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Spitz nevus (large spindle cell and/or epithelioid cell nevus)

Age-related involvement of the suprabasal epidermis

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Summary. The Spitz nevus (large spindle and/or epithelioid cell nevus) is a benign acquired melanocytic tumour found predominantly in children and adolescents. Depending on the architecture (junctional, compound, dermal) and cytology (predominance of spindle or epithelioid cells, or presence of both cell types) several variants have been distinguished. A histological feature occasionally leading to diagnostic difficulties is the involvement of the suprabasal epidermis. The present study details the occurrence of intraepidermal involvement (pagetoid spread, nesting of cells, trans-epidermal elimination) according to the age of the patients. 89 cases of Spitz nevus were reviewed. There were 19 compound Spitz nevi with evidence of epidermal involvement, 56 cases of compound Spitz nevi without evidence of epidermal involvement and 14 cases of dermal Spitz nevi. The epidermal involvement mainly consisted of nesting of nevus cells above the basal cell layer, 9 cases clearly showing evidence of transepidermal elimination of cell nests. Upward spread of single melanocytes (pagetoid spread) was minimal and always associated with nesting or trans-epidermal elimination. The mean age of patients was significantly lower in the group of compound nevi with intraepidermal involvement (7.16 ± 4.52 years), than in the group of compound nevi without epidermal involvement (13.18 ± 8.88 years). The age of the latter group was significantly lower than the group of pure intradermal nevi (30.14 ± 11.25 years). Thus, involvement of the suprabasal epidermis is not a feature of Spitz nevi in adults; in such a case the diagnosis of malignant melanoma should be considered.

Key words: Spitz nevi – Architectural patterns – Age distribution

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The great majority of common melanocytic nevi appear after birth. Between infancy and early adulthood – and especially during puberty – they increase in number progressively. Thereafter, their number decreases with age, only isolated nevi being found in the elderly (Mackie et al. 1985; Stegmaier 1959). These clinical observations are corroborated by the presumed biological evolution of the acquired common melanocytic nevi. The nevus cells first appear isolated and in nests at the tips of epidermal ridges, and constitute junctional nevi. The nevus then becomes a compound nevus by migration of cells into the dermis and finally an intradermal nevus when the junctional component is lost. The migration of nevus cells into the dermis is characterized by differentiation into a variety of patterns, which, in general, is characterized by increased fibrogenesis, leading to nesting of the cells and decreased melanogenesis. The intradermal nevus may also regress and eventually disappear.

A particular form of acquired nevus is the Spitz nevus, also known as benign juvenile melanoma or as large spindle and/or epithelioid cell nevus (Spitz, 1948). Clinically, this tumour is usually asymptomatic, dome shaped and rounded, pink, tan or reddish. Occasionally, the lesion may be brown, polypoid or verrucous, but is rarely ulcerated. They are found in children and adolescents primarily, and their incidence decreases decade by decade in older age groups.

Histologically (Allen and Spitz 1953; Weedon 1985), the Spitz nevus is composed of large spindle and/or epithelioid nevus cells arranged in elongated fascicles. The architecture of the lesion is symmetrical. Junctional, compound and intradermal forms are described, the compound form accounting for at least two third of the cases. At the dermoepidermal junction, the nevus cells pro-

liferate in nests and extend from their site of origin in a hyperplastic epidermis into an expanded papillary dermis, then into the reticular dermis and sometimes into the subcutaneous fat.

Within the papillary and the reticular dermis, the cells proliferate in fascicles and nests. In the deepest part of the lesion, the cells may spread from nests or fascicles and infiltrate as single cells or small aggregates. There is an increasing maturation of nevus cells from superficial to deep areas, but the degree of maturation is much less pronounced than in common acquired melanocytic nevi. The mitotic rate is variable, mitoses being usually confined to the upper part of the tumour. Two types of cells have been described: spindle cells and epithelioid cells. The spindle cells are elongated cells with oval vesicular nuclei, dark nuclear membranes and finely, evenly dispersed chromatin within the nuclear membranes. There are variable amounts of amphophilic or slightly basophilic cytoplasm which is not usually pigmented. The epithelioid cells are mostly round to polygonal and associated with a greater amount of cytoplasm than the spindle cells. The nuclear and cytoplasmic characteristics are essentially the same as in the spindle cells, although binucleated or multinucleated cells are frequent.

According to architectural and cytological criteria, Paniago-Pereira et al. (1978) distinguished several forms of Spitz nevi in a study of 200 cases:

A compound form with spindle cells predominanting (37.5%) a compound form with epithelioid cells predominanting (10%); a compound form with both spindle and epithelioid cells (18.5%); a dermal form with spindle cells predominanting (9.5%); a dermal form with epithelioid cells predominanting (9%); a dermal form with both spindle and epithelioid cells (6%); a junctional form with spindle cells predominanting (7%); and a junctional form with epithelioid cells predominanting (2%).

Among these forms there are rare miscellaneous types presenting special features; these have been described as desmoplastic, pyogenic granuloma-like, granulomatous, lichenoid or halo Spitz nevi.

