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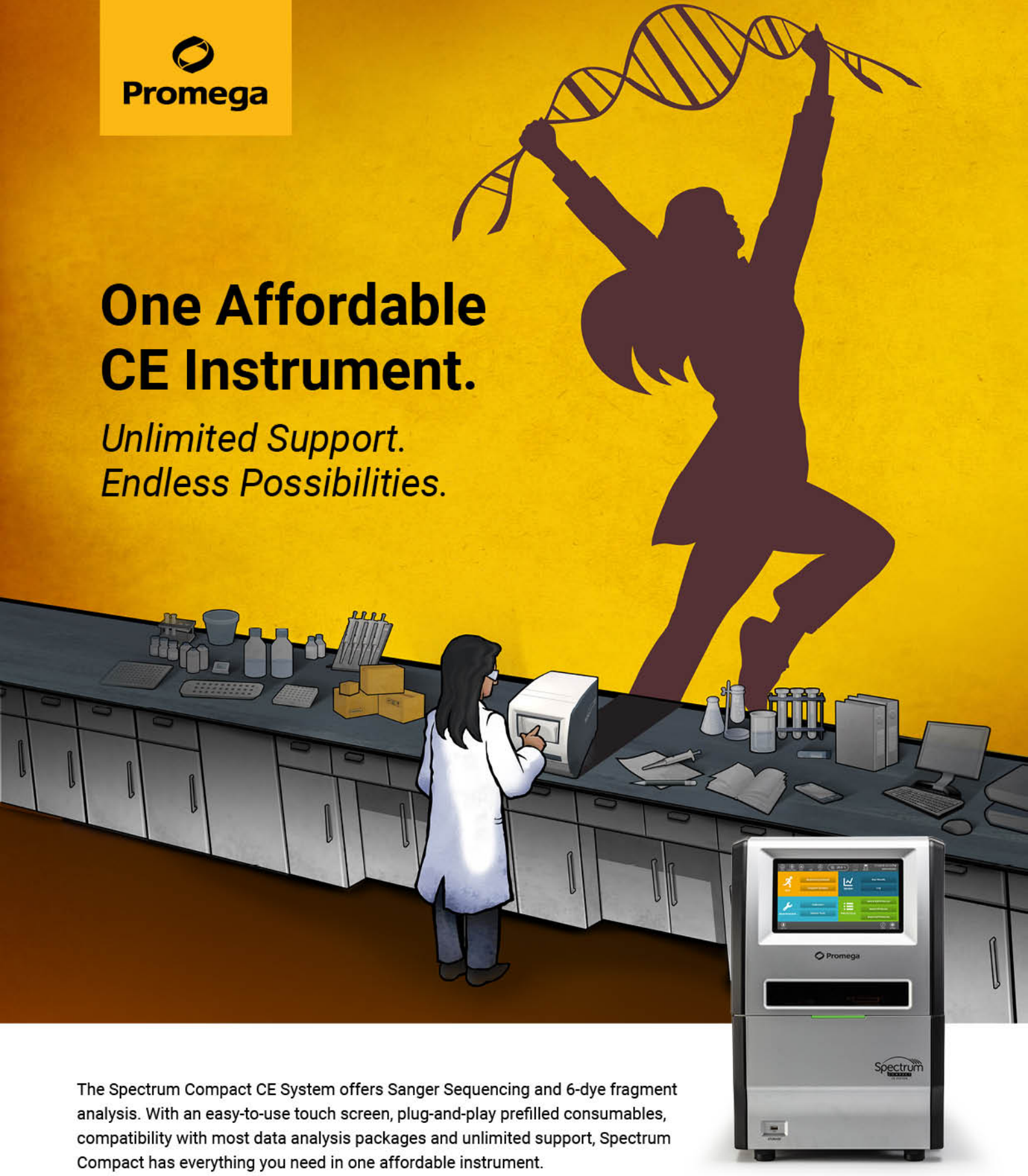

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Histopathology

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Lesson of the Month

Papillary immature squamous metaplasia of the anal canal: a rare but probably underdiagnosed entity

DOI: 10.1111/his.14368

Case summary

A 63-year-old man presented with a condylomatous hemicirconferential exophytic lesion of the anal canal. He had a history of anal squamous cell carcinoma (cT2N0M0) that had been treated with radiochemotherapy, and some recurrent condylomata that had been treated with electrocoagulation. Given this background and the morbidity of an abdominoperineal amputation, a mucosectomy was performed. Histopathological examination demonstrated a squamous mucosa with papillary architecture, lined by a population of immature cells (Figure 1). There was little maturation. p16 remained immunohistochemically negative. Ki67 was immunohistochemically positive, essentially in the lower half of the epithelium, with some rare positive cells being seen in the upper layers (Figure 2). A diagnosis of papillary immature metaplasia of the anal canal was made.

