Spitz tumours

Alan T Evans

Abstract

The traditional dichotomous classification of Spitz naevus versus Spitzoid melanoma is challenged by a group of lesions that deviates from the prototypic Spitz naevus; these lesions (Spitzoid tumours of uncertain malignant potential [STUMP]) remain difficult to define using objective criteria. Clinical series and comparative molecular genetic studies support the concept that Spitzoid lesions form a family of melanocytic tumours distinct from ordinary naevi and common types of melanoma. A bipolar classification of naevus versus melanoma does not readily accommodate the recognized diverse spectrum of pathological features and behaviour observed in Spitz lesions and it has been proposed that they be viewed as part of a continuum with significant modification of the current terminology. These proposals remain controversial.

Keywords classification; pathological features; spitz naevus; spitzoid melanoma; spitz tumour of uncertain malignant potential (STUMP)

Introduction

In 1948 Sophie Spitz described a group of melanocytic lesions in childhood that shared many histological features with adult melanomas but were generally associated with a benign course.[1] Spitz labelled these lesions 'juvenile melanoma'. This term was eventually replaced with the eponymous label Spitz naevus or the more descriptive title of naevus of large spindle and/or epithelioid melanocytes. It is worth noting from the title of her paper, 'Melanomas of childhood', that Spitz did not equate these lesions as a variant of benign naevus but as a special subtype of melanoma. Indeed, one 12-year-old female in Spitz's original series of 13 cases succumbed to metastatic disease, effectively encapsulating the recurring difficulty for the modern pathologist in reliably distinguishing Spitz naevus from Spitzoid melanoma. In recent years the introduction of a category of Spitz tumours possessing atypical features that are considered to imply indeterminate (but potentially aggressive) biological potential has lead to further problems for the pathologist and clinician. Currently, we are in the position of trying accurately to categorize a generally benign melanocytic tumour (the Spitz naevus) that mimics the histological features of melanoma in the knowledge that this entity itself has a potentially lethal malignant mimic (Spitzoid melanoma). It is not surprising that pathologists approach the diagnosis of Spitz tumours with trepidation.

Misdiagnosis of Spitzoid lesions is a recognized problem. Underdiagnosis of melanoma as Spitz naevus is revealed when metastatic disease ensues – a problem well documented by medical insurers.[2] Statistics detailing overdiagnosis of Spitz naevus as an atypical Spitz tumour, Spitzoid melanoma or conventional melanoma are more elusive although in one study, 6.5% of all new melanomas referred to a regional melanoma service in Australia proved, after review, to be Spitz naevi.[3]

Pathologists prefer to use robust reproducible criteria to compartmentalize diseases into well-defined groups with the aim of facilitating the correct treatment and prognosis. Spitz lesions challenge this ideal; very rarely lesions diagnosed confidently by a panel of experts as a Spitz naevus prove fatal,[4] whilst a significant proportion of Spitzoid melanomas have a favourable outcome. It may be more logical to view Spitz lesions as part of a continuum rather than as two or three distinct entities. Proposals that the conventional groupings of Spitz naevus, atypical Spitz naevus and Spitzoid melanoma are replaced by the term 'Spitz tumour', qualified by a stratified evaluation of the risk of metastasis,[5,6] will be discussed.

Spitz naevus

The conventional term 'Spitz naevus' will be used. This entity is synonymous with Spitz tumour, naevus of large spindle and/or epithelioid melanocytes, and also with the effete terms juvenile melanoma and benign juvenile melanoma.

Clinical features

Spitz naevi are not uncommon, accounting for some 1% of childhood naevi. Typically, they present as a solitary dome-shaped lesion on the head, neck or extremity.[7] Melanin pigment production varies and the presence of a rich stromal vasculature may result in misdiagnosis as a haemangioma. The reported age range is wide; in one study of 247 lesions, 66% of cases occurred in patients older than 20, although this high figure may reflect referral bias.[8] In adult females the leg is most commonly involved, whilst in adult males (over 40) the trunk is the most common site. Lesions on acral skin are rare. Occasional examples have been described on the oral labial mucosa,[9] the glans penis[10] and the tongue in association with pseudoepitheliomatous hyperplasia mimicking granular cell tumour.[11]

Lesions are generally solitary but rarely Spitz naevi occur in a grouped (agminate) form, in a zosteriform distribution or in an eruptive pattern when several hundred small papular lesions may develop.[12] Lesions are generally 5–6 mm in diameter and rarely exceed 10 mm. Ulceration of the epidermis may generate concern but in an otherwise typical lesion traumatic excoriation should be considered (especially in children with a lesion at an accessible site).

Early lesions showing junctional growth alone present as macules. Most lesions are compound tumours and present as papules, nodules, polyps or verrucose lesions. Some lesions (particularly in adulthood) may be largely intradermal, poorly pigmented and associated with desmoplastic stroma, thereby mimicking a dermatofibroma clinically and histologically.

