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BRIEF REPORTS

Confocal and dermoscopic features of basal cell carcinoma in Gorlin–Goltz syndrome: A case report

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ABSTRACT

Gorlin–Goltz (GS) syndrome is an autosomal dominant disease linked to a mutation in the *PTCH* gene. Major criteria include the onset of multiple basal cell carcinoma (BCC), keratocystic odontogenic tumours in the jaws and bifid ribs. Dermoscopy and reflectance confocal microscopy represent imaging tools that are able to increase the diagnostic accuracy of skin cancer in a totally noninvasive manner, without performing punch biopsies. Here we present a case of a young woman in whom the combined approach of dermoscopy and RCM led to the identification of multiple small inconspicuous lesions as BCC and thus to the diagnosis of GS syndrome.

Key words: confocal laser microscopy, dermoscopy, Gorlin–Goltz syndrome.

INTRODUCTION

Naevoid basal cell carcinoma syndrome (NBCC), also known as Gorlin–Goltz syndrome (GS), is an inherited autosomal dominant condition with high penetrance and variable expressivity. It is characterises by the classical triad of multiple basal cell carcinomas (BCC), keratocystic odontogenic tumours in the jaws and bifid ribs. In addition to the classical triad described by Gorlin and Goltz, calcification of the falx cerebri, palmar and plantar epidermal pits, spine and rib anomalies, relative macrocephaly, facial milia, frontal bossing, ocular malformation, medulloblastomas, cleft lip or palate, and the development of mental malformations have also been established as features of the syndrome.[1] Estimates of the incidence of NBCC in the general population vary between 1:57 000 and 1:150 000, with a male-to-female ratio of 1:1.[2]

In the case of NBCC it is of great importance to make an early diagnosis since the severity of complications such as malignant skin and brain tumours can be reduced, and maxillofacial deformities related to the jaw cysts can be avoided.[3] The relatively recent introduction of new diagnostic imaging tool such as dermoscopy and reflectance confocal microscopy (RCM) may assist clinicians to identify NBCC patients.[4] Here we report a case of a young woman who underwent a clinical and modern imaging examination.

CASE REPORT

A 21-year-old woman was referred to our department because she had a previous diagnosis of BCC on her face. A physical examination showed the presence of ocular hypertelorism, multiple suspicious papular and nodular lesions, located in both sun-exposed areas and non–sun-exposed areas such as the trunk, face and arms. Clinically, round or oval-shaped lesions were seen. They were small in diameter, with a smooth surface. All these lesions were lightly pigmented and brownish in colour. The differential diagnosis included dermal naevus or fibropapillomas.

A dermatoscopy examination was carried out on each single lesion. Multiple grey-blue dots and structureless areas were observed, leading to the possible diagnosis of dermal naevi or BCC (Figs 1,2). A RCM examination revealed the presence of tightly packed basaloid islands with peripheral palisading suggestive of a BCC diagnosis.

Furthermore, palmar pits were identified on clinical grounds as punctate depressions. On dermatoscopy, the

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Abbreviations:

BCC	basal cell carcinoma
GS	Gorlin–Goltz syndrome
NBCC	naevoid basal cell carcinoma syndrome
RCM	reflectance confocal microscopy

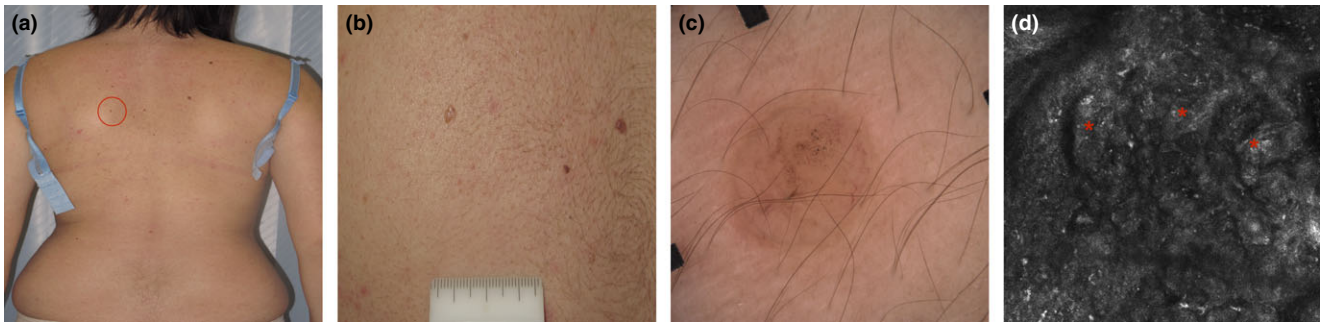

Figure 1 (a) The back of a 21-year-old woman with small papules (circle) that appear as (b) translucent lesions 3 × 2 mm in size. (c) Dermoscopic image: presence of small grey dots. (d) High resolution reflectance confocal microscopy image reveals the presence of tightly packed cells arranged to form basaloid nests and cords (red asterisks).

