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Collision skin lesions—results of a multicenter study of the International Dermoscopy Society (IDS)

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ABSTRACT **Background:** Collision lesions as two independent and unrelated skin tumors often manifest an atypical morphology.

Objective: To determine the combinations of collision skin lesions (CSLs).

Methods: Twenty-one pigmented lesion clinics in nine countries included 77 histopathologically proven CSLs in this retrospective observational study.

Results: Seventy-seven CSLs from 75 patients (median age 59.8 years) were analyzed; 24.7% of CSLs were located on the head and neck area, 5.2% on the upper extremities, 48.1% on the trunk, and 11.7% on the lower extremities; 40.3% revealed a melanocytic component (median age 54.7 years), followed by 45.5% with a basal cell carcinoma (BCC) (median age 62.4 years) and 11.7% with a seborrheic keratosis (median age 64.7 years). CSLs with a BCC component were more often found on the head and neck area compared to tumors with a melanocytic component (34.3% versus 16.1%). Lesions with a melanocytic component were more often detected on the trunk compared to lesions with a BCC (64.5% versus 37.1%). Patients with CSLs with epidermal-epidermal cell combination were older than patients with epidermal-dermal cell combination (63 versus 55.2 years), were more often male than female (63% versus 43.3%), more often had the lesion on the head and neck area (32.6% versus 13.3%), and less often on the upper (2.2 % versus 10%) or lower extremities (8.7% versus 16.6%).

Conclusions: CSLs consist of a heterogeneous group of lesions of varying cell types. They are associated with advancing age and cumulative UV-exposure. CSLs manifest a complex morphology making it challenging to diagnose correctly.

Introduction

Human skin consists of several layers with different cell types. Any possible intrinsic or extrinsic stimulation can trigger any one of these cells to proliferate, which can lead to the development of various combinations of skin tumors, both benign and malignant (Table 1). The challenge for the patient and clinician is to correctly diagnose these lesions with the aim of excising early skin cancer and minimizing the biopsy or excision of benign lesions.

Derm(at)oscopy is a noninvasive tool that helps improve the clinician's diagnostic sensitivity and specificity. Dermoscopy is widely accepted and used for the diagnosis of primary and recurrent pigmented and non-pigmented lesions of the skin, nail apparatus, hair, acral skin and mucosal areas [1-7] with a high diagnostic accuracy [8-12].

While the dermoscopic features of single lesions have been well described (Table 1), the possibilities and causes of collision skin lesions (CSLs) remain to be characterized. A Medline search performed before starting this study revealed a few case reports [13-31], and a few dermoscopic observations of a collection of CSLs with 17 pigmented actinic keratoses [32] in 3/130 dermatofibromas (2.3%) [33] and in 9/412 basal cell carcinomas (BCCs) (2.2%) [34].

In an effort to accrue a larger number of cases of CSLs, the International Dermoscopy Society (IDS) launched this multicenter retrospective, observational study. The aim of the study was to characterize the dermoscopic features of CSLs, to determine the most common lesions that occur in CSLs and to analyze possible reasons.

Methods

Patient Selection and Design

In this retrospective, observational study, patients' data and dermoscopic images of histopathologically diagnosed CSLs were included from 21 pigmented lesion clinics in nine countries: Argentina (2 centers), Australia, Brazil (3), Germany (4), Italy (4), Romania, Serbia, Spain (3), and United States of America (2).

CSLs were collected from July through December 2012 via an e-mail request sent to all IDS members. For each lesion, a patient data intake form, digital dermoscopic polarized and/or non-polarized and in-focus image(s) in JPEG format were requested. The CSLs had to fit within the field of view of the image to be included in the study. The following data variables were recorded for each lesion: gender, age, anatomic site, and the histopathology report. CSLs of the nails and mucosa were excluded. Anatomic sites were classified into head and neck, upper extremities, trunk, and lower extremities. The micro-anatomical location of the skin was classified as epidermal or dermal. Based on this the different subpopulations of cells within the CSLs were subdivided into epidermal-epidermal, epidermal-dermal and dermal-dermal combination according to the histopathology reports.

All data and digital images were assigned unique identifiers, anonymized, and sent via e-mail to the study coordinator (AB). The approval for this study was waived by the Ethics Committee of the Medical Council Baden-Wuerttemberg, Stuttgart, Germany.

TABLE 1. Skin lesions or tumors with their original cell types of the different skin layers (focused only on skin lesions detectable by dermoscopy)

Layer of the Skin	Cell Type or Functional Structure	Associated Proliferations/Neoplasms
Epidermis	Keratinocytes	Solar lentigo Seborrheic keratosis Actinic keratosis Bowen's disease Keratoacanthoma Squamous cell carcinoma
	Basal cell layer (non-differentiated folliculo-sebaceous-apocrine germ)	Trichoblastoma Basal cell carcinoma
	Melanocytes	Melanocytic nevus Melanoma
	Merkel cells	Merkel cell carcinoma
Dermis	Blood capillaries	Angioma
	Melanocytes	Melanocytic (dermal or blue) nevus Melanoma
	Fibroblasts	Dermatofibroma Dermatofibrosarcoma protuberans
	Non-Langerhans cells/histiocytes	Xanthogranuloma
	Infundibulo-follicular-sebaceous unit	Sebaceous hyperplasia, milia, cyst, pilomatrixoma, trichoepithelioma, adnexal (benign or malignant) tumor
	Myocytes	Kaposi sarcoma

Classification of Dermoscopic Images

During the process of evaluating and recording the dermoscopic criteria present in each image the researchers were aware of the histopathology diagnosis [35].

Results

General Data

The study consisted of 77 CSLs from 27 females (35.1%) and 43 males (55.8%); for seven patients (9.1%) the gender was not recorded. The mean age of the patients was 59.8 years (range from 24 to 88 years); for 10 patients (12.9%) the age was not provided. Regarding the anatomic site, 19 CSLs were located on the head and neck (24.7%), four on the upper extremities (5.2%), 37 on the trunk (48.1%), and nine on the lower extremities (11.7%); for eight lesions this data was not available (10.3%) (Table 2).

