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Collision Lesions: Genuine Collision (Conflict) or not?

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ABSTRACT By definition, the term "collision lesion" refers to two or more tumors coinciding in the same anatomic position or visceral organ. Collision lesions coexisting on the same skin location are defined as collision skin lesions (CSLs). Although this term implies a conflict between the tumors, this is not the case. CSLs appear to be rare, but still pose a significant diagnostic problem in everyday clinical practice and clinicians should be aware of their existence. The aim of this study was to elucidate the problem of CSLs in clinical practice, with an emphasis on classification of CSLs according to position dependence, tumor histogenesis, etiology, and possible lesion combinations in CSLs, as well as diagnostic possibilities. According to our results, accurate clinical diagnosis could be only rarely reached, requiring lesion excision and pathohistological confirmation of CSLs. Considering the fact that tumors in CSLs can be partially or completely overlying or can even be positioned one within the other, the existence of two or more tumors is extremely difficult to detect.

KEY WORDS: collision skin lesions, etiology, histogenesis, diagnostics

INTRODUCTION

Collision skin lesions (CSLs) are two or more independent and unrelated skin tumors coinciding at the same skin location or visceral organ and often manifesting atypical morphology (1). Collision lesions coexisting on the same skin location are defined as collision skin lesions. Although such lesions appear to be rare, they pose a significant diagnostic problem in everyday clinical practice. The aim of our study was to elucidate the problems associated with the CSLs in everyday practice as well as their incidence and most frequent combinations, and possible diagnostic methods and interpretations.

PATIENTS AND METHODS

For the purpose of this cross-sectional study, 61 samples of collision skin lesions were collected and compared at the pathohistological laboratory of the Department of Dermatovenerology, Rijeka University Hospital Center, Rijeka, Croatia over a two-year period. CSLs were diagnosed based on the clinical and dermoscopy findings and were histopathologically confirmed.

RESULTS

In total, we analyzed 61 CSLs; 60 of them with coexistence of two different tumors, and one present-

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ing with three coexisting lesions. Our results show CSLs to be more frequent in women (36 women, 59.01%) compared with men (25 men, 40.98%). Regarding the anatomic site location, CSLs were more often detected on the trunk (41 CSLs, 67.21%), and head area (14 CSLs, 22.95%) while a smaller percentage was found on the extremities (6 CSLs, 9.84%). As to the tumor types, we detected 33 cases (54.09%) of CSLs combining two benign tumors and 28 cases (45.9%) of CSLs combining benign and malignant tumors, while the collision involving two malignant tumors was not observed. The most common combinations of tumors in the CSLs observed were seborrheic wart with nevus (7 cases, 11.47%) and compound nevus combined with dysplastic nevus (7 cases, 11.47%) followed by dysplastic nevus with hemangioma (5 cases, 8.19%) and basal cell carcinoma (BCC) with solar lentigo (5 cases, 8.19%). Other tumor combinations in CSLs are illustrated in Table 1. The results of this study show the most common tumors in CLSs to be nevi (29 CSLs, 47.54%) and seborrheic warts (19 CSLs, 31.14%). Based on data from the literature and our results and due to histopathology, we analyzed the examined CSLs with regard to the position dependence of the two lesions and divided them into four different types of CSLs: juxtaposition, overlying, tumor within a tumor, and combinations (juxtaposition and overlying), as shown in Figure 1. The majority of the lesions were arranged in juxtaposition, as it was the case of CSL of angioma and nevus (Figure 2). The second most common type of CSLs was the overlying of collision tumors, as shown in the case of nevus and syringoma combination (Figure 3). Table 2 displays the frequency of tumor types detected in CSLs. Clinical and dermoscopic examination helped in achieving the correct diagnosis in 6 cases (9.83%) cases and the partially correct diagnosis in 46 cases (75.4%), while 9 cases (14.75%) were misdiagnosed.

