Benign skin lesions – Part 3
Vascular, dermal and adnexal tumours

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This month we conclude a three-part article on benign skin 'lumps and bumps' that may be encountered in general practice. Part 3 focuses on vascular, dermal and adnexal tumours.

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This short series of articles covers a range of benign skin lesions, some very common and others seen only occasionally, with a focus on aetiology, issues of clinical significance, and management. This, the final instalment in the three-part series, discusses a range of vascular, dermal and adnexal tumours.

HAEMANGIOMA

The most common haemangiomas are 'cherry haemangiomas' or Campbell de Morgan spots (Figure 1), which increase in prevalence with age. Most people over 60 years of age have at least one haemangioma and it is common to have a moderate to large number. They may multiply during pregnancy.

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Appearance

Haemangiomas are tiny to medium in size (up to 5 mm) and appear as bright red or crimson macular dots to papules. They can be polypoid and occasionally bleed with trauma (Figures 2 and 3). Occasionally a haemangioma may thrombose and turn a dark, almost black-crimson colour and be mistaken for a melanoma. A crimson hue under the dermoscope is a helpful clue that the lesion is benign – as long as other features of melanoma are lacking.

Points of interest

If haemangiomas are eruptive, the rare POEMS syndrome should be considered. This is a plasma cell dyscrasia with multiple features (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes). Common skin features are diffuse hyperpigmentation, lower limb oedema, hypertrichosis, sclerodermoid skin thickening and eruptive cherry angiomas, often in association with glomeruloid haemangiomas.

Treatment

Haemangiomas are generally of cosmetic concern only and the lesions are usually left alone. If desired, they can be removed with electrosurgery, shave excision or excision, or by destructive or vascular lasers.

PYOGENIC GRANULOMA

Pyogenic granuloma is a poorly named tumour because it is not caused by infection and the pathology is not granulomatous. It is better called a lobular capillary haemangioma, and may be a form of reactive neovascularisation. It occurs most commonly in children and young adults.

Appearance

Pyogenic granuloma is a solitary red papule or polypoid nodule. It grows fairly rapidly, over weeks to a few months, to usually less than 1 cm (sometimes up to 2 cm), then stabilises in size. There is often a thin colarette of soggy keratinous skin around the base (Figure 4). It can persist indefinitely if not removed.

About one-third of pyogenic granulomas develop after minor trauma. They most commonly occur on the hands, feet or digits, but also on the gingivae (particularly during pregnancy), lips, tongue or face. The lesions are friable, bleed easily, and are prone to ulceration.

Points of interest

The cause of pyogenic granuloma often cannot be identified. Occasionally, the lesions develop while a patient is taking systemic retinoids (isotretinoin or acetretin) or, less often, indinavir and anti-EGFR therapies.

There is a disseminated eruptive form that occurs rarely.

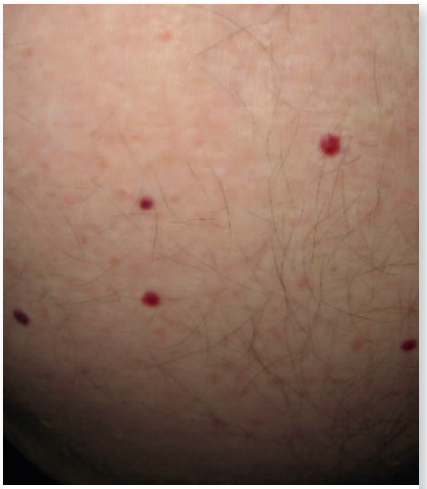

Figure 1. Campbell de Morgan spots on a man's back.