Various Combinations of CSLs

The 77 cases were subclassified as follows (Figure 1): in the first step the CSLs were analyzed for the presence of any melanocytic features (benign or malignant) (n= 31; 40.3%); in the second step, lesions were analyzed for any BCC features (n=35; 45.5%); in the third step the lesions were analyzed for features of a seborrheic keratosis (n= 9; 11.7%) and the remaining lesions comprised one solar lentigo in combination with an angioma (1.3%) and one clear cell acanthoma with a dermatofibroma (1.3%). Patients with CSLs in which a melanocytic tumor occurred were younger compared to patients with CSLs with BCC and seborrheic keratoses (54.7 versus 62.4 and 64.7 years). CSLs with melanocytic or basal cell carcinoma were more often observed in males than in females (64.5% and 65.7%) compared to lesions with seborrheic keratoses (33.3%). CSLs with BCC were more often found on the head and neck area compared to lesions with melanocytic parts (34.3% versus 16.1%). Finally, lesions with melanocytic parts were more often detected on the trunk compared to lesions with BCC (64.5% versus 37.1%) (Table 2).

Regarding the 31 CSLs with a melanocytic component, 22 were nevi, one was a severe melanocytic dysplasia and eight were melanomas. With these 31 melanocytic lesions, 14 seborrheic keratoses (Figure 2), seven angiomas (Figure 3), six BCCs, three dermatofibromas and one squamous cell carcinoma were found as part of the CSLs. The case of the severe melanocytic dysplasia was associated with an angioma (Figure 4). Four melanomas were associated with a seborrheic keratosis (Figure 5), three melanomas with a BCC (Figure 6) and one melanoma with a squamous cell carcinoma in situ.

With regard to the 35 CSLs with a BCC component, 18 seborrheic keratoses (Figure 7), five angiomas (Figure 8),

TABLE 2. Overview of age, gender and anatomic site data for all CSLs (which include the single lesion of a solar lentigo with an angioma, a clear cell acanthoma with a dermatofibroma and six lesions with additional inflammations), lesions with a melanocytic part (Melanocytic), basal cell carcinomas (BCC), and seborrheic keratoses (Seb.-ker.).

	All lesions (n=77)	Melanocytic (n=31)	BCC (n=35)	Seb.-ker. (n=9)
Median age in years (range in years)	59.8 (24-88)	54.7 (24-86)	62.4 (24-88)	64.7 (48-81)
Male (%)	43 (55.8)	20 (64.5)	23 (65.7)	3 (33.3)
Female (%)	27 (35.1)	8 (25.8)	10 (28.6)	4 (44.4)
Missing data for gender (%)	7 (9.1)	3 (9.7)	2 (5.7)	2 (22.2)
Head and Neck (%)	19 (24.7)	5 (16.1)	12 (34.3)	2 (22.2)
Upper extremities (%)	4 (5.2)	1 (3.2)	2 (5.7)	-
Trunk (%)	37 (48.1)	20 (64.5)	13 (37.1)	3 (33.3)
Lower Extremities (%)	9 (11.7)	1 (3.2)	6 (17.1)	2 (22.2)
Missing data for anatomic site (%)	8 (10.3)	4 (12.9)	2 (5.7)	2 (22.2)

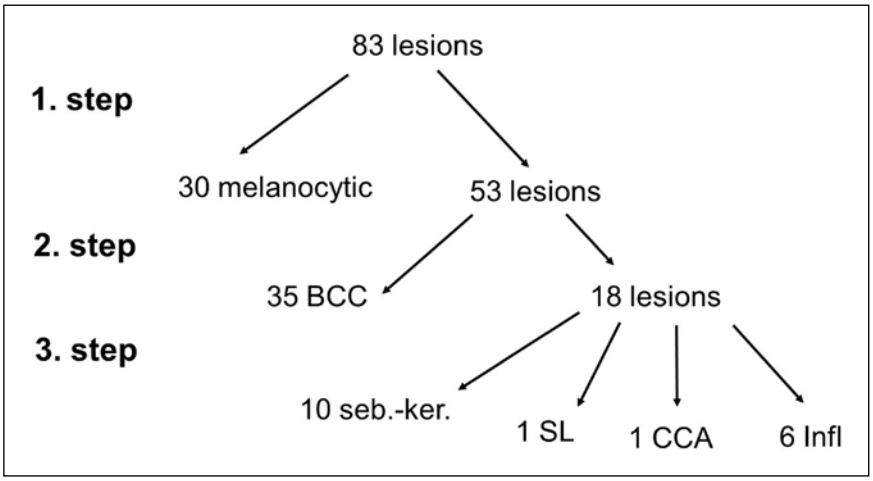

Figure 1. Subdivision of the 77 CSLs according to any detectable melanocytic origin (n= 31, melanocytic) in the first step, followed by any present basal cell carcinoma (n=35, BCC) in the second step, and finally nine seborrheic keratosis (seb.-ker.), one solar lentigo (SL) with an angioma and one clear cell acanthoma (CCA) with a dermatofibroma detected. [Copyright: ©2017 Blum et al.]

five dermatofibromas (Figure 9), two actinic keratoses, two hyperplasias of sebaceous glands, one clear cell acanthoma (Figure 10), one keratoacanthoma and one solar lentigo were found.

The nine CSLs with a seborrheic keratosis component (and without a melanocytic or BCC component), two solar lentigines (Figure 11), four angiomas (Figure 12), one hyperplasia of sebaceous glands and two squamous cell carcinomas were found.

Referencing Table 1, the data were additionally classified based on the combination of cells within the CSLs as either epidermal cells only, epidermal and dermal cells, and dermal cells only (Table 3). The epidermal-epidermal combination was found in 46 cases, the epidermal-dermal combination in 30 cases and the dermal-dermal combination in only one case (dermal nevus with an angioma, not listed in Table 3).

