Acta Derm Venereol 2014; 94: 492–493

QUIZ SECTION

A Perianal Erythematous Plaque: A Quiz

Hirohisa Ishibuchi[1], Akira Shimizu[2]*, Izumi Negishi[3] and Osamu Ishikawa[2]

*Departments of Dermatology, [1]Tatebayashi Kosei Hospital, Tatebayashi, [2]Gunma University Graduate School of Medicine, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, and [3]Ota Memorial Hospital, Ota, Japan. *E-mail: ashimizu@med.gunma-u.ac.jp*

An 83-year-old man with a 4-month history of an itchy perianal lesion was referred to our hospital. A physical examination revealed a round, well-demarcated, erythematous, erosive plaque involving the perianal skin (Fig. 1a).

The histopathological examination of the patient's lesion (Fig. 1b) revealed the presence of atypical tumour cells with an abundant pale-staining cytoplasm and large atypical nuclei in all layers of the epidermis. Immunohistochemically, the tumour cells were positive for carcinoembryonic antigen (CEA), cytokeratin (CK) 7, CK20 and caudal-related homeobox gene nuclear transcription factor (CDX2) (Fig. 1c), while they were negative for gross cystic disease fluid protein (GCDFP)-15 and human papillomavirus (HPV). PCR using HPV consensus primers was negative. Neither colonoscopy nor surgery was performed because of the patient's refusal.

What is your diagnosis? See next page for answer.

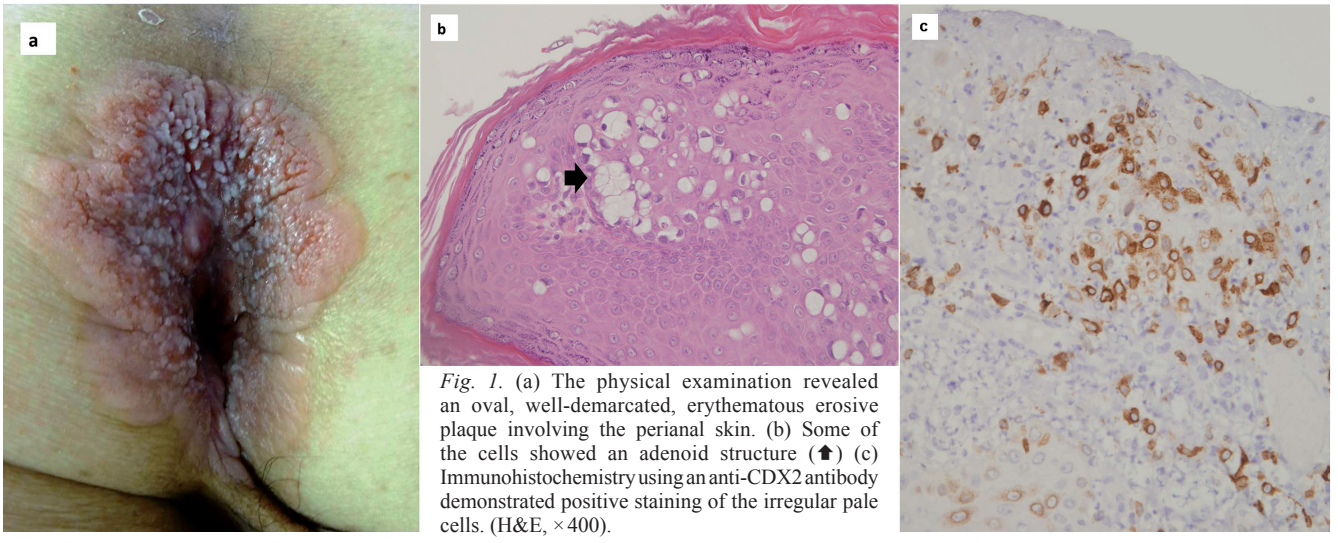

Fig. 1. (a) The physical examination revealed an oval, well-demarcated, erythematous erosive plaque involving the perianal skin. (b) Some of the cells showed an adenoid structure (⬆) (c) Immunohistochemistry using an anti-CDX2 antibody demonstrated positive staining of the irregular pale cells. (H&E, ×400).

doi: 10.2340/00015555-1734

© 2014 The Authors.
Journal Compilation © 2014 Acta Dermato-Venereologica. ISSN 0001-5555

ANSWERS TO QUIZ

A Perianal Erythematous Plaque: Commentary

Acta Derm Venereol 2014; 492–493.

Diagnosis: Secondary extramammary Paget's disease from adenocarcinoma of the anorectal region

The patient was diagnosed to have secondary extramammary Paget's disease (EMPD) from adenocarcinoma of the anorectal region. EMPD of the perianal area is classified into 2 types: the primary type of cutaneous origin and the secondary type due to the cutaneous spread of either adenocarcinoma of the anorectal region or of urothelial carcinoma (1). Primary and secondary EMPD can share similar clinical findings and are characterised histologically by intraepidermal invasion. Ackerman (2) described the characteristic histological findings of primary and secondary EMPD. In cases of primary EMPD, the distribution of the tumour cells is homogenous, and a glandular lumen is rarely seen. On the other hand, secondary EMPD is associated with disarrayed tumour cells, and a glandular lumen is frequently seen. In our cases, disarrayed tumour cells and glandular lumens were clearly seen, which was compatible with a diagnosis of secondary EMPD (Fig. 1c).