DISCUSSION

Regarding the combination of tumors in CSLs, there are cases reporting combinations of two benign tumors, combinations of benign and malignant tumors, combinations of more malignant tumors, combinations of two tumor metastases, combinations of metastatic tumors and malignant tumors, as well as combinations of tumors and cysts. A review of the literature listed below reveals cases combining two benign tumors, such as combination of eccrine syringofibroadenoma in association with clear-cell acanthoma (2), cases with combinations of one benign and one malignant tumor, such as trichofolliculoma in association with BCC (3) or a blue nevus combined with BCC (4), and combinations of two malignant tumors, such as melanoma malignum (MM) with squamous cell carcinoma (SCC) (5). In addition to that, CSLs can also be combinations of different malignant tumors such as metastatic MM colliding with BCC (6). Cyst and tumor collisions occur rarely, and one of the documented cases reports a combination of Merkel cell tumor with a trichilemmal cyst (7). The results of our study show the occurrence of the combination of two benign tumors to be the most frequent (54.09%), followed by CSLs including benign and malignant tumors (45.9%), while a collision involving two malignant tumors was not observed. Regarding histopathogenesis, different combinations of CSLs are also possible: combinations of two epidermal tumors, combinations of two mesenchymal tumors, or combinations of epidermal and mesenchymal tumors. Less commonly documented

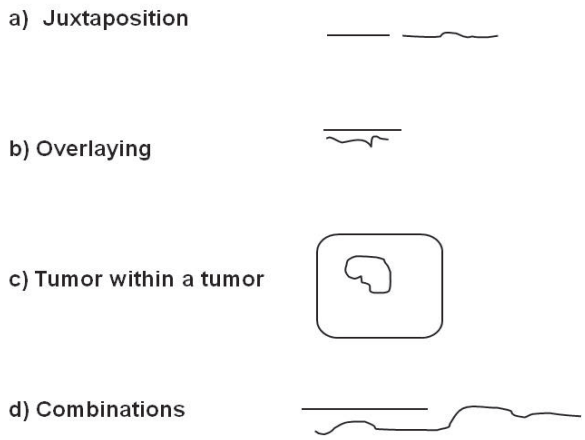

Figure 1. Collision lesions according to tumor position dependence

Table 1. Tumor combinations in CSLs: frequency and percentage

Collision lesion	Frequency	Percentage (%)
Seborrheic wart with nevi	7	11.47
Compound nevus with dysplastic nevus	7	11.47
Dysplastic nevus with hemangioma	5	8.19
BCC with solar lentigo	5	8.19
Nevus with foreign body granuloma	4	6.55
Fibropapiloma with dermatofibroma	2	3.27
BCC with fibropapiloma	2	3.27
BCC with sebaceous hyperplasia	2	3.27
Dysplastic nevus with neurofibroma	2	3.27

CSL - collision lesion, BCC - basal cell carcinoma

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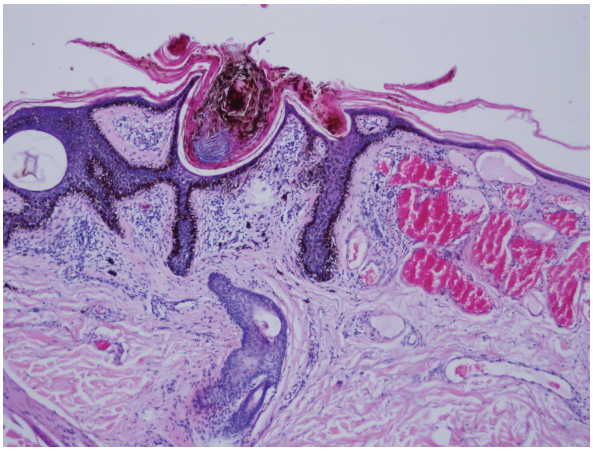

Figure 2. Collision between dysplastic nevus and hemangioma (HE stain x100).

are different combinations of mesenchymal tumors: proliferation with melanocytic and desmoplastic nevi (Spitz nevus) and leiomyoma (8). Combinations of melanocytic lesions with epidermal, follicular, and adnexal tumors have also been described (8). Alves *et al*. reported an unusual collision case of BCC and atypical fibroxanthoma (9). Interestingly, combinations of different malignant tumors (MM and BCC) as well as combinations of malignant tumors (MM) and benign tumors (seborrheic warts) do not display the pattern in which malignant tumors have a tendency to "destroy" less malignant or benign tumors. The term "collision skin lesion" should therefore be brought into question, since a genuine collision seems to be absent. Namely, the term "collision" indicates a conflict, a clash and a struggle, while the aforesaid tumors peacefully coexist and, in certain combinations, actually act jointly against their human host. In fact, most of the combined tumors are anatomically close yet separated. Therefore, more appropriate terms seem to be combination, association, or coexistence. Other authors share our opinions regarding the CSLs combinations (10): either suspecting tumor association (7,11) or tumor coexistence (4,12). Moreover, certain authors introduced the terms "colonization tumors" or "bi-phenotypic tumors" (6,13,14). However, such terminology is quite rare and mostly refers to malignant tumor combinations (10).