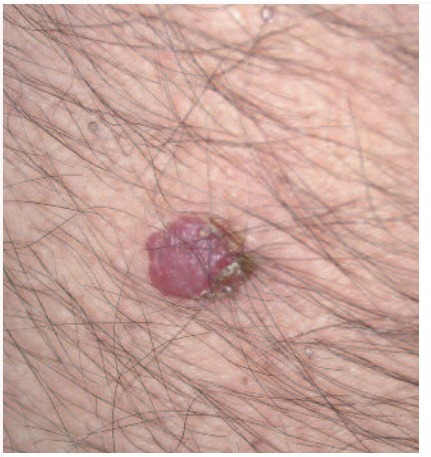

Figure 2. Haemangioma with some crusting after minor trauma on the abdomen.

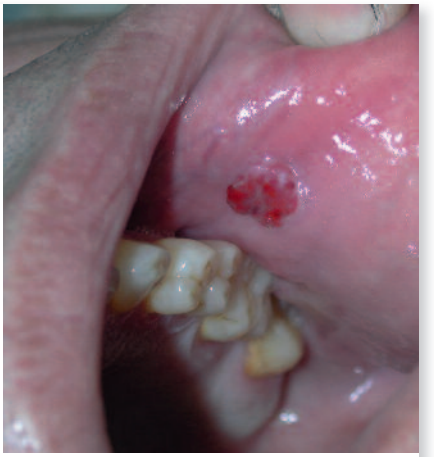

Figure 3. Haemangioma on the buccal mucosa. The lesion was prone to bleeding from biting so was excised.

Treatment

If possible a pyogenic granuloma should be excised and the skin edges sutured but this can be difficult on a distal digit or certain other sites. On awkward sites, lesions can be excised and the defect closed with a small, full-thickness skin graft or left to heal by secondary intention. The lesions can also be removed with shave excision or electrosurgery, but they are more likely to recur if these latter methods are used because the wounds heal via granulation. Multiple satellite lesions occasionally develop in this situation. It is vital that the tumour be sent for histopathology because occasionally malig - nancies such as amelanotic melanoma present like a pyogenic granuloma.

Other treatments that may be effective are cryotherapy, laser ablation, repeated applications of silver nitrate, 5% imiquimod cream applied daily under occlusion, sclerotherapy or tight strangling of the base of a polypoid lesion with an absorbable suture. Biopsy is recommended before trying these methods.

JUVENILE XANTHOGRANULOMA

Juvenile xanthogranuloma (JXG) is a benign tumour of differentiated histiocytic cells (of monocyte–macrophage lineage). Histopathology shows a mixed cellular dermal infiltrate dominated by histiocytes, lymphocytes and eosinophils, often with giant cells with a wreath-like arrangement of nuclei (Touton giant cells). Later, foamy lipid-laden histiocytes appear, which correlate with the typical yellow hue of JXG.

Immunohistochemistry suggests that JXGs arise from dermal dendrocytes. Most appear in infancy (half by 6 months of age) or early childhood. They appear suddenly, then spontaneously regress months to years later. Resolution is marked by gradual replacement by fibrous tissue. Their cause is unknown. There is no link between JXG and dyslipidaemias.

Appearance

JXGs appear as asymptomatic, small red-yellow papulonodules with an orange hue (Figure 5). Later they become a little more brown. There may be one lesion or a few, and they are usually between 3 and 6 mm in size but can be larger. Resolution may leave small atrophic scars.

JXGs are usually seen on the face, neck, scalp or upper trunk, but can occur anywhere, including on the oral mucosa. Ocular JXGs can affect any part of the eye, but most often the iris or other parts of the uveal tract.

More aggressive, deep dermal JXGs, occur rarely and may infiltrate skeletal muscle. There are occasional reports of disseminated JXGs in a variety of internal organs; this presentation is sometimes fatal.

Treatment

JXGs are mainly of cosmetic concern, but a patient with a cutaneous lesion should be assessed by an ophthalmologist for ocular JXG because around 50% of

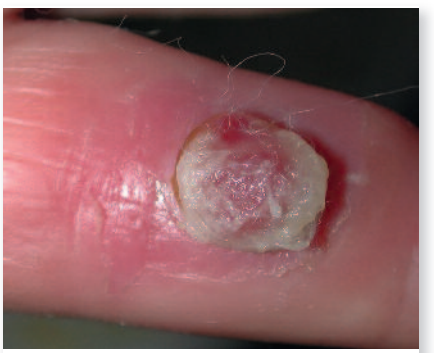

Figure 4. Pyogenic granuloma. Note the typical marginal colarette.