Patients with the epidermal-epidermal combination were older than patients with the epidermal-dermal combination (63 versus 55.2 years), were more likely to be male than female (63% versus 43.3%), and more often had the lesions on the head and neck area (32.6% versus 13.3%) and less often on the upper (2.2% versus 10%) and lower extremities (8.7% versus 16.6%).

Discussion

Any possible combination of benign and malignant collision skin lesions (CSLs) comprising melanocytic, epithelial, dermal

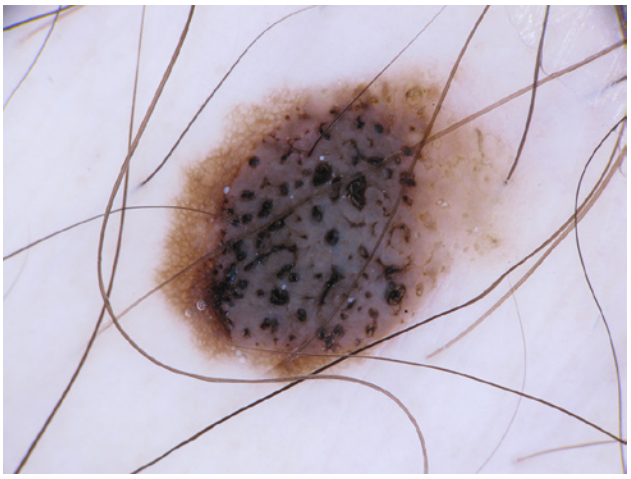

Figure 2a. CSL of a melanocytic nevus and a seborrheic keratosis in a 48-year-old male. [Copyright: ©2017 Blum et al.]

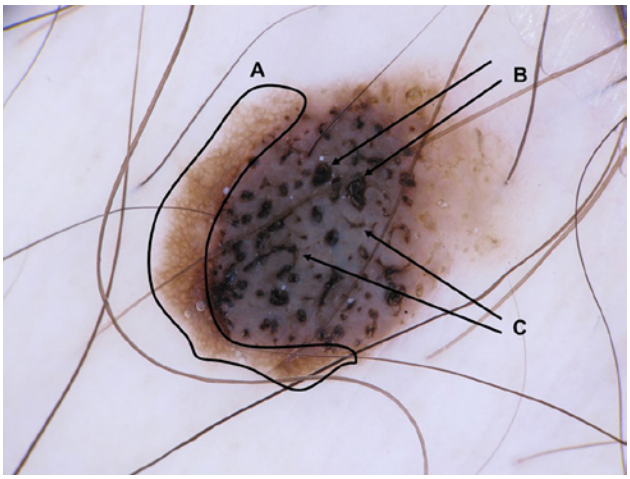

Figure 2b. Melanocytic nevus with regular brown network (A), and a seborrheic keratosis with comedo-like openings (B) and sulci/crypts (C). [Copyright: ©2017 Blum et al.]

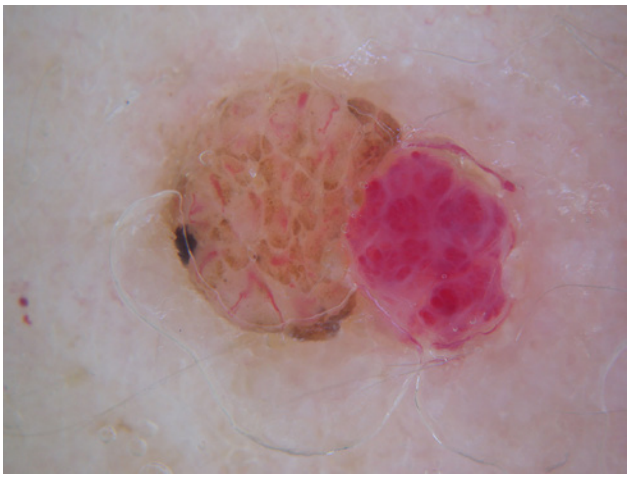

Figure 3a. CSL of a dermal nevus and an angioma in a 41-year-old female on her trunk. [Copyright: ©2017 Blum et al.]

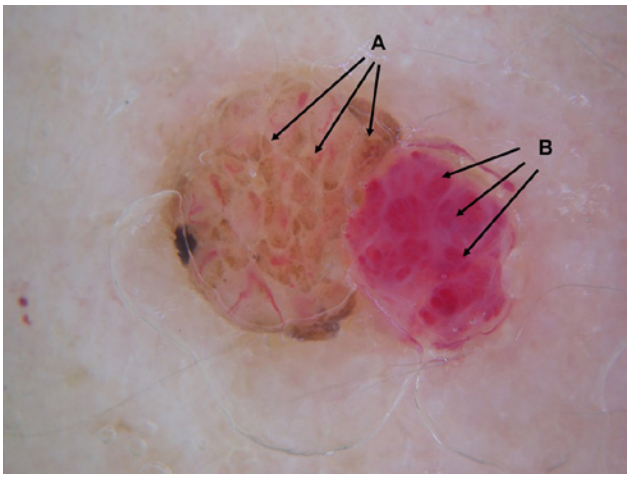

Figure 3b. Dermal nevus with distinct brown globules (A), and an angioma with red lacunas (B). [Copyright: ©2017 Blum et al.]

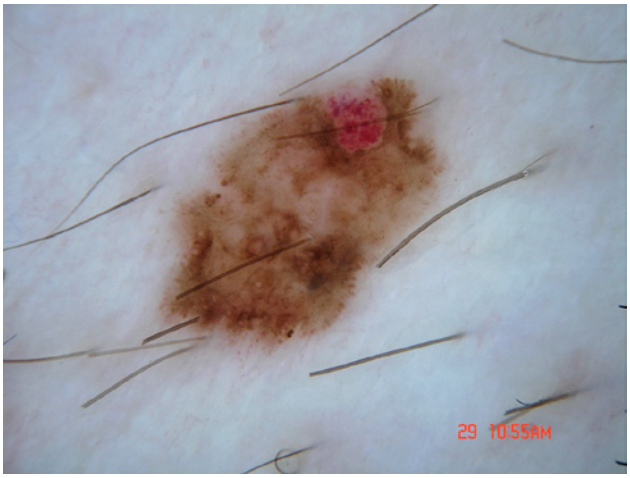

Figure 4a. CSL of a severe melanocytic dysplasia and an angioma (unknown age, gender or area of lesion). [Copyright: ©2017 Blum et al.]

