

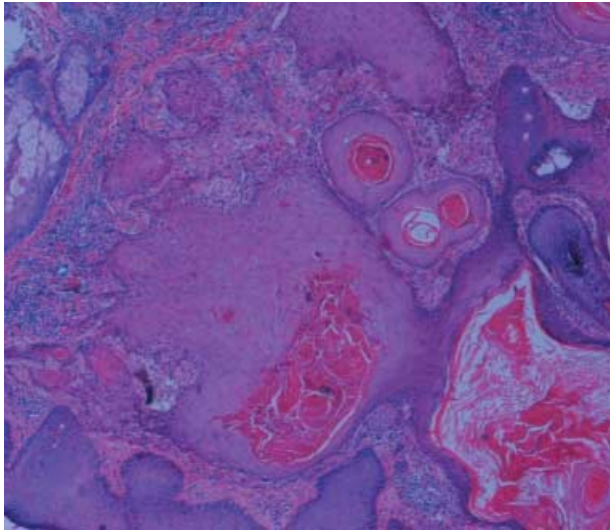


fig. 2 Huge amount of squamous cells in the derma, with irregular arrangement, abnormal nucleus, and abundant keratotic bead formation.

The reason for dilated pore occurrence is not clear. Dilated pore has previously resulted from secondary inflammation of a ruptured infundibular cyst or some infundibular cysts have led directly to dilated pore.^{2,3} Some dilated pores may contain a histological focus of epidermolytic hyperkeratosis.⁴

Dilated pore is a specific follicular infundibular cyst. It looks like a great open comedo. It commonly occurs on the face, neck and upper chest, or in the external ear canal, and there is a male predominance. Dilated pore is usually solitary, but occasionally grouped lesions may be present. Duration may reach as long as 40 years.^{1,3,5-8}

Benign follicular neoplasms and basal cell carcinoma may arise from a common pluripotential stem cell and thus may coexist in a single cutaneous lesion.^{5,9}

No prior report of squamous cell carcinoma with a dilated pore has been documented in the literature. Epidermal appendageal tumours can contain combinations of several tumour types within the same tumour due to differentiation along different pathways.⁶ Squamous cell carcinoma may arise in a dilated pore by the same mechanism.

The best treatment for the condition is excision. Superficial measures such as superficial desiccation, cauterization, coagulation or abrasion will not eradicate this lesion because of its extreme depth.^{1,4} If the lesion is diagnosed as benign neoplasms by histopathology, surgical operation is the first choice of treatment. We suggest that excision should be extended at least 2 or 5 mm beyond the lesion. Cauterization or laser may be useful for a smaller lesion. However, for malignant tumours, surgical excision is necessary.

L Zhao,*† J Xu,‡ F Fang,† G Qian,† Y Wang,† Q-Q Wang†
†Department of Dermatologic Surgery, Institute of Dermatology,
Chinese Academy of Medical Sciences & Peking Union Medical
College, 12 Jiang-wang-miao Road, Nanjing 210042, ‡Chengdu
University of TCM, Chengdu 610075, China,

*Corresponding author, tel. +86 25 85478041;
fax +86 25 85414477;

E-mail: zhaoliang210042@hotmail.com

References

- 1 Winer LH. The dilated pore, a trichoepithelioma. *J Invest Dermatol* 1954; **23**: 181–188.
- 2 Requene L, Sanchez E, Simon P *et al*. Induction of cutaneous hyperplasia by altered stroma. *Am J Dermatopathol* 1996; **18**: 248–268.
- 3 Morikawa T, Takizawa H, Ohnishi T *et al*. Dilated pore: a case report and an immunohistochemical study of cytokeratin expression. *J Dermatol* 2003; **30**: 556–558.
- 4 Tokura Y, Takigawa M, Yamada M. Epidermolytic hyperkeratosis associated with a dilated pore. *J Dermatol* 1987; **14**: 286–288.
- 5 Kate N, Ueno H. A pedunculated follicular hamartoma: a case showing a central trichofolliculoma-like tumor with multiple trichogenic tumors. *J Dermatol* 1991; **18**: 465–471.
- 6 Kim L, Dennis A, Deborah F. Trichoid basal cell carcinoma found in a dilated pore on the nose. *Dermatol Surg* 2000; **26**: 874–876.
- 7 Konohama A, Kobayashi T. Aggregated dilated pores. *J Dermatol* 1999; **26**: 332–333.
- 8 Ayoub OM, Timms MS, Mene A. Winer's dilated pore: rare presentation in the external ear canal. *Auris Nasus Larynx* 2001; **28**: 349–352.
- 9 Dennis A, Deborah F. Regarding trichoid basal cell carcinoma found in a dilated pore on the nose. *Dermatol Surg* 2000; **26**: 1084.