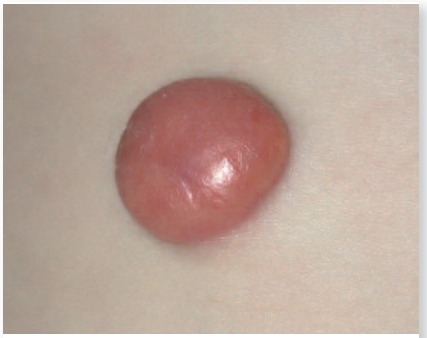

Figure 5. Solitary prominent juvenile xanthogranuloma (JXG) on the abdomen of a 21-month-old girl. Ophthalmological examination was normal. This type of lesion is often not as prominent as shown here. The brown, slightly yellow colour and the patient's age are important clues to the diagnosis.

individuals with ocular lesions have skin lesions, and up to 10% with cutaneous lesions have ocular lesions. Ocular JXG is the most common cause of spontaneous hyphema in children and can result in secondary glaucoma and eventual blindness. The cutaneous lesions are usually not treated because they resolve spontaneously.

DERMATOFIBROMA

A dermatofibroma (DF) is a common benign tumour of fibroblast origin. Immunohistochemistry shows the cells have some features of dermal dendrocytes or myofibroblasts so their histogenesis may vary. DFs are also called fibrous histiocytoma.

Appearance

DFs usually occur on the trunk and limbs. On first viewing, they look like small flat to nodular moles (Figure 6). They are usually asymptomatic but are occasionally sore. DFs are usually smaller than 8 mm but are occasionally larger. They appear as light brown or red-brown papules to nodules with a firm rubbery consistency. The colour is often more at the periphery.

Lateral pressure causes DFs to indent into the skin. They can be almost flat and occasionally depressed. They occur on the limbs more often than on the trunk and are usually solitary or few in number. Uncommon variants include:

- cellular DF (5% of lesions, Figure 7); this lesion is larger than a normal DF and more likely to recur if excised
- aneurysmal DF, which clinically mimics a vascular tumour and can be rapid growing and quite large; the lesion is also more likely to recur if excised
- deep DF, a rare form that grows entirely in the subcutaneous tissue, deeper soft tissue or exceptionally in organs
- histological variants, including types with atypical cells that can lead to misdiagnosis or with more epithelioid histiocyte-like cells.

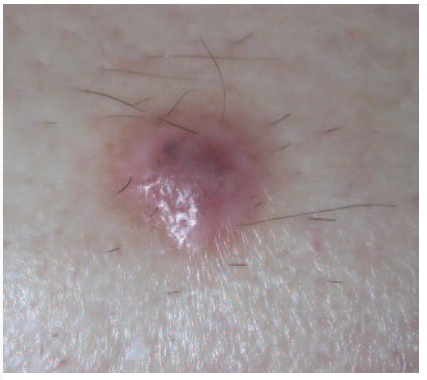

Figure 6. Typical red-brown dermato - fibroma (DF) on the shin.

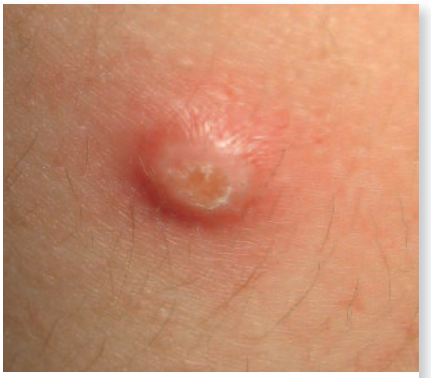

Figure 7. Likely cellular type dermato - fibroma (DF) on the arm. It was not excised.