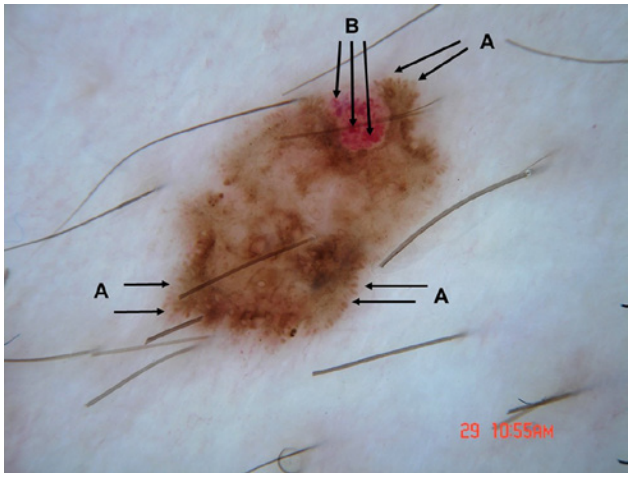

Figure 4b. Severe melanocytic dysplasia with asymmetrical radial streaks (A) and an angioma with red lacunas (B). [Copyright: ©2017 Blum et al.

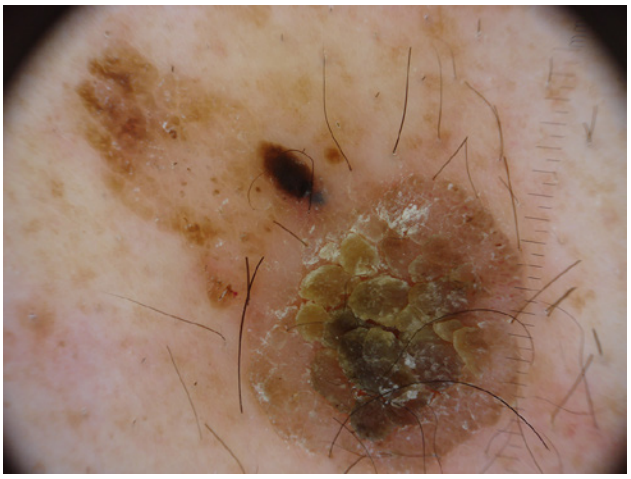

Figure 5a. CSL of an invasive melanoma and a seborrheic keratosis in a 62-year-old male on his belly. [Copyright: ©2017 Blum et al.]

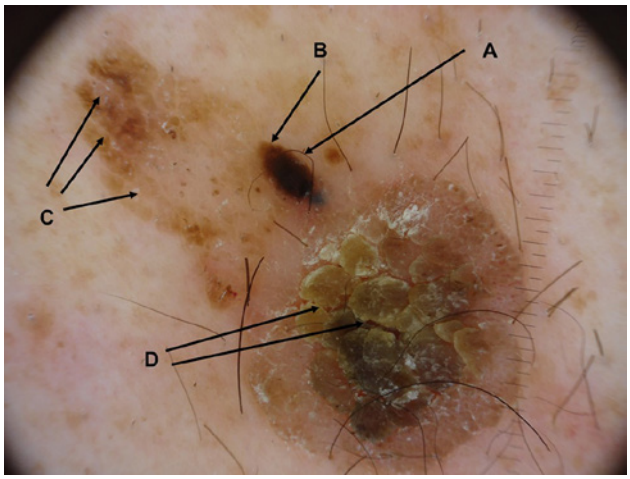

Figure 5b. Invasive melanoma with a brown-to-black homogenous symmetric pigmented single blotch (A) with distinct radial asymmetric streaming (B), and a seborrheic keratosis with sulci/crypts in early (C) and advanced stages (D). [Copyright: ©2017 Blum et al.]

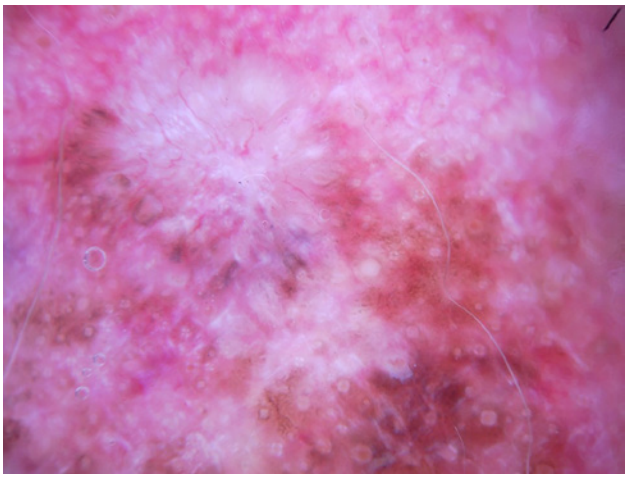

Figure 6a. CSL of a lentigo maligna and a basal cell carcinoma of a male at his face (unknown age). [Copyright: ©2017 Blum et al.]

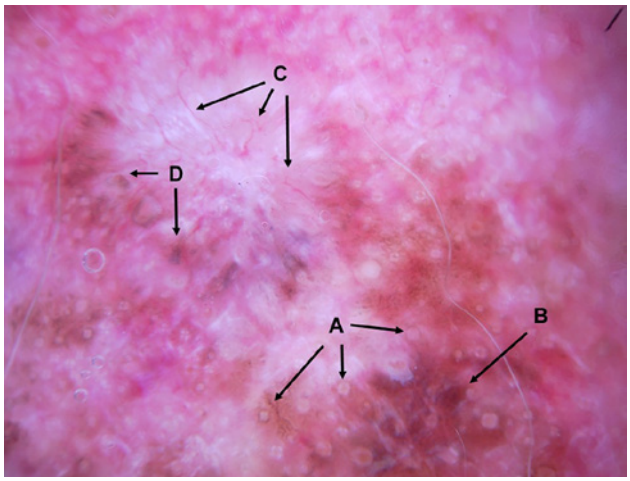

Figure 6b. Lentigo maligna with pigmented follicles (A) and destroyed follicle with patchy pigmentation (B), and a basal cell carcinoma with arborizing vessels (C) and pigmented blue-grayish globules (D). [Copyright: ©2017 Blum et al.]

