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REVIEW

Sebaceous lesions of the skin

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Summary

Sebaceous differentiation is commonly seen in cutaneous neoplasms, both in the context of lesions showing predominantly sebaceous differentiation (e.g., sebaceous adenoma, sebaceoma and sebaceous carcinoma), or as more focal sebaceous components in neoplasms with other primary lines of differentiation. Sebaceous changes can also be a component of benign cystic lesions or epidermal tumours, and sebaceous hyperplasia is commonly encountered. This review is intended to provide an overview of the cutaneous lesions with sebaceous differentiation, with a particular emphasis on facilitating histological diagnosis of neoplasms. In addition, the role of immunohistochemical studies is outlined, as well as the evaluation of potential cases of Muir–Torre syndrome.

Key words: Sebaceous neoplasms; sebaceous hyperplasia; sebaceous adenoma; sebaceoma; sebaceous carcinoma; Muir–Torre syndrome.

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INTRODUCTION

Sebaceous glands are holocrine glands widely distributed in the skin, recognised histologically by a characteristic lobular architecture, with a peripheral germinative component and central component of multivacuolated sebocytes. There is a limited list of neoplasms with predominant sebaceous differentiation, typically restricted to sebaceous adenoma, sebaceoma and sebaceous carcinoma, though some rarer and more controversial entities (e.g., reticulated acanthoma with sebaceous differentiation) might also be included. Sebaceous hyperplasia is a common clinical finding and can be induced by medications or present with unique clinical features (e.g., juxtaclavicular beaded lines). In addition, sebaceous components can be seen in neoplasms with primarily follicular or apocrine differentiation, which is unsurprising given the embryological relationship of these adnexal structures. A sebaceous component is recognised in cystic lesions such as steatocystoma and frequently in dermoid cysts.

This group of lesions can present significant diagnostic challenges in: the recognition of sebaceous differentiation; the separation of sebaceous differentiation from mimics characterised by a vacuolated or clear cell appearance; and the separation of some entities within the sebaceous group. Importantly, sebaceous neoplasms can be an important clue to the recognition of Muir–Torre syndrome.

EMBRYOLOGY AND NORMAL ANATOMY

The sebaceous glands are holocrine glands and develop from an epithelial bud arising from the outer root sheath of embryological hair follicles at approximately 13–15 weeks gestation.[1] They can normally be found at all cutaneous locations, apart from the palms and soles, and are most numerous on the face and scalp. As their origin suggests, they are usually seen in association with hair follicles. Exceptions to this rule include sebaceous glands on the buccal mucosa and lip vermillion (Fordyce's spots), areolae (Montgomery's tubercles), glans penis (Tyson's glands), labia minora and the eyelids (Meibomian glands).

Sebaceous glands are lobulated structures encased by a thin fibrous capsule. At the periphery of these lobules one can discern a layer of germinative cells, with relatively large nuclei, prominent nucleoli and basophilic cytoplasm without vacuolation. The more differentiated, centrally located cells (sebocytes) have a characteristic vacuolated cytoplasm, with a small central nucleus which demonstrates scalloping due to compression by the numerous lipid vacuoles. Centrally these cells disintegrate and discharge the resulting mix of lipid and cellular debris (sebum) into the excretory duct. This duct is lined by keratinising squamous epithelium with a finely crenelated surface and opens into the hair follicle at the base of the infundibulum. Several sebaceous lobules typically share the same excretory duct. The presence of cells resembling mature sebocytes is the major morphological feature used to identify sebaceous differentiation. However, in the setting of neoplastic lesions, sebocytes can show differing morphologies to those seen in the normal sebaceous glands. Examples include cells with granular eosinophilic cytoplasm, cleared cytoplasm or signet ring forms.[2]

Development and activation of the sebaceous glands is dependent on androgens, and the effect of transplacental maternal androgens results in relatively well-developed glands being present in the newborn. *In utero*, they contribute to the vernix caseosa, a protective layer over the developing skin which is comprised of a mixture of fetal sebaceous secretions, shed epithelial cells and lanugo hairs.[3] However, after birth the level of androgens decreases and the sebaceous glands undergo atrophy. The immature sebaceous glands which result from this process are known as the mantle, a structure which may be visualised on histological sections as cords of epithelial cells arising from either side of a hair follicle.[2] Sebaceous glands enlarge again in puberty under the influence of increased androgens, and they tend to be larger and more active in males for the same reason. In this context, it is unsurprising that sebaceous neoplasms are very rare in children and uncommon in adolescence.[4]

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SEBACEOUS HYPERPLASIA

Circumscribed sebaceous hyperplasia is a common lesion, and can be identified in approximately 1 in 4 older adults.[5,6] The classical clinical presentation is of solitary or multiple skin coloured to yellow papules, typically occurring on the face (particularly the forehead). There is frequently central umbilication, corresponding to a patulous follicular infundibulum. Transient sebaceous hyperplasia, which presents as small papules on the face, can be identified in up to nearly 50% of full-term neonates as a result of exposure to maternal hormones.[7,8] Other clinical scenarios include lesions in rows in the juxtaclavicular area (juxtaclavicular beaded lines),[9] presentation in a linear arrangement elsewhere,[10–13] presentation with a diffuse distribution,[14] formation of large masses,[15] anogenital involvement,[16] and presentation in younger individuals with familial disease.[17] Sebaceous hyperplasia can also be seen as a side effect of treatment with cyclosporine in the setting of organ transplantation[18,19] and has been reported in association with antiretroviral treatment of HIV.[20]