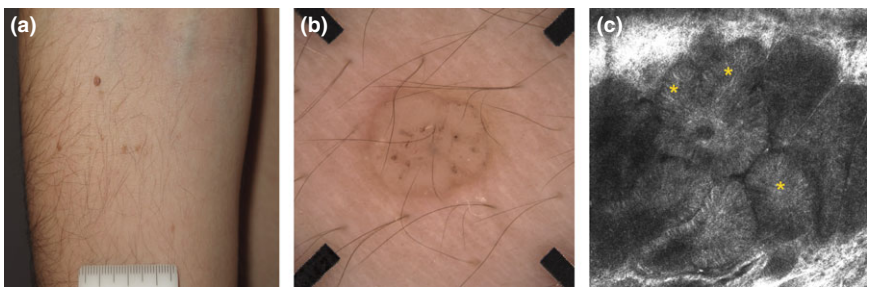

Figure 2 (a) Translucent 2 × 2 mm papule located on the arm. (b) Dermoscopic image: presence of grey-blue dots and structureless areas. (c) Reflectance confocal microscopy shows tightly packed basaloid nests with palisading, which correspond to basaloid islands (yellow asterisks).

palmar pits appeared as pigmented spots with barely visible grey-blue dots. Upon RCM examination, the pits showed the presence of tightly packed basaloid islands with peripheral palisading suggesting the diagnosis of pigmented BCC rather than palmar pits (Fig. 3).

Taken together, all findings (i.e., young age, multiple BCC, palmar BCC) pointed towards a diagnosis of GS, which was confirmed by blood genetic test that revealed the mutation of the *PTCH* gene. The lesions identified as BCC by means of dermoscopy and RCM were scheduled for surgical excisions and other treatment (imiquimod and photodynamic therapy) without performing a skin biopsy. Thus, the use of RCM saved time and unnecessary procedures before noninvasive treatments.

DISCUSSION

Early diagnosis and treatment of GS syndrome, as well as family screening and genetic counselling, are essential as it may be associated in 10% of the patients with aggressive BCC and malignant neoplasia. The diagnosis is based upon established major and minor clinical and radiological criteria and it should be confirmed by DNA analysis. The diagnostic criteria for naevoid BCC, established by Evans

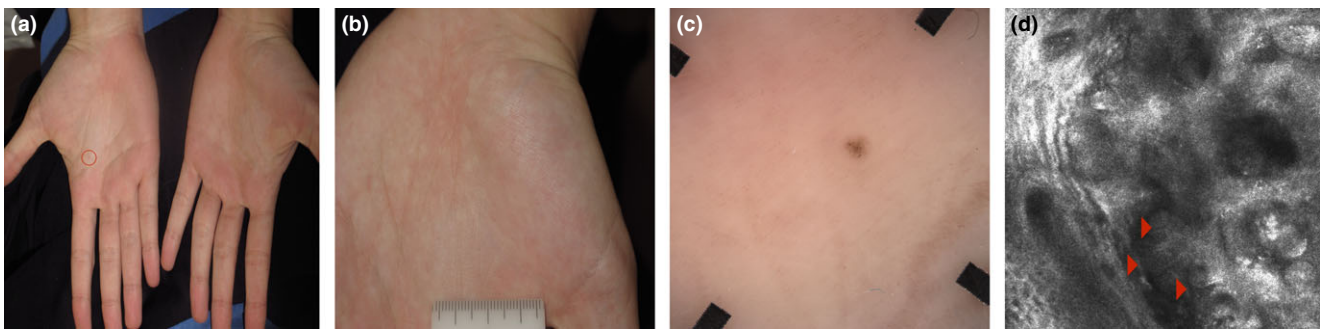

Figure 3 (a) Palms of the patient with few brown spots (b) of 2 × 1 mm in diameter (circle) (c) Dermoscopy shows the presence of brown dots. (d) Detail of confocal laser microscopy showing the presence of tightly packed basaloid islands (red arrows) with peripheral palisading suggestive of a basal cell carcinoma diagnosis.

and colleagues and modified by Kimonis and colleagues in 1997, state that two major or one major and two minor criteria should be present for the diagnosis.[5,6]

In our case report the young patient displayed two major clinical criteria that were suggestive of GS: multiple BCC and palmar BCC, which were further confirmed by a genetic test. Multiple BCC constitute the most characteristic feature of the syndrome. However, BCC in GS may reveal clinically and dermoscopically unusual pattern and thus, their diagnosis can be challenging.