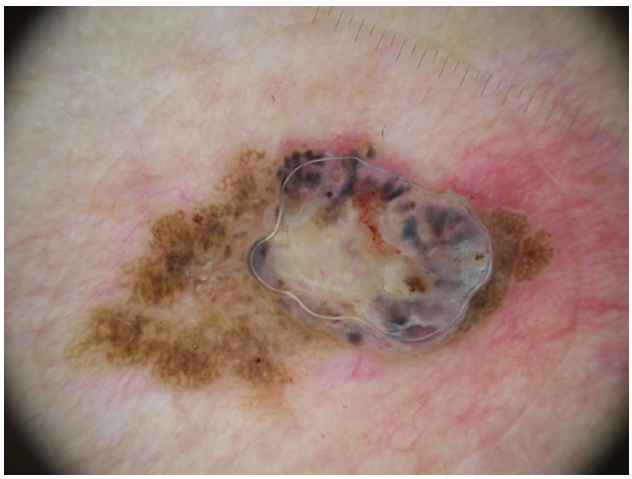

Figure 7a. CSL of a basal cell carcinoma and a seborrheic keratosis in a 65-year-old male on his arm. [Copyright: ©2017 Blum et al.]

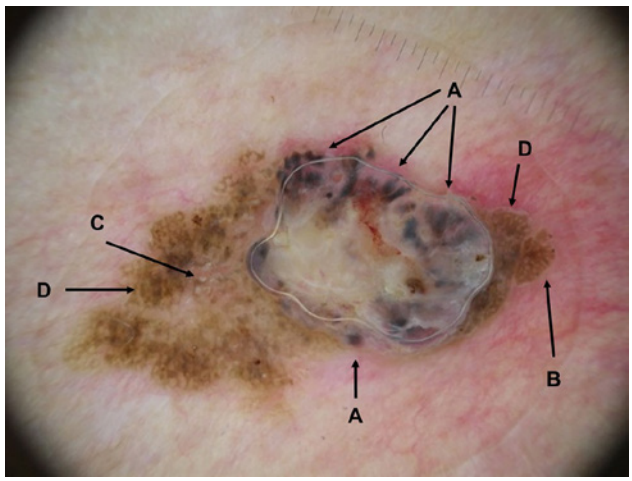

Figure 7b. Basal cell carcinoma with ovoid blue-gray nests (A) and a seborrheic keratosis with brown fat-fingers (B), pseudo horn cysts (C) and sulci/crypts (D). [Copyright: ©2017 Blum et al.]

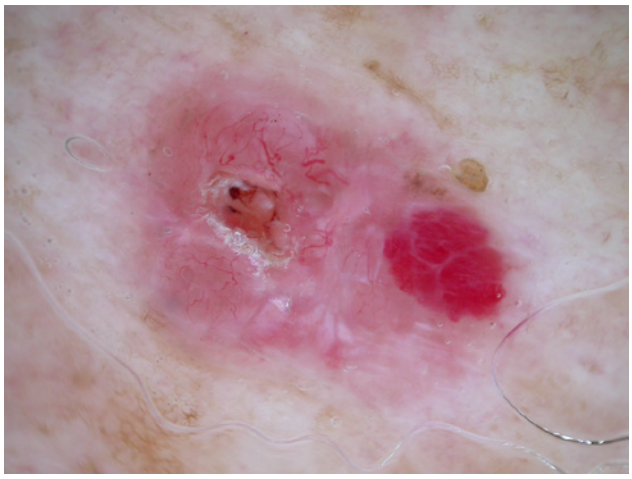

Figure 8a. CSL of a basal cell carcinoma and an angioma in a 67-year-old male on his back. [Copyright: ©2017 Blum et al.]

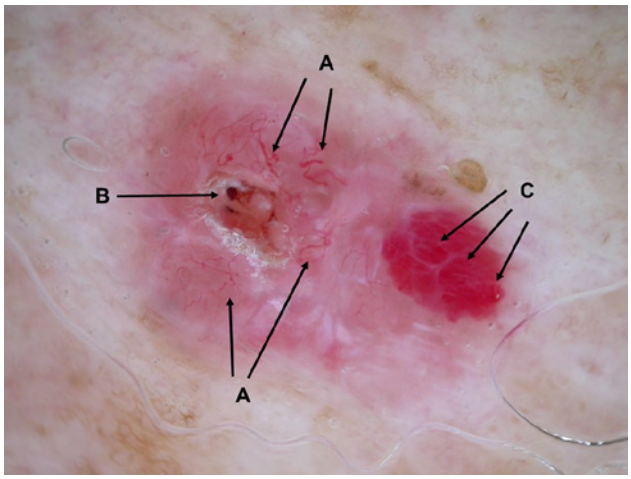

Figure 8b. Basal cell carcinoma with arborizing vessels (A) and one pigmented blue-grayish globule (B) and an angioma with red globules/lacunas (C). [Copyright: ©2017 Blum et al.]

