of the topical application of Carmoisine vital stain as part of the operative skin preparation of patients with a clinical diagnosis of cutaneous squamous neoplasia, which is poorly visible. It requires no additional equipment such as ultraviolet light with its accompanying protective precautions. Operative time is not increased, and the pathology department is not encumbered more. It may be used with equal facility by developing healthcare systems and by financially constrained systems in developed nations. We have found that it is a simple, extremely inexpensive, and rapid aid to improve identification of the extent of poorly defined cutaneous neoplasia.

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