Considering the above, there is a certain amount of "fair play" between the tumors in CSLs which might have a certain recognition mechanism preventing them from attacking each other. However, CSLs consisting of combinations of malignant and benign tumors or combinations of two malignant tumors do endanger their human host. The latter consideration

Table 2.Tumor types in CSLs: frequency and percentage

Tumor	Frequency	Percentage (%)
Nevus	29	47.54
Seborrheic wart	19	31.14
BCC	19	31.14
Hemangioma	7	11.47
Fibropapiloma	6	9.83
Solar lentigo	5	8.19
Superficial BCC	5	8.19
Actinic keratosis	3	4.81
Bowen's disease	3	4.81
Sebaceous hyperplasia	3	4.81
Keratoacanthoma	3	4.91
Dermatofibroma	2	3.27
Neurofibroma	2	3.27

CSL – collision lesion, BCC - basal cell carcinoma

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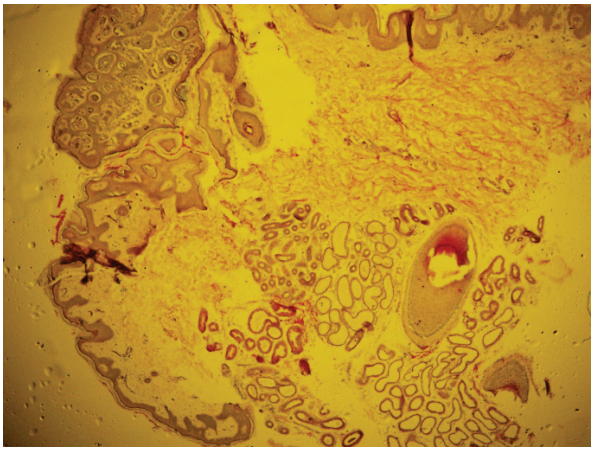

Figure 3. Collision lesion between compound nevus (papillomatosus) and syringoma in down position (HE stain x100).

is of great relevance in understanding tumor behavior in order to adopt the best approaches to collision lesions. As to the position-dependence of collision tumors, we differentiate between the four types (Figure 1) of CSLs, and the majority of analyzed lesions were in juxtaposition (Figure 1a, Figure 2) followed by overlying of collision tumors (Figure 1b, Figure 3). We also detected a case of a dysplastic nevus underlying a seborrheic wart. Figuratively speaking, juxtaposition includes adjacent positions, while overlying tumors suggests the presence of "one tumor under another". A tumor within a tumor position appears to be quite rare; as suggested previously in a cases of MM within SCC and BCC (10), MM within BCC (10,14,15), a MM within a seborrheic wart (16), as well as in a case of a seborrheic wart within MM (17) (Figure 1c). The combination of juxtaposition and overlying is also possible (Figure 1d).

It should be noted that clinical and dermoscopic diagnosis is mostly applicable to juxtaposed CSLs, since the latter appear on the skin surface. As to overlying, partial overlying and tumor within tumor positions (cases when one tumor is completely invisible or partially visible) CSLs types can only be speculated on, with only the surface tumor possibly being diagnosed. Interestingly, we detected a case of a papillomatous nevus overlying a syringoma (Figure 3), while other authors describe the overlying of syringoma and Spitz nevus (18). In clinical practice, patients sometimes report recent changes and growth of previously unchanging tumor lesions. However, these cases usually involve the upper tumor being pushed upwards by the lower tumor, thus creating the illusion of growth and change of the upper tumor. Furthermore, in the reviewed literature authors described collision cases involving three tumors: for example eccrine poroma, seborrheic wart and viral wart (19), a combination of melanocytic nevus, BCC, and seborrheic wart (20), and a combination of MM, SCC, and BCC (10). Our study also includes a CSL combining three different tumors: Mb Bowen, seborrheic wart (reticulated type), and lichen planus-like keratosis. Various authors reported a collision of MM with BCC (12-14,21,22), and histopathology demonstrated a distinct separation of the aforesaid tumors, or tumor cells (21). However, exceptionally infrequent cases documented tumor cells mixing in tumor within tumor position dependence (22-24). As to etiology, it has been suggested that a tumor might induce the other tumor's growth, could be transfected into another one, or a mutation in the BRAF gene could be present (25). Thus, CSLs might be random events or induced by the attraction or induction method. The literature presents cases of MM cell trans-differentiation into a leiomyosarcoma, such as MM cells trans-differentiating into a leiomyosarcomatoid phenotype (26). Therefore, a question of tumors transferring into other tumors arises. Tumor clonality is also possible, as described in a case of BCC and epidermal nevus collision (27).