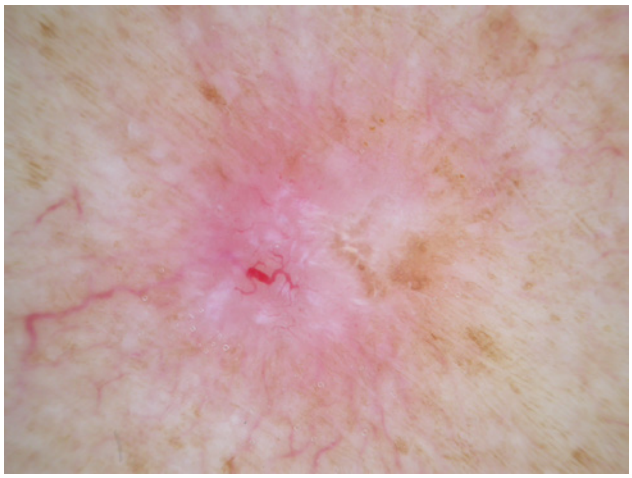

Figure 9a. CSL of a basal cell carcinoma and a dermatofibroma in a 40-year-old female on her arm [39]. [Copyright: ©2017 Blum et al.]

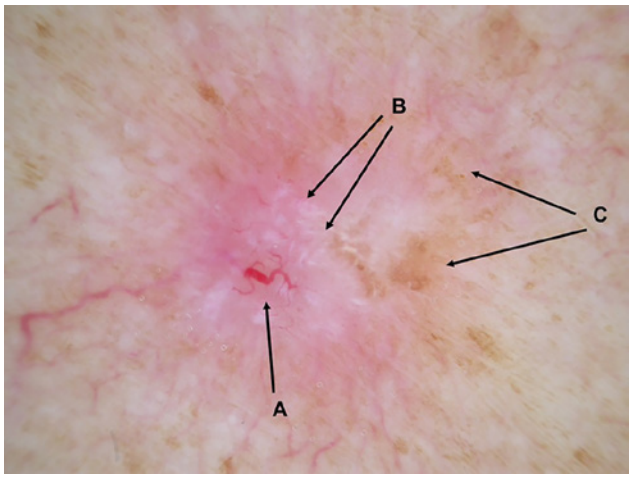

Figure 9b. Basal cell carcinoma with arborizing vessels (A) and a dermatofibroma with a central white patch and shiny white lines (B) and post-inflammatory peripheral hyperpigmentation (C) [39]. [Copyright: ©2017 Blum et al.]

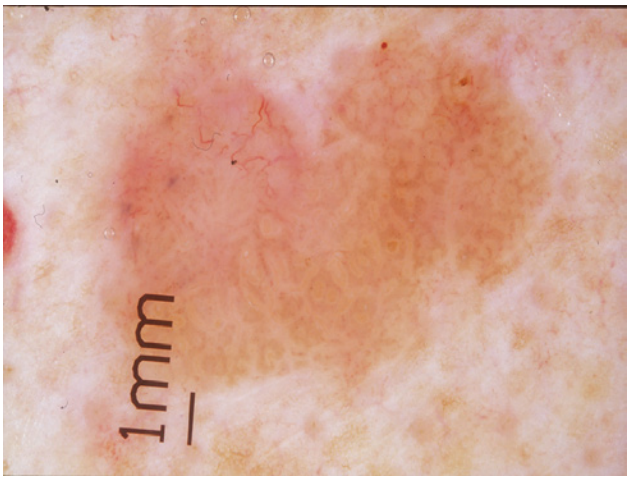

Figure 10a. CSL of a basal cell carcinoma, a clear cell acanthoma and a seborrheic keratosis (unknown age, gender and area of lesion). [Copyright: ©2017 Blum et al.]

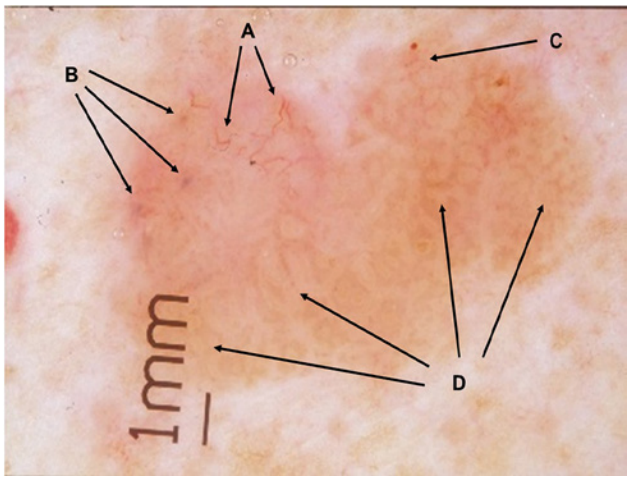

Figure 10b. Basal cell carcinoma with arborizing vessels (A) and pigmented blue-grayish globules (B), a clear cell acanthoma with dotted vessels in a line (C) and a seborrheic keratosis with brown fingerprint-like structures (D). [Copyright: ©2017 Blum et al.]

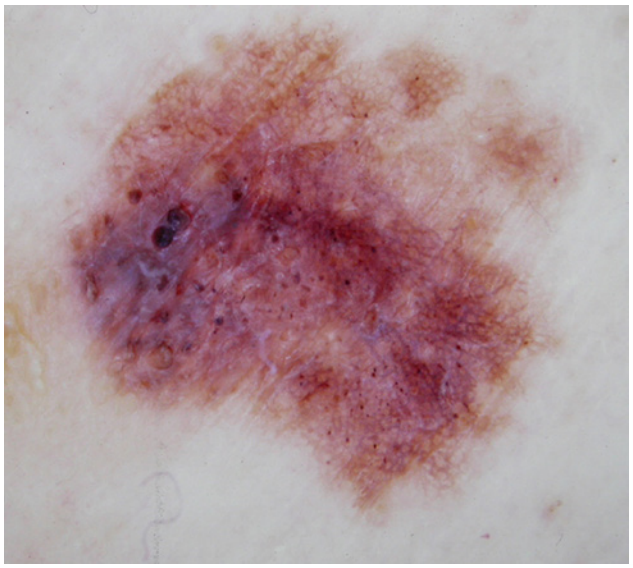

Figure 11a. CSL of a seborrheic keratosis and a solar lentigo in an 81-year-old male on his trunk. [Copyright: ©2017 Blum et al.]