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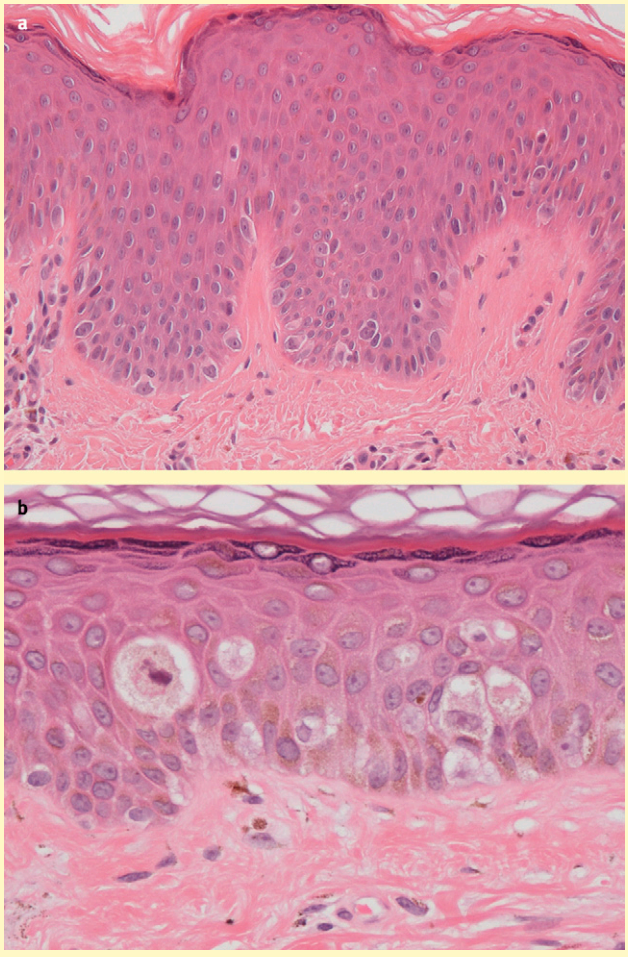
Histological features

Spitz naevi recapitulate the growth patterns of usual acquired naevi in that junctional, compound and intradermal variants are described.

Junctional (including pagetoid) Spitz naevus

Junctional Spitz naevi where the proliferation is confined to the epidermis are rare. These tumours present as a small (< 4 mm diameter) pigmented macule and the leg of young females is a favoured site. The lesion is characterized by large epithelioid cells (often with some retraction artefact) distributed in solitary units or small nests in the basal layer (Figure 1a). In some cases there is a tendency to pagetoid scatter, particularly within the lower half of the epidermis, and the designation pagetoid Spitz naevus is used (Figure 1b). This stage in the evolution of a Spitz naevus is important to recognize as it may mimic melanoma in situ; however, the clinical setting combined with the small size of the lesion, sharp peripheral circumscription, epidermal acanthosis and lack of marked cytonuclear atypia favour a diagnosis of Spitz naevus over melanoma.[13]



Junctional Spitz naevus. **a** An early junctional Spitz with plump epithelioid cells distributed singly within the basal epidermis. **b** This junctional lesion shows some variation in nuclear morphology and pagetoid scatter.

Figure 1

Compound Spitz naevus

Most Spitz naevi encountered in routine practice are compound lesions.

The epidermis in a Spitz naevus characteristically displays acanthosis and hyperkeratosis. Occasionally the epidermal proliferation is so florid that it constitutes pseudoepitheliomatous hyperplasia. In lesions where melanin pigment production is marked, there may be pigmented parakeratosis.

At scanning magnification the Spitz naevus generally appears symmetrical with sharp circumscription of the junctional component. These two features are often emphasized as strong indicators of benignity; although their presence gives reassurance, it is not so difficult to find examples of melanomas (of nodular, naevoid and indeed Spitzoid type) that display excellent side-to-side symmetry and abrupt circumscription. Similarly, the presence of some asymmetry with an untidy 'shouldered' junction does not always indicate malignancy; e.g. Spitz lesions at acral and near acral sites may have an untidy low power architecture.

The junctional component typically shows a nested growth pattern, although there may be short lentiginous runs of cells or foci where the cells are distributed singly in the basal layer. By definition the cells are of spindle and/or epithelioid type. The cells have vesicular nuclei often with a single large acidophilic nucleolus, although multiple nucleoli may be found. Most cells retain ample cytoplasm and, although the nuclei may appear worryingly enlarged, the overall nuclear:cytoplasmic ratio remains relatively low. Cytoplasmic nuclear pseudoinclusions are common and in childhood lesions there may be frequent naevus giant cells (including multinucleate forms), especially in the subepidermal zone – a feature stressed by Spitz.[1] In some Spitz naevi, marked cytonuclear pleomorphism may be apparent but this is generally focal and rarely as widely distributed as in melanoma (Figure 2a).

Junctional nests of spindle cells often show vertical alignment. Artefactual clefting (a processing artefact) around nests is commonplace and sometimes clefting may even be identified around single intraepidermal cells, reflecting shrinkage of their voluminous cytoplasm (Figure 2b). Transepidermal elimination of nested groups of melanocytes is generally observed in childhood lesions (Figure 2c). A degree of pagetoid epidermal invasion by single melanocytes (pagetoid melanocytosis) is not uncommon, particularly towards the centre of the lesion, but is generally focal and often limited to the lower half of the epithelium.[14,15] Pagetoid spread of melanocytes is reported to be more conspicuous in Spitz naevi at acral/near acral sites and in lesions subjected to trauma. Eosinophilic globules of basement membrane material (Kamino bodies) along the dermo-epidermal junction are common in Spitz naevi, where they often coalesce to form aggregates, but are also found in ordinary naevi and in 12% of melanomas (Figure 2d).[16,17]

The dermal component in a Spitz naevus characteristically shows a diminution in both nest and cell size from the top to the bottom of the lesion. Towards the base the nested architecture is progressively lost and cells (often resembling those of an ordinary naevus) ramify between the reticular dermal collagen (Figure 3a).[14] Ultrastructural studies reveal loss of organelles, indicating that the process is in fact atrophy rather than 'maturation'. This characteristic stratified pattern of reduction in nest size combined with cell atrophy may be highlighted by