Points of interest

The cause of DF is unknown. For years it has been suggested that a DF can arise as a result of an insect bite or local skin trauma, but this is based on flimsy evidence. DFs are clinically and histologically distinct from keloids or hypertrophic scars. The presence of multiple DFs (more than five) is occasionally a pointer to lupus erythematosus or immunosuppression, including HIV infection.

Treatment

Generally, DFs are not excised because the resultant scar is prone to becoming unsightly, spreading and sometimes hypertrophic. If a DF is troublesome (for instance, by being repeatedly cut during shaving), shave excision (partial or complete) can be performed to flatten it, but the scar will still be unsightly and the DF prone to recur. If excised, a larger lesion needs a somewhat wider margin to minimise the risk of recurrence.

FIBROUS PAPULE

Fibrous papule is a form of angiofibroma. It is of fibroblast or dermal dendrocyte origin.

Appearance

Fibrous papules appear mainly on the face, often on or around the nose. They may be solitary or few in number (Figure 8). The lesions are firm, small papules, which are red and occasionally lightly pigmented. There will sometimes be telangiectatic vessels on the papule or nearby.

Points of interest

Fibrous papules are of cosmetic significance only. They may be confused with a papular mole or a basal cell carcinoma (BCC). Other forms of angiofibromas are

'pearly penile papules' and the multiple angiofibromas of the face (Figure 9). The latter are a feature of tuberous sclerosis (where they were previously and incorrectly named 'adenoma sebaceum') and multiple endocrine neoplasia type 1 (which features endocrine tumors, particularly of the parathyroid gland but also gastrinomas, insulinomas, prolactinomas, and carcinoid tumours).

Treatment

Fibrous papules are easily removed with electrosurgery, shave excision, formal excision-punch excision or, if available, destructive laser. However, the appearance of the resultant scar needs to be considered.

FORDYCE SPOTS

Fordyce spots are ectopic sebaceous glands found in skin that normally lacks hair follicles (usually sebaceous glands are part of a hair follicle). They are extremely common. It is probable that 80% of the elderly population has at least a few of them.

Appearance

Fordyce spots appear as multiple, slightly yellow, small grains just under the epidermis. They occur on the vermillion of the lips (Figure 10), oral mucosa (labial or buccal, particularly inside the commissures and sometimes in the retromolar regions), the distal penis (mainly the foreskin) and the labia minora.

Treatment

Fordyce spots are of cosmetic significance only, and patients are usually happy to be reassured they are safe and, if located on the genitals, not sexually transmitted. The spots can be physically destroyed with light diathermy or destructive laser, if desired.

SEBACEOUS HYPERPLASIA

Sebaceous hyperplasia is a common benign condition that affects adults from middle age and becomes more common with age. It is more common in organ transplant recipients.[1] Sebaceous hyperplasia may be related to cyclosporin therapy (which often causes hypertrichosis), but it does not seem to be associated with other immunosuppressive drugs. The condition is not premalignant and is not a part of the Muir–Torre syndrome (see below).

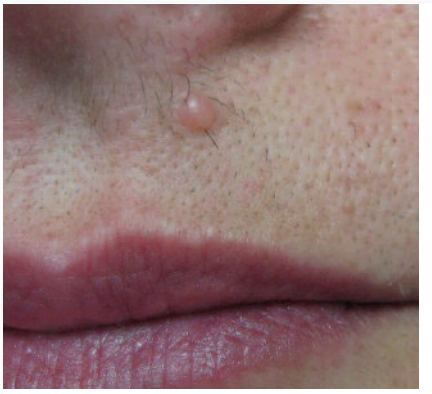

Figure 8. Fibrous papule on a woman's face.