Comments

Anal squamous cell carcinoma and anal squamous dysplasia are strongly related to human papillomavirus (HPV) infection (88%).[1] The current iteration includes two types of anal squamous dysplasia, i.e. low-grade and high-grade. Low-grade anal squamous dysplasia includes what were previously classified as mild dysplasia, anal intraepithelial neoplasia (AIN) I, anal squamous intraepithelial lesion I, and condyloma accuminatum; these lesions are not believed to progress to cancer.[2] High-grade anal squamous dysplasia comprises precancerous lesions, i.e. Bowen disease, squamous cell carcinoma *in situ*, moderate and severe dysplasia, AIN II, AIN III, and Bowenoid papulosis. The three-tiered dysplasia was associated with poor reproducibility.[3] The therapeutic possibilities range from a 'watch and see' strategy to surgery with a risk of faecal incontinence.

Cervical dysplasia is another precancerous lesion mediated by HPV (nearly 100%), and also involves the maturation of a squamous mucosa. Since 1992, an entity comprising a low-grade lesion with a high-grade pattern has been observed and recognised. This lesion, initially called immature condyloma, is related to low-risk HPV (HPV6 and HPV11), and is described as a papillary formation lined by immature cells with some atypia. It is now called papillary immature metaplasia. It can occur together with low-grade dysplasia, contain koilocytes, or be found adjacent to high-grade lesions. Possible transformation to high-grade dysplasia is matter of discussion. Immunohistochemistry often shows patchy positivity or negativity for p16, and positive Ki67 staining in the lower third of the epithelium. The architectural form and the immature aspect of the cells can, however, lead to a

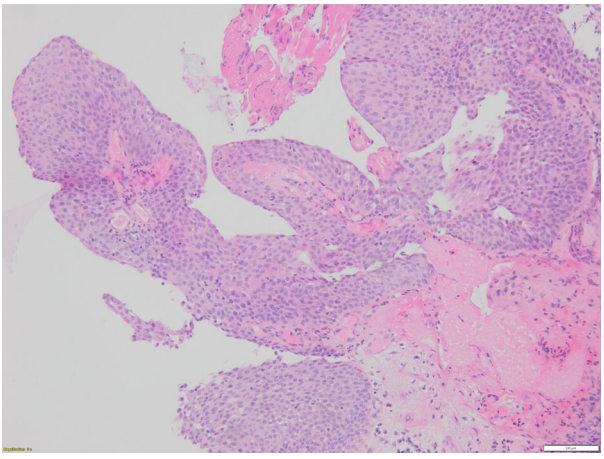

Figure 1. Squamous mucosa with papillary architecture, lined by immature squamous metaplastic cells.

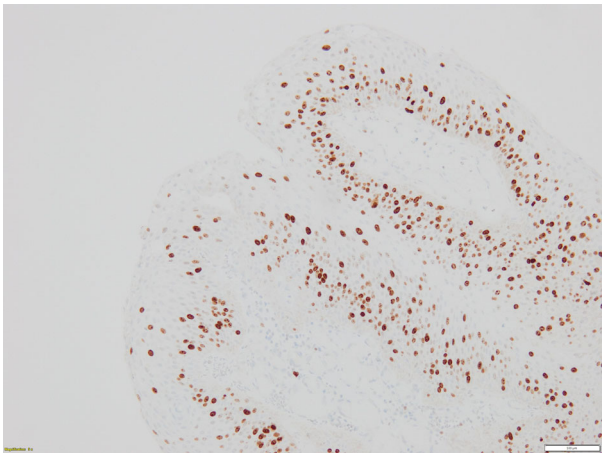

Figure 2. Ki67 immunohistochemical staining with positivity essentially in the lower half of the epithelium.

misdiagnosis of high-grade dysplasia, and hence overtreatment.[4] Recently, Roberts *et al*. performed a cohort study on cases of anal canal dysplasia.[5] Among 1500 subjects, they found 15 histopathological patterns (1%) that were similar to those of papillary immature metaplasia of the cervix. The immunohistochemical negativity of p16 and the absence of high-risk HPV were strong arguments against a diagnosis of high-grade dysplasia. The authors concluded that papillary immature metaplasia also occurs in the anal canal, and that there is no evidence that this is a premalignant condition.[5] The absence of keratinisation distinguishes it from squamous papilloma of the anal canal.[6]

Papillary immature metaplasia of the anal canal is probably underdiagnosed, as anal screening is not widespread. Pathologists should be aware of this entity and be able to recognise it in order to avoid unnecessary therapeutic interventions.

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

F. Lifrange and P. Demetter collected clinical data and wrote the first draft of the manuscript. All authors approved the final version.

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