DOI: 10.1111/j.1468-3083.2006.01849.x

Is serum galectin-3 a potential predictor of the response to active specific immunotherapy in melanoma patients?

Editor

Active immunotherapy with tumour-specific antigens has emerged in recent years as a promising new treatment modality against cancer, and more particularly against melanoma. This is the result of the identification of a large number of tumour antigens and of an improved understanding of the immune responses directed against

tumoral cells. Experimental models and clinical immunotherapy trials support further development of this approach. However, exactly to what extent remains uncertain because the effectiveness of immunotherapeutic strategies may be limited to certain subgroups of patients.

Recently, it has been shown that melanoma cells frequently express galectin-3 (Gal-3) at a high level and an increased level of this protein has been detected in the serum of some cancer patients, including melanoma patients.¹⁻⁴ Gal-3 is a 29–35 kDa mammalian lectin encoded by the LGALS3 gene. This lectin, which binds beta-galactoside residues on glycoproteins, can be detected in the cytoplasm, in the nucleus and on the cell membrane. It can also be secreted into the extracellular space. Gal-3 can be isolated as a monomer but can also form dimers or oligomers. The protein lacks a classical signal peptide as well as a transmembrane peptide. The mechanism by which it is secreted is not known. Theoretical and experimental considerations suggest a multifaceted role of this protein in cell growth, cell adhesion, neoplastic transformation and progression.⁵ This protein, which has a NWGR motif in common with Bcl-2, has been described as an anti-apoptotic factor and has been shown to modulate a wide variety of cellular functions. More precisely, Gal-3 can exert an anti-apoptotic effect on inflammatory cells in order to sustain the inflammatory response.⁶⁻⁸ Because this proinflammatory action might be involved in the immune response to cancer, we investigated the predictive value of serum Gal-3 for efficiency of response to immunotherapy in melanoma patients.

Serum samples were collected from 18 patients with AJCC stage 3 or stage 4 (M1) metastatic melanoma before they entered various melanoma vaccine trials, which have been described elsewhere.⁹ All patients received repeated vaccinations with synthetic peptide(s), a recombinant MAGE-3 protein, or with a recombinant ALVAC virus encoding tumour antigens. Following this they were categorized either as patients with tumour regression (complete, partial or mixed response, $n = 8$) or as patients without tumour regression (progressive disease without mixed response, $n = 10$). The corresponding protocols had been approved by the ethics committee. Concentrations of Gal-3 were measured by enzyme-linked immunosorbent assay (ELISA) in accordance with the manufacturer's instructions (BMS 279, Bender MedSystems GmbH, Vienna, Austria). The results were expressed as medians, and the difference between the two groups was analysed by a non-parametric Mann-Whitney *U*-test (Table 1). No differences in serum Gal-3 measurement could be demonstrated between the two groups (regressors and non-regressors). These Gal-3 serum levels were similar to those obtained in control patients, as published recently.⁴

Table 1 Results of Gal-3 measurement (ng/mL) in vaccinated melanoma patients

	Regressors	Non-regressors
<i>n</i>	8	10
AJCC stage 3	7	6
AJCC stage 4 (M1)	1	4
Lowest value	6.390	5.587
Highest value	10.134	9.317
Median	7.552	6.810
95% CI for the median	6.4217–10.0391	6.2075–8.6983

In conclusion, the results obtained in our small cohort of patients do not support the hypothesis that Gal-3 serum levels can predict tumour response following vaccination with tumour-specific antigens in patients with metastatic melanoma. Further investigations are needed to understand immune privilege in immunotherapy-responding melanoma patients.

Acknowledgement

This work was supported by an Erasmus Foundation grant (VP).

Pierre Vereecken,* Michel Heenen, Sajida Babar,
Nicolas Van Baren

Department of Dermatology, CHU-Brugmann – Erasme-Bordet,
Université Libre de Bruxelles and, Ludwig Institute for Cancer
Research, Brussels Branch, Belgium, *Corresponding author,
17 Avenue Nellie Melba, B-1070 Brussels, Belgium,
tel. +32 497 47 77 77;

E-mail: pierre.vereecken@chu-brugmann.be

References

- May A, Berthier-Vergnes O, Apoil PA *et al.* Expression of the galactose binding protein Mac-2 by human melanoma cell lines. *Cancer Lett* 1994; **81**: 155–163.
- Iurisci I, Tinari N, Natoli C *et al.* Concentrations of galectin-3 in the sera of normal controls and cancer patients. *Clin Cancer Res* 2000; **6**: 1389–1393.
- Vereecken P, Debray C, Petein M *et al.* Expression of galectin-3 in primary and metastatic melanoma: immunohistochemical studies on human lesions and nude mice xenograft tumors. *Arch Dermatol Res* 2005; **296**: 353–358.
- Vereecken P, Zouaoui Boudjeltia K, Debray C *et al.* High serum galectin-3 in advanced melanoma: preliminary results. *Clin Exp Dermatol* 2006; **31**: 105–109.
- Califice S, Castronovo V, Van Den Brule F. Galectin-3 and cancer (Review). *Int J Oncol* 2004; **25**: 983–992.
- Rubinstein N, Alvarez M, Zwirner NW *et al.* Targeted inhibition of galectin-1 gene expression in tumor cells results

in heightened T cell-mediated rejection; A potential mechanism of tumor-immune privilege. *Cancer Cell* 2004; **5**: 241–251.