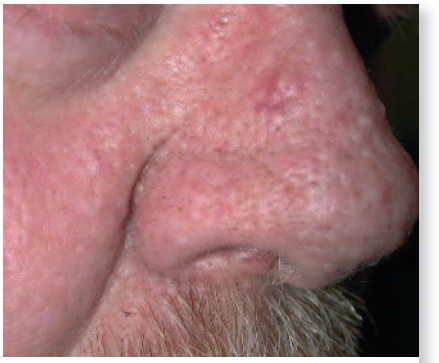

Figure 9. Angiofibromas on the nose and medial cheek in an epileptic man with tuberous sclerosis.

Appearance

Sebaceous hyperplasia appears as a single papule or (more commonly) multiple flesh-coloured papules with a yellowish tinge. They are 1 to 4 mm in size, usually with a small central umbilication. The papules are generally 1 to 4 mm in size. There may be the occasional telangiectatic vessel visible so a papule can be mistaken for a BCC. Dermoscopy is helpful, showing small yellow ovaloid globules radially around the central punctum.

Sebaceous hyperplasia occurs mainly on the face – commonly on the cheeks, temples, forehead (Figure 11) and nose. Uncommonly, it may be seen on other areas, such as the chest, areola, genitalia or mouth. Papules tend to continue to gradually appear. Rarely, many diffuse small papules occur on the face, neck and upper chest, which can give the whole area a yellow hue.

Treatment

Sebaceous hyperplasia can safely be left alone. If desired, the lesions are easily destroyed with light diathermy under

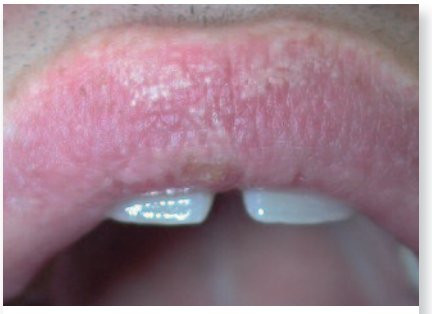

Figure 10. Fairly subtle Fordyce spots on the upper lip of a teenage boy.

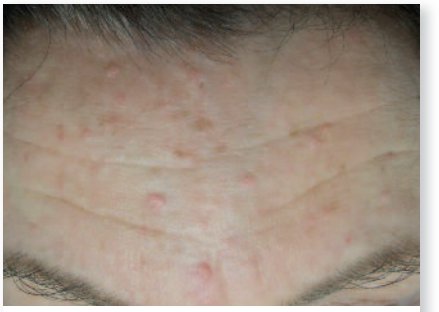

Figure 11. Sebaceous hyperplasia on the forehead.

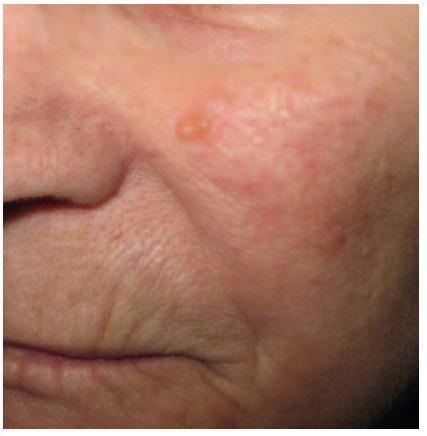

Figure 12. Solitary sebaceous adenoma. This patient had no other features of Muir–Torre syndrome.

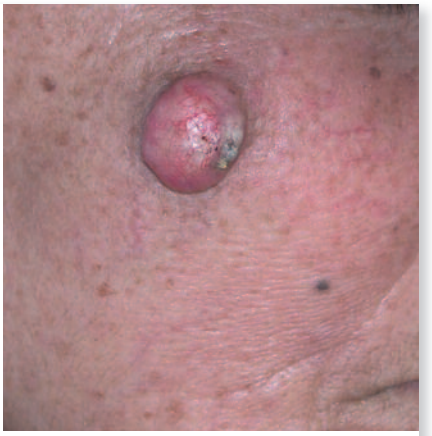

Figure 13. Sebaceous carcinoma on the cheek. This patient had no other features of Muir–Torre syndrome.

local anaesthetic or EMLA (lignocaine/prilocaine cream); it is wise to perform a test treatment to see if unsightly post-inflammatory hypo- or hyperpigmentation occurs, particularly in people with darker skin. This treatment will leave small burn-like scars, but often the cosmetic result is good. Sebaceous hyperplasia can also be destroyed by destructive lasers and, less reliably, by cryotherapy or chemical peels.