In sebaceous hyperplasia the sebaceous glands are increased in size and number, but retain a normal structure (Fig. 1A,C). The lobules are typically attached to a central hair follicle, which may be dilated. A criterion of four or more sebaceous lobules attached to a single hair follicle has been suggested as an arbitrary diagnostic point.[21] Distinction from sebaceous adenoma is based on an increase in the number of germinative cells in adenoma (Fig. 1C,D), in some cases with sebocytes displaying eosinophilic cytoplasm or architectural abnormalities, including replacement of the follicular epithelium with sebaceous elements.[2] The presence of overlying epithelial proliferation, somewhat resembling seborrhoeic keratosis, has been proposed as a diagnostic clue for the recognition of underlying sebaceous hyperplasia in superficial biopsy samples.[22]

SEBACEOUS ADENOMA

Sebaceous adenoma is a benign neoplasm, typically present as solitary or multiple nodules which may be tan, skin-coloured, pink or yellow in colouration. Most lesions are less than 1 cm in size, although rare examples measuring 5 cm or more have been documented.[23] They are usually asymptomatic and slow growing.

Histologically these lesions are multilobulated and architecturally recapitulate the organisation of the normal sebaceous gland, with centrally located sebocytes surrounded by germinative cells (Fig. 1B,D). They usually demonstrate an attachment to the epidermis or follicular infundibulum.[2,23] Indeed, the sebaceous cells may focally replace the keratinocytes in the region of these attachments. The lesions may be polypoid and occasional examples may be pedunculated.[23] The lobules maintain a circumscribed outline and show a 'pushing' relationship with the surrounding dermis. Stromal-stromal clefting may also be a feature. The lobules may vary in size and shape, but the lesions are generally relatively symmetrical. The progression of germinative cells at the periphery of the lobules to mature sebocytes in the central portions is maintained, although in this neoplastic lesion it

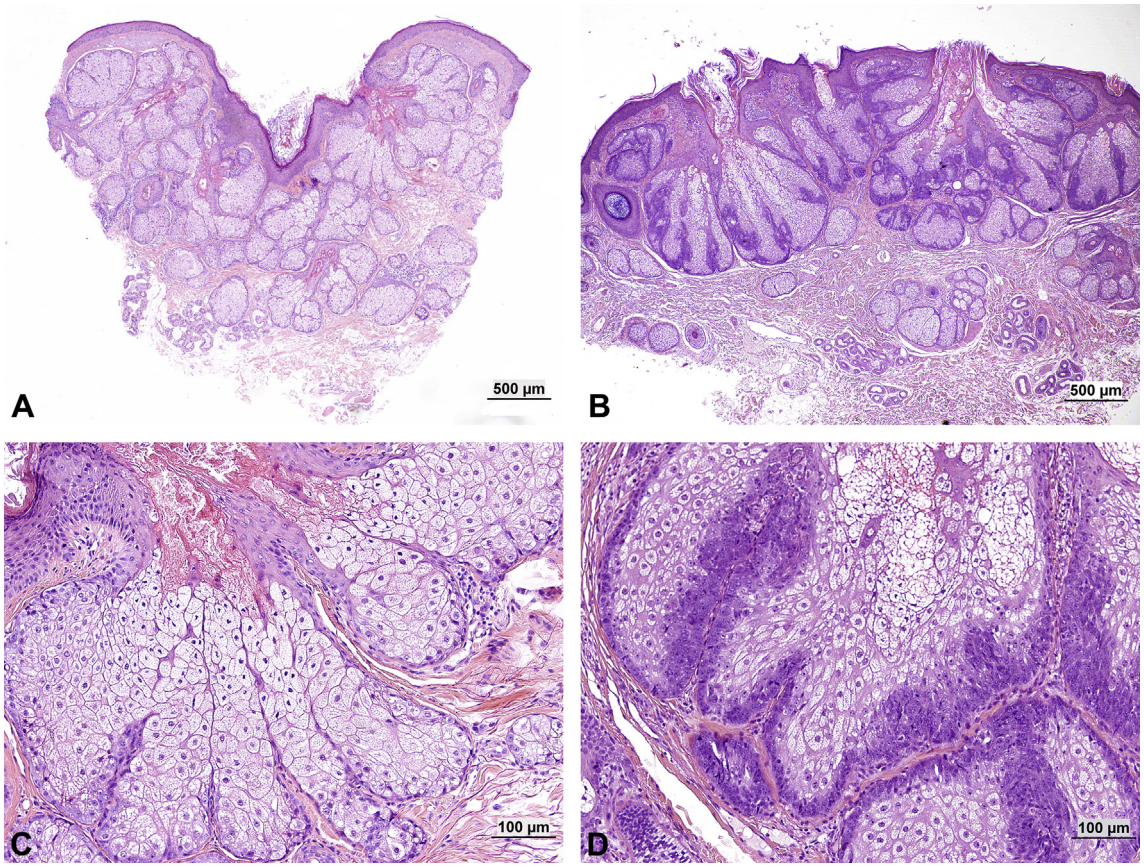

Fig. 1 (A,C) A comparison of sebaceous hyperplasia with (B,D) sebaceous adenoma (H&E). Both lesions show a similar architecture, but sebaceous adenomas are characterised by greater numbers of germinative cells and a population of less than fully mature sebocytes.

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