- 7 Almkvist J, Karlsson A. Galectins as inflammatory mediators. *Glycoconj J* 2004; **19**: 575–581.
- 8 Fukumori T, Takenaka Y, Oka N *et al*. Endogenous galectin-3 determines the routing of CD95 apoptotic signaling pathways. *Cancer Res* 2004; **64**: 3376–3379.
- 9 Balch CM, Buzaid AC, Soong SJ *et al*. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. *J Clin Oncol* 2001; **19**: 3635–3648.

DOI: 10.1111/j.1468-3083.2006.01853.x

Umbilical endometriosis

Editor

Endometriosis (formerly 'external endometriosis') is defined by the presence of endometrial tissue outside of the uterus.¹ Several pathogenic causes have been suggested, including implantation after menstrual regurgitation, metaplasia, and metastasis. It must be clearly distinguished from adenomyosis (formerly 'internal endometriosis'), which is characterized by the presence of endometrial tissue within the uterine musculature, with a completely dissimilar pathogenesis, epidemiology and clinical picture. However, both conditions may develop in the same patient. Endometriosis is a common disorder in women of reproductive age, with a mean age at diagnosis of 25–29, without ethnic predominance.² Isolated umbilical presentation has rarely been reported. We report a case, and review differential diagnoses.

A 40-year-old Malian-born black woman presented with an umbilical nodule that had been developing for the past 8 months. Her medical history included two deliveries, which included one by caesarean section. The patient reported neither abortion nor secondary infertility. She did not use any oral contraception and had a regular menstrual cycle. Clinical examination revealed a firm, haemorrhagic, polypoid bluish-grey tumour (fig. 1). The key clinical feature that led to the correct diagnostic hypothesis before further investigation was that the lesion was intermittently haemorrhagic, in accordance with the menstruation cycle. Histopathology of the umbilical nodule showed endometrial glands and stroma in the dermis, accompanied by adjacent oedema and fibrosis (fig. 2). These glands had irregular and inflated lumen, and regular epithelium. The epidermis was unaffected. Perl's stain revealed iron deposition in the dermis. Staging investigation, including endovaginal ultrasonography and MRI, revealed endometriomas of the peritoneum and the bladder (the patient did not have haematuria), and adenomyosis. Three



fig. 1 A polypoid, bluish-grey, firm umbilical tumour. Menstrual bleeding was reported by this 40-year-old woman.

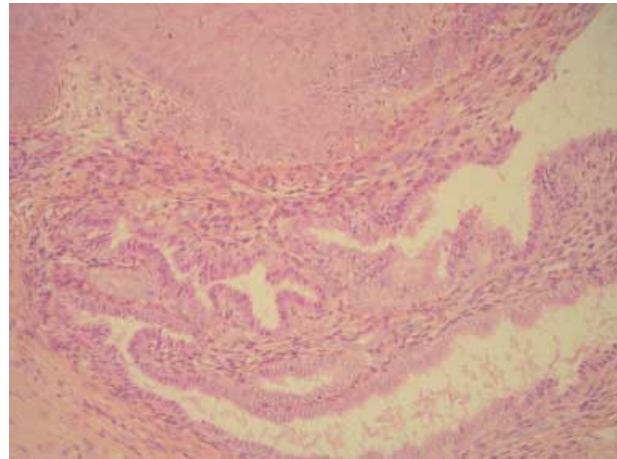


fig. 2 A skin specimen was fixed in formalin, embedded in paraffin, and stained with haematoxylin and eosin. Endometrial glands and stroma are present in the dermis, and surrounded by oedema and fibrosis (magnification, $\times 20$).

months later, intense dysmenorrhoea and peri-menstrual cystalgia gradually appeared. As surgical intervention was rejected by the patient treatment with oral noregestrol acetate was introduced.

The gold standard for the diagnosis of endometriosis is histopathology, showing endometrial glands and stroma in the dermis, with a normal overlying epidermis. Biopsy methods include laparoscopy and skin biopsy. Isolated cutaneous presentation is rare³ and the most frequent clinical symptoms are pelvic or abdominal pain, secondary dysmenorrhoea, dyspareunia, and infertility.² Rare cutaneous or mucosal locations have been reported on the perineum, vagina, groin, umbilicus, as have surgical scars. Cutaneous endometriosis should be suspected whenever a woman of reproductive age presents with a