In patients with many papules, oral isotretinoin will clear many lesions – at least temporarily. This can be used as an alternative to multiple biopsies if BCCs need to be excluded (for example, in a transplant recipient with sun-damaged skin).

SEBACEOUS ADENOMA AND EPITHELIOMA

Sebaceous adenoma and epithelioma (sebaceoma) are uncommon, clinically similar, benign tumours with distinct but overlapping histopathology. They feature incompletely differentiated sebaceous cells of varying degrees of maturity. Their cause is unknown and, despite their location on sun-exposed sites, they are not known to be caused by sun exposure or other carcinogens.

Appearance

These are slow-growing, generally solitary, dome-shaped nodules, usually less than 1 cm in size (Figure 12). Older lesions may form a plaque or ulcerate. They are flesh-coloured to red, often with a slight yellow hue, and most commonly occur on the face or scalp. Occasionally, they are pedunculated. They are easily mistaken for a BCC or squamous cell carcinoma.

Points of interest

Sebaceous adenoma and epithelioma are not known to be premalignant; however, sebaceous carcinoma is a well recognised entity (Figure 13). Sebaceous carcinoma may arise from normal skin sebaceous glands, the Meibomian glands and glands of Zeis of the eyelid or a naevus sebaceous (an epidermal hamartoma with sebaceous elements occurring in a naevoid distribution often on the head and neck), and has significant metastatic potential.

The presence of any sebaceous neoplasm apart from sebaceous hyperplasia or naevus sebaceous raises the possibility of the rare Muir–Torre syndrome (MTS), which is the cause of multiple types of internal and skin malignancies. MTS is a rare subset (1 to 2% of cases) of the hereditary nonpolyposis colorectal carcinoma (Lynch type II) syndrome.[2,3] MTS is defined as the presence of benign or malignant sebaceous neoplasms and at least one internal malignancy. Less often seen is keratoacanthoma, typically showing a degree of sebaceous differentiation. The internal malignancies are particularly colorectal and gynaecological (especially endometrial or ovarian); less common are malignancies of the small bowel, stomach, upper gastrointestinal tract, hepatobiliary system, breast, renal pelvis, bladder, lymphomas, CNS and others. These internal malignancies tend to occur at younger than expected ages. The cutaneous neoplasm may precede or follow the internal malignancy by many years.

Hereditary nonpolyposis colorectal carcinoma syndrome is an autosomal dominant inherited germline mutation in one of the DNA mismatch repair genes – in MTS, most commonly *MSH-2* and, less commonly, *MSH-6* or *MLH-1*. The primary human DNA polymerase is quite error prone, and DNA mismatch repair gene proteins increase the accuracy of DNA replication 100- to 1000-fold. Loss of expression of these repair proteins can be demonstrated by immunohistochemical methods on routine biopsy or excision tissue. If this is found, it is putative evidence of MTS and the patient should be referred, preferably to a genetic cancer specialist, for full evaluation.

Treatment

Clinical points of significance are discussed above. Apart from these, sebaceous adenoma and epithelioma are of cosmetic significance only. Their malignant potential is unknown. They should be excised with a narrow margin, with lesions located on an eyelid being removed by an oculoplastic surgeon.