To date, pigmented BCC in patients with GS have been described as having tree-like vessels, ulceration, fine telangiectasia, blue-grey ovoid nests, dots and globules. By using dermoscopy, BCC can be detected in early stages by the presence of blue-grey globules in lesions less than 3 mm in diameter. In larger lesions, arborising telangiectasia may also be present. No other dermatoscopic features have been reported.[7,8] Notably, in our patient BCC were typified by the presence of few dots without any vascular pattern, making a dermoscopic diagnosis extremely difficult. The systematic use of RCM on those multiple inconspicuous lesions permitted the clinicians to arrive at a diagnosis of BCC in a few minutes and with high confidence, since clear-cut confocal criteria were observed.

Typically, BCC on RCM display the presence of tightly basaloid islands, peripheral clefting and increased dermal vasculature.[9–11]

In the literature, palmar pits are described as small punctiform depressions (with a diameter ranging from 2 to 3 mm and a depth from 1 to 3 mm) that show small red dots upon dermoscopy. Surprisingly, in our patient, dermoscopy showed the presence of brown dots. The RCM examination revealed the presence of tightly packed basaloid islands with peripheral palisading: these findings were suggestive of BCC diagnosis.

Palmar pits have long been considered as lesions that are not able to evolve towards epithelial skin tumours. However, recently some authors have hypothesised that these pits could represent precursor lesion for BCC and few anecdotal cases of patients with palm–sole BCC arising within the context of numerous pits have been recently reported.[12,13]

CONCLUSIONS

The difficulty in the recognition GS patients is justified by its rarity and phenotypic variability. Diagnosis is often delayed, especially when it is in an attenuated form. Once a diagnosis has been made, family screening, including genetic testing, is indicated. For clinically doubtful lesions a biopsy is routinely performed, leading to inevitable scarring. In the modern era the use of non-invasive methods such as dermoscopy and RCM allows the identification of small tumours in their initial stage of development and their differential diagnosis from other neoplasia. Our case highlights the benefits of using a combined approach with dermoscopy and RCM to identify patients with inconspicuous lesions without performing multiple biopsies.

REFERENCES

1. Gorlin RJ, Goltz RW. Multiple nevoid basal cell epithelioma, jaw cysts and bifid rib: a syndrome. *N. Engl. J. Med.* 1960; **262**: 908–12.
2. Amezaga AOG, Arregui OG, Nuño SZ *et al.* Gorlin–Goltz syndrome: clinicopathologic aspects. *Med. Oral Patol. Oral Cir. Bucal* 2008; **13**: 338–43.
3. Acocella A, Sacco R, Bertolai R *et al.* Genetic and clinicopathologic aspects of Gorlin–Goltz syndrome (NBCC): presentation of two case reports and literature review. *Minerva Stomatol.* 2009; **58**: 43–53.
4. Segura S, Puig S, Carrera C *et al.* Non-invasive management of non-melanoma skin cancer in patients with cancer predisposition genodermatosis: a role for confocal microscopy and photodynamic therapy. *J. Eur. Acad. Dermatol. Venereol.* 2011; **25**: 819–27.
5. Kimonis VE, Goldstein AM, Pastakia B *et al.* Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. *Am. J. Med. Genet.* 1997; **69**: 299–308.
6. Evans DG, Ladusans EJ, Rimmer S *et al.* Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J. Med. Genet.* 1993; **30**: 460–4.
7. Kolm I, Puig S, Iranzo P *et al.* Dermoscopy in Gorlin–Goltz syndrome. *Dermatol. Surg.* 2006; **32**: 847–51.
8. Tom WL, Hurley MY, Oliver DS *et al.* Features of basal cell carcinomas in basal cell nevus syndrome. *Am. J. Med. Genet. A* 2011; **155A**: 2098–104.
9. Nori S, Rius-Díaz F, Cuevas J *et al.* Sensitivity and specificity of reflectance-mode confocal microscopy for in vivo diagnosis of basal cell carcinoma: a multicenter study. *J. Am. Acad. Dermatol.* 2004; **51**: 923–30.
10. Longo C, Lallas A, Kyrgidis A *et al.* Classifying distinct basal cell carcinoma subtype by means of dermatoscopy and reflectance confocal microscopy. *J. Am. Acad. Dermatol.* 2014; **71**: 716–24.
11. Segura S, Puig S, Carrera C *et al.* Dendritic cells in pigmented basal cell carcinoma: a relevant finding by reflectance-mode confocal microscopy. *Arch. Dermatol.* 2007; **143**: 883–6.
12. Holubar K, Matras H, Smalik AV. Multiple palmar basal cell epitheliomas in basal cell nevus syndrome. *Arch. Dermatol.* 1970; **101**: 679.
13. Howell JB, Freeman RG. Structure and significance of the pits with their tumors in the nevoid basal cell carcinoma syndrome. *J. Am. Acad. Dermatol.* 1980; **2**: 224.