The perianal secondary EMPD accounts for 5% of all cases of EMPD (3). Seventy-five percent of the reported perianal cases of secondary EMPD in Japan originated from anal canal cancer, and 25% from rectal cancer (4). Although primary EMPD is an *in situ* lesion, secondary EMPD is a direct invasion from anal canal or rectal cancer. The differential diagnosis of primary and secondary EMPD is necessary, because there are significant differences in the surgical approaches and prognosis.

Immunohistochemistry is useful to distinguish primary EMPD from secondary EMPD. It has been recommended that immunohistochemical staining with antibodies against CK7, CK20, GCDFP15 and uroplakins (UPs) can be used for the differential diagnosis of different types of EMPD. EMPD secondary to urothelial carcinoma is positive for CK7 and CK20, but negative for GCDFP-15, while UPs are positive in EMPD of urothelial origin (5). UPs Ia, Ib, II and III, transmembrane proteins constituting the asymmetrical unit membrane of urothelial umbrella cells, were the first specific urothelial differentiation markers described (6) based on the consistently $CK7^+$ and $CK20^-$ immunophenotype of the primary forms, and the frequent $CK20^+$ and $CK7^-$ immunoprofile of the secondary forms of anorectal origin (7). However, some anorectal adenocarcinomas are $CK7^+$, and some are $CK20^-$ (8). CEA is also a useful marker for distinguishing EMPD of urothelial origin, which is CEA negative. Like CK7 and CK20, CEA expression cannot always be used safely to discriminate urothelial and anorectal cancers, because the latter can be also CEA negative. Therefore, an immunohistochemical analysis using CK7, CK20 and CEA is not specific and sensitive enough to identify the origin of tumour cells in the secondary type of perianal EMPD.

CDX2 is a gene involved in the regulation of intestinal cell proliferation/differentiation. It is considered specific for enterocytes and has been used for the diagnosis of primary and metastatic colon adenocarcinoma (9). Approximately, 97% of rectal cancers are positive (10), and metastatic rectal cancers are also positive (10–12). De Nisi et al. (1) examined 16 cases of primary EMPD and 5 cases with secondary EMPD immunohistochemically using a CDX2 antibody. All of the cases of primary EMPD were positive for CK7 and negative for CK20 and CDX2, while all of the cases of the secondary EMPD were positive for CDX2. Therefore, CDX2 is useful for distinguishing between primary and secondary perianal EMPD associated with underlying colorectal malignancies.

REFERENCES

1. De Nisi MC, D'Amuri A, Toscano M et al. Usefulness of CDX2 in the diagnosis of extramammary Paget disease associated with malignancies of intestinal type. Br J Dermatol 2005; 153: 677–679.
2. Ackerman AB. Differential diagnosis in dermatopathology. III, Lea & Febiger, Philadelphia: 1993: 130–133.
3. Ohnishi T, Kawabata Y, Ohara K, Sawada T, Okuno T. A case of perianal paget's disease. Rinsho Derma (Tokyo) 1994; 36: 207–211.
4. Moritani Y, Tomioka N, Izumi A, Takiue T, Kobayashi N, Shirakawa Y, et al. A case of anal gland carcinoma accompanied by pagetoid spread. Journal of Japan Society of Coloproctology (Tokyo) 2009; 62: 121–126.
5. Brown HM, Wilkinson EJ. Uroplakin-III to distinguish primary vulvar Paget disease from Paget disease secondary to urothelial carcinoma. Human Pathology 2002; 33: 545–548.
6. Moll R, Wu XR, Lin JH, Sun TT. Uroplakins, specific membrane proteins of urothelial umbrella cells, as histological markers of metastatic transitional cell carcinomas. Am J Pathol 1995; 147: 1383–1397.
7. Ohnishi T, Watanabe S. The use of cytokeratins 7 and 20 in the diagnosis of primary and secondary extramammary Paget's disease. Br J Dermatol 2000; 142: 243–247.
8. Zhang PJ, Shah M, Spiegel GW, Brooks JJ. Cytokeratin 7 immunoreactivity in rectal adenocarcinomas. Appl Immunohistochem Mol Morphol 2003; 11: 306–310.
9. Lora V, Kanitakis J. CDX2 Expression in cutaneous metastatic carcinomas and extramammary Paget's disease. Anticancer Res 2009; 29: 5033–5038.
10. Barbareschi M, Murer B, Colby TV, Chilosi M, Macri E, Loda M, Doglioni C. CDX-2 homeobox gene expression is a reliable marker of colorectal adenocarcinoma metastases to the lungs. Am J Surg Pathol 2003; 27: 141–149.
11. Fraggetta F, Pelosi G, Cafici A, Scollo P, Nuciforo P, Viale G. CDX2 immunoreactivity in primary and metastatic ovarian mucinous tumours. Virchows Arch 2003; 443: 782–786.
12. Yatabe Y, Koga T, Mitsudomi T, Takahashi T. CK20 expression, CDX2 expression, K-ras mutation, and goblet cell morphology in a subset of lung adenocarcinomas. J Pathol 2004; 203: 645–652.