TRICHOEPITHELIOMA AND TRICHOBLASTOMA

Pathologists argue about the degree of relatedness of these uncommon tumours of hair follicle origin. Histopathology

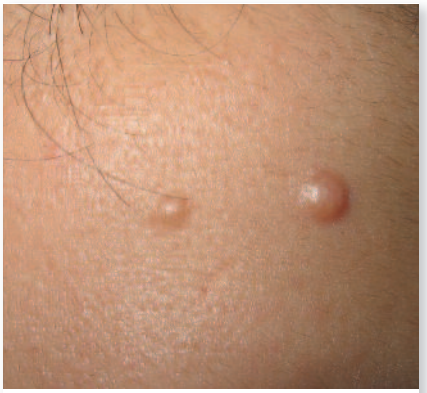

Figure 14. Trichoepitheliomas on the forehead in a young woman.

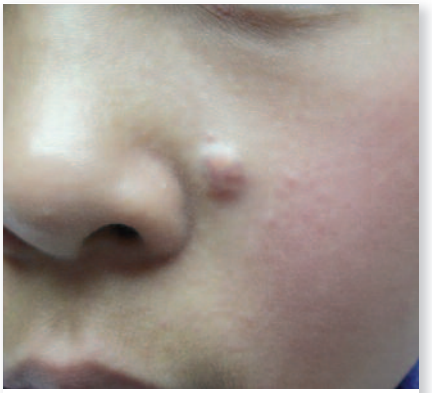

Figure 15. Pilomatricoma in an 11-year-old boy.

shows that trichoblastomas lack the keratinising cysts seen in trichoepitheliomas and have a more prominent mesenchymal component (with the amount depending on the subtype). Desmoplastic trichoepitheliomas have a densely collagenous stroma. All these tumours have some pathological similarities to BCCs, but they are benign.

Appearance

Trichoblastomas are usually solitary, flesh-coloured nodules about 1 cm in size. They are typically located on the head and neck, and particularly on the scalp.

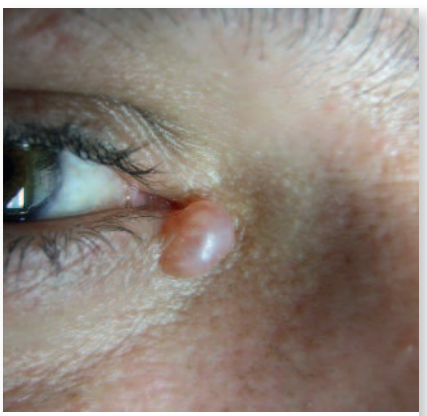

Figure 16. Apocrine hidrocystoma in a middle-aged man, which was excised by an oculoplastic surgeon.

Trichoepitheliomas, which are more common than trichoblastomas, are solitary or multiple flesh-coloured nodules, usually less than 1 cm in size (Figure 14). They occur mainly on the face, particularly on or near the nose.

Desmoplastic trichoepitheliomas, which are very uncommon, are usually solitary, firm, small, flesh-coloured nodules or plaques, often with a central indentation. They usually occur on the face.

Giant trichoepitheliomas are a more rapidly growing nodule, often pedunculated, several centimetres in size. They often appear on the lower trunk, particularly the perianal area. These tumours are very uncommon.

Points of interest

The malignant potential of these tumours is very low. Solitary trichoepitheliomas are usually sporadic. Multiple trichoepitheliomas occur in a number of settings: sporadic; as a sole entity, inherited (autosomal dominant) and mapped to chromosome 9;[4] or as part of the Brooke–Spiegler syndrome, inherited (autosomal dominant) and due to mutations of the *CYLD* oncogene on chromosome 16.[5] In Brooke–Spiegler syndrome, there are various combinations of multiple trichoepitheliomas and two other adnexal tumours – cylindroma and spiradenoma (both of uncertain histogenesis, probably of hair or sweat gland origin). Patients may develop other tumours, including BCCs and benign or malignant salivary gland tumours.

Trichoblastomas are the most common tumours to develop in naevus sebaceous; previously, many of these were erroneously labelled BCCs.