Tumor location could also be an important factor in development of CSLs. In our study, most CSLs were detected on the trunk (67.21%) and head area (22.95%), similarly to previous findings (28). CSLs were also more frequent in women (36 women, 59.01%) compared with men (25 men, 40.98%). The use of dermoscopy in diagnosing CSLs partially facilitates the distinction and recognition of collisions, although most authors question its accuracy since tumor position dependence in collisions appears to be the most relevant factor (16,17,20,25). Several authors claim reflectance confocal microscopy to be more reliable than dermoscopy in the differentiation of collision tumors (1,29).

The most frequent tumors reported in our clinical study were nevi (47.54%), followed by BCC and seborrheic warts (31.14%). Other authors documented the most frequent tumors to be seborrheic warts followed by nevi (1). It should be noted that clinical practice often detects combinations of angiomas and nevi (different types) as well as seborrheic warts and angiomas. However, such CSLs are mostly diagnosed by clinical assessment and dermoscopy, and further histopathological verification is not necessary. Generally, the incidence rate of CSLs is around 1.5% (30). Although such lesions appear to be statistically rare, we are well-aware that they are more frequent in clinical practice. Surgical excision of a tumor lesion is applied when malignancy is suspected. However, the question is how many possible (hidden) malignant lesions are not detected by clinical examination of CSLs.

In case of overlying tumors or tumor within a tumor positioning, when the malignant part of the CSL is not visible, clinical assessment and dermoscopy only reveal the benign lesion. Accordingly, surgical excision is not applied and the malignant lesion could remain undetected. CSLs are not easily diagnosed, which has been confirmed by other authors (20,31). Dermoscopy cannot help in cases overlying and tumor in tumor collision types. Therefore, when an atypical cutaneous tumor is encountered in clinical practice, CLS should also be suspected. According to our results, accurate diagnosis based only on clinical and dermoscopy examination of CSLs was only established in 9.83% cases. However, in 75.4% of cases one of the two tumors in CSLs was correctly diagnosed since clinical examination and dermoscopy did reveal "different and unusual" features, giving rise to a suspicion and resulting in excisional biopsy. We should point out that we have detected a high percentage of CSLs (45.9%) due to a combination of malignant and benign tumors. Therefore, although the clinical diagnosis regarding the presence of a collision lesion was not accurate in some cases, the diagnostic procedure undertaken turned out to be correct since it ultimately led to the detection of a malignant tumor part.

CONCLUSIONS

With regard to position dependence of collision tumors, we could differentiate between juxtaposed positions, overlying position, tumor within a tumor, and combinations (juxtaposed and overlying). Histopathogenetic aspects also vary, and CSLs may include combinations of two epidermal tumors, combinations of two mesenchymal tumors, or a combination of an epidermal and a mesenchymal tumor. The etiology of CSLs is still not well understood and includes several theories: a tumor might be attracted to or induced by another tumor. Additionally, tumor clonality or trans-differentiation into other tumors are also possible. We believe that clinical and dermoscopic examination are insufficient in establishing accurate diagnosis in cases of CSLs, probably due to position dependence, since compounding lesions of CSLs could be partially or completely overlying. Therefore, the existence of two or more tumors can only be suspected and the correct diagnosis of CSL is hampered. Finally, it should be pointed out that the term "collision skin lesion" is also questionable since a real collision (conflict) between the tumors appears to be absent. More appropriate terms, already adopted by several authors, seems to be tumor combination, association, or coexistence.

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