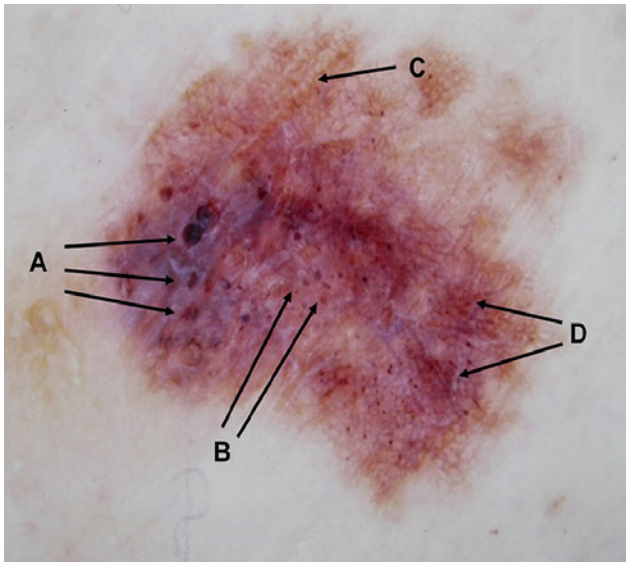

Figure 11b. Seborrheic keratosis with comedo-like openings (A) and initial sulci/crypts (B) and a solar lentigo with brown homogenous (C) and more prominent network (D). [Copyright: ©2017 Blum et al.]

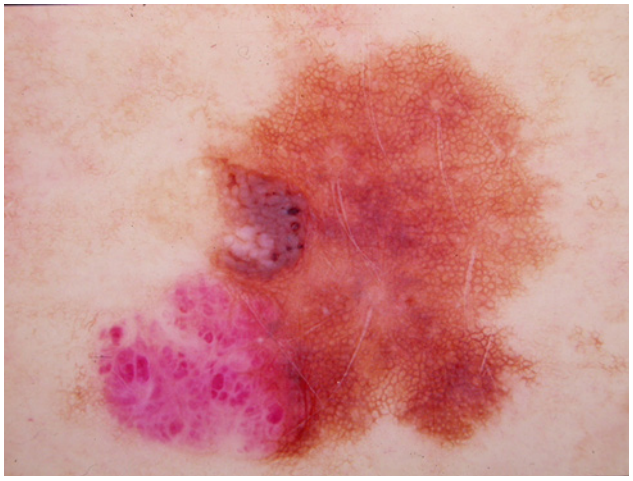

Figure 12a. CSL of a seborrheic keratosis, an angioma and a solar lentigo in a 67-year-old female on her belly. [Copyright: ©2017 Blum et al.]

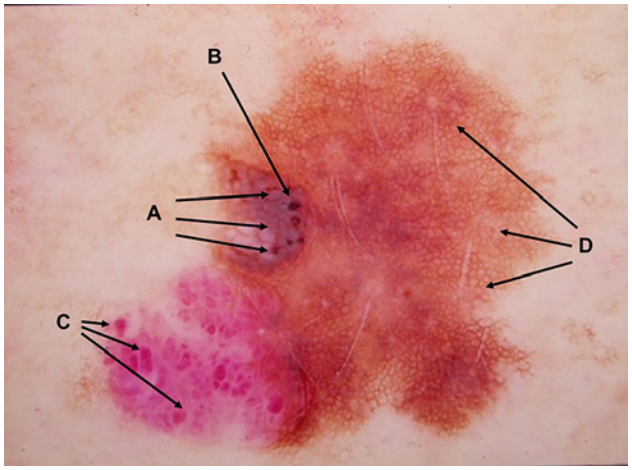

Figure 12b. Seborrheic keratosis with initial sulci/crypts (A) and comedo-like opening (B), an angioma with red lacunas (C) and a solar lentigo with brown homogenous network (D). [Copyright: ©2017 Blum et al.]

or adnexal cells can occur in human skin [13-34,36-43]. Both intrinsic and extrinsic factors contribute to the likelihood of having two unrelated skin lesions occurring adjacent and contiguous with each other [44].

Age is an intrinsic factor, and although skin lesions are not found in abundance during youth or adolescence, when present, most of the lesions are melanocytic nevi. During adulthood more skin lesions from different cell types occur from epithelial more than melanocytic cells [45,46]. In this retrospective observational study, CSLs with a melanocytic component were found more often in patients younger than 60 years of age. This can be explained by the fact that there is a progressive reduction of nevi with advancing age [47]. In contrast, in the groups of CSLs with BCC and seborrheic keratosis components, the median age was older than 60 years. Once again, this can be explained by the fact that BCCs and seborrheic keratoses are more prevalent the older we get. Interestingly, in our image database we found melanocytic lesions with one squamous cell carcinoma and six with BCCs, which contradicts the observation of the literature and our study about the age distribution and the origin of melanocytic and epithelial skin lesions. This confirms again that probabilities are observed, but exceptions are always possible [13-34,36-43].

Skin type is also a known intrinsic factor. In Fitzpatrick skin types I and II, more epithelial skin lesions can occur dur-

TABLE 3. Overview of age, gender and anatomic site data according to the combination of epidermal-epidermal cells and epidermal-dermal cells of the CSLs

	Epidermal – epidermal cells (n=46)	Epidermal – dermal cells (n=30)
Median age in years (range in years)	63.0 (24-88)	55.2 (24-85)
Male (%)	29 (63.0)	13 (43.3)
Female (%)	13 (28.3)	13 (43.3)
Missing data for gender (%)	4 (8.7)	4 (13.4)
Head and Neck (%)	15 (32.6)	4 (13.3)
Upper extremities (%)	1 (2.2)	3 (10.0)
Trunk (%)	22 (47.8)	14 (46.7)
Lower Extremities (%)	4 (8.7)	5 (16.6)
Missing data for anatomic site (%)	4 (8.7)	4 (13.4)

ing a lifetime compared to skin types III and IV [46,48]. This observation could not be investigated in this study because the data were not available.