Treatment

Solitary trichoepitheliomas and trichoblastomas are best treated by excision. This may not be practical for multiple trichoepitheliomas – if excision is to be undertaken, the patient will need to be advised about the likely continuing occurrence of new lesions (as well as about surgical morbidity).

Multiple trichoepitheliomas can be flattened with shave excision, diathermy, laser ablation or dermabrasion, but the recurrence rate is high and sometimes quite rapid. These procedures can be done repeatedly. Scarring is an issue.

PILOMATRICOMA

Pilomatricoma (pilomatrixoma), the most common hair follicle tumour, is a benign hamartoma of the hair matrix whose cells resemble those of the hair matrix, cortex and inner root sheath. Mimicking hair development, the cells in the tumour degenerate into 'shadow cells', which lack a nucleus. They often develop calcification, which is prone to inflammation. This or haematoma can cause rapid enlargement of the tumour. About half of the reported cases of pilomatricoma have occurred in people younger than 20 years (with 12% of cases in children aged 5 years or under), with a smaller peak in the 50- to 70-year-old age group. It is more common in females.[6]

Appearance

Pilomatricomas appear as solitary, skin-coloured to faint-blue nodules (Figure 15). Their size is between 0.5 and

3 cm (typically between 0.8 and 1.5 cm), but they can be much bigger. If calcified, the nodules have a firm to hard consistency and may show white-yellow flecks. The calcium may cause redness or soreness from inflammation and occasionally perforates the surface. Most nodules are located on the head, neck or upper extremities, particularly the face.

Pilomatricomas grow at a variable rate, from slowly to moderately quickly. They are often mistaken for epidermoid cysts.

A very uncommon variant is pilomatricoma with anetoderma (loss of surrounding elastic tissue), which causes a firm nodule in soft baggy skin. Multiple pilomatricomas are quite uncommon.

Points of interest

It has been shown that many pilomatricomas and some other adnexal neoplasms carry beta-catenin gene mutations; these mutations influence cell differentiation and proliferation.[7] Most tumours are sporadic, but patients with multiple pilomatricomas may have other genetic conditions, including myotonic dystrophy, Turner's syndrome and familial adenomatous polyposis (Gardner syndrome).

Treatment

Although malignant transformation in a pilomatricoma is very rare, these lesions are generally excised.

HIDROCYSTOMA

Hidrocystoma (apocrine or eccrine) is a sweat-filled cystic tumour distinguished histologically, the apocrine form being quite common and the eccrine form rare. It is mainly seen in adulthood, at any age.

Appearance

Hidrocystomas appear as smooth-surfaced, translucent papulonodules with a well-defined dome-shape (Figure 16). They are asymptomatic and usually flesh-coloured, but some have a blue-grey or even blue-black tinge (the pigmentation may affect only part of the cyst). The translucent appearance means that these lesions are easily mistaken for BCCs. They increase in size slowly, but most are small. They most often occur on the eyelids or nearby; occasionally they are located off the face. Eccrine hidrocystomas may enlarge if the patient becomes overheated.

Hidrocystomas are generally solitary, but occasionally multiple hidrocystomas occur. Multiple lesions may be seen in the very rare Schöpf–Schulz–Passarge syndrome, a form of ectodermal dysplasia featuring hypotrichosis, hypodontia, nail dystrophy, palmoplantar keratoderma and apocrine hidrocystomas.

Treatment

Hidrocystomas should be treated by excision. If a lesion is located close to the eyelid margin then it is best removed by an oculoplastic surgeon.

CONCLUDING COMMENTS

In this series, I have tried to cover the more common, or more important, of a myriad of benign skin lesions. By necessity, these articles are not comprehensive. The importance of these benign skin lesions lies in distinguishing them from skin malignancies. It is also important to consider the appearance of a benign skin lesion and a patient's desire to have a lesion removed. For some lesions, determining malignant potential or association with other conditions is also important. MT

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FURTHER READING

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COMPETING INTERESTS: None.