The total lifetime dosage of UV radiation is considered an extrinsic reason for having CSLs [16,21,31,32,48]. UV-induced proliferation of benign or malignant cell types can occur resulting in various combination of CSLs. Our study confirmed this observation: BCCs were more often found in sun-exposed areas (head and neck followed by the trunk) compared to melanocytic lesions (trunk followed by head and neck). Patients with CSLs with epidermal-epidermal tumor combinations were older than patients with the epidermal-dermal tumoral combinations, more males than females had CSLs, and the CSLs were more often on the head and neck area—these three observations suggest that UV exposure is associated with CSLs and that the lifetime UV-exposure load may be greater in men then in women [45,48].

Viral infections in the elderly could also be an extrinsic factor for proliferation of epidermal skin cells, which could lead to Bowen's disease or squamous cell carcinoma—but this hypothesis is still under discussion [49]. Any further investigation was not possible in this present study.

CSLs can pose diagnostic challenges. CSLs composed of two or more benign lesions can manifest a clinically irregular morphology leading to unnecessary biopsies or excisions. However, and more importantly, CSLs composed of benign and malignant lesions can sometimes be diagnosed as benign lesions due to anchoring bias (also known as confirmation bias) [50]. This occurs when the observer anchors their diagnosis on the benign features within a CSL and stops searching for features suggestive of malignancy. Such errors in visual perception can lead to the missed opportunity to biopsy or excise a skin cancer. Being aware of anchoring bias prevents the observer from placing so much emphasis on dermoscopically prominent features within a CSL that the clinician stops searching for potentially subtler features that may be present and would assist in detecting skin cancer [51]. A good rule to follow is to evaluate, especially in benign lesions, all four quadrants of a lesion and to ensure that there are no signs of malignancy in any quadrant [50,52]. In complex dermoscopic images the switch between polarized and non-polarized light may be helpful as well [53,54].

This study has several limitations. (1) CSLs were only classified dermoscopically according to the histopathology reports given to the study coordinator. A further project with the collected images of CSLs should be the evaluation of diagnostic accuracy with a higher number of dermoscopists blinded to the histopathological result. (2) The specific diagnosis of the melanocytic nevi was rarely given (e.g., lentiginous or compound or dermal nevus), which could have influenced the analysis of the level of cell layers.

In conclusion, CSLs are found increasingly in the aging population with higher accumulative lifetime UV exposure (Figure 13). Many of these lesions will manifest a complex clinical morphology, including when the CSL consists of two benign lesions, leading, at times, to unnecessary biopsies and excisions. Dermoscopy may assist in correctly identifying the benign components of the CSLs that are composed of two or even more benign entities. However, dermoscopy can also lead to anchoring errors, resulting in the missed opportunity to biopsy a CSL that is composed of a benign and malignant entity. Awareness of this pitfall should help the observer in avoiding it. Reflectance confocal microscopy could be a new additional and helpful diagnostic tool for these CSLs [26,55-57]. However, uncertain or non-classifiable lesions still need a complete excision for the final, correct diagnosis.

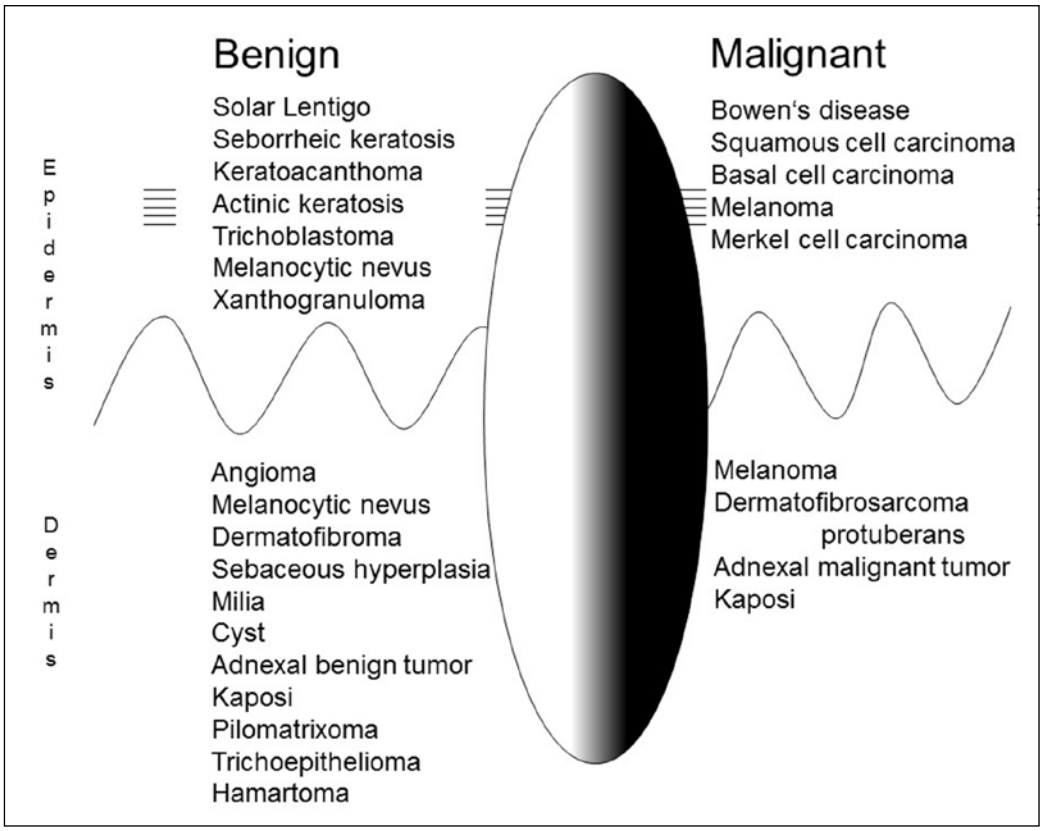

Figure 13. Skin model for collision skin lesions with benign and malignant lesions from the epidermal and dermal origin. [Copyright: ©2017 Blum et al.]

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