Spitz nevi and malignant melanomas have many histological features in common (Allen and Spitz 1953; Paniago-Pereira et al. 1978; Peters and Goellner 1986). Among these is the invasion of the overlying epidermis by melanocytic cells. This feature has not yet been described in detail in Spitz nevi; we therefore investigated its incidence in the different age groups of patients with this nevus.

Material and method

We reviewed the histological slides from nevi diagnosed as Spitz nevi between 1950 and 1986 at the Dermatopathology Laboratory of the University, Department of Dermatology, Lausanne, Switzerland. Spitz nevi were diagnosed as such according to the well accepted criterias of Allen and Spitz 1953; Paniago-Pereira et al. 1978; Reed et al. 1975 and Weedon 1985. They are as follows:

Major criteria:

1) Cell type: spindle and/or epithelioid. We did not include those cases with a combination of one (or both) of these cell types and a significant number of common nevus cells – a so-called combined Spitz nevus (Fletcher and Sagabiel 1981; Rogers et al. 1984). Furthermore, we did not include the junctional form of Spitz nevus with large spindle cells. This type of nevus, being in general heavily pigmented, is best classified as pigmented spindle cell nevus (Reed et al. 1975). According to Reed et al. (1975) and Sagebiel et al. (1984), pigmented spindle cell nevus and Spitz nevus can be separated from each other because of their growth pattern and their capacity to form melanin pigment.

2) Symmetry. The lesion appears roughly triangular in shape, the tip in the dermis or hypodermis. The tumour has a sharp lateral demarcation of the junctional component, without horizontal extension of individual melanocytes.

3) There are or no single melanocytes above the epidermal basal cell layer (upward or pagetoid spread).

4) There is progressive maturation of nevus cells with depth.

5) Eosinophilic globules are seen (Arbuckle and Weedon 1982; Kamino et al. 1979). These globules are usually lacking in the pure junctional forms.

Other features of Spitz nevi include clefting between nests of cells and surrounding epidermis, superficial dermal edema and telangiectasia, presence of giant nevus cells; especially in the epithelioid cell variant. Loss of cellular cohesion, especially in the upper part of the lesion. Mitoses only occur in the upper half of the lesion; there is almost complete absence of atypical mitotic cells, absence of or minimal nuclear pleomorphism, a perivascular inflammatory infiltrate, rather than intra-lesional inflammatory infiltrate. A dense lympho-histocytic infiltrate invading the whole tumour without any other histological evidence of malignancy, was referred as an histological "halo phenomenon" ("halo-Spitz-nevus"). Finally single outlying cells in the deep dermal part of the nevus are also sometimes seen.

Nevi satisfying the first four major criteria were confirmed as Spitz nevi and assessed for their intraepidermal involvement, classified as upward spread of single melanocytes (pagetoid spread), nests of nevus cells above the epidermal basal cell layer (intraepidermal nesting). and transepidermal elimination of nevus cell nests.

The Student's *t*-test for small populations was used in analysis.

Results

Among the 109 cases reviewed, 89 were definitively interpreted as Spitz nevi. The other cases included 5 combined nevi, 9 pigmented spindle cell nevi and 6 malignant melanomas.

Of the 89 patients with Spitz nevi, 49 were females and 40 males (male to female ratio 0.84).

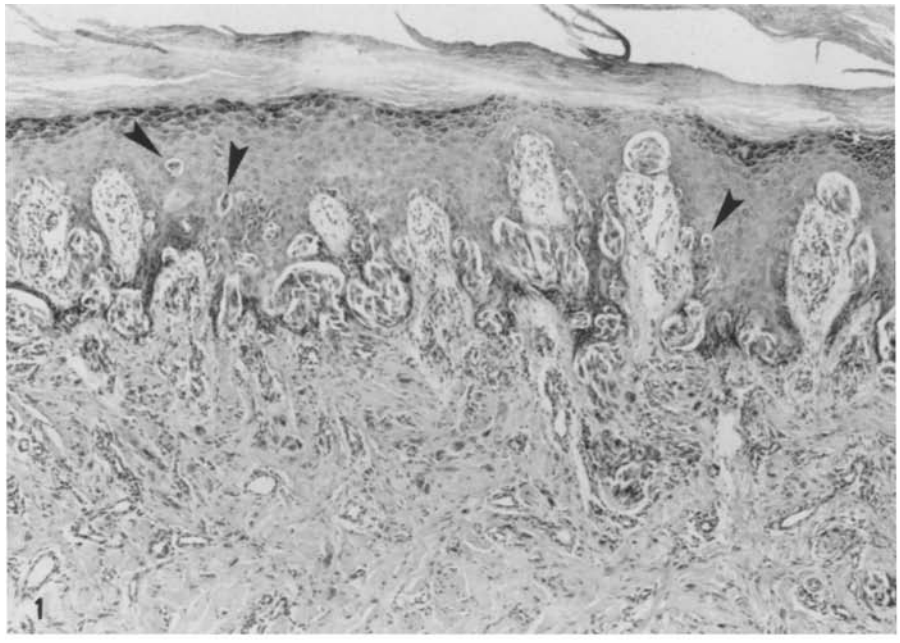

Fig. 1. Spitz nevus: suprabasal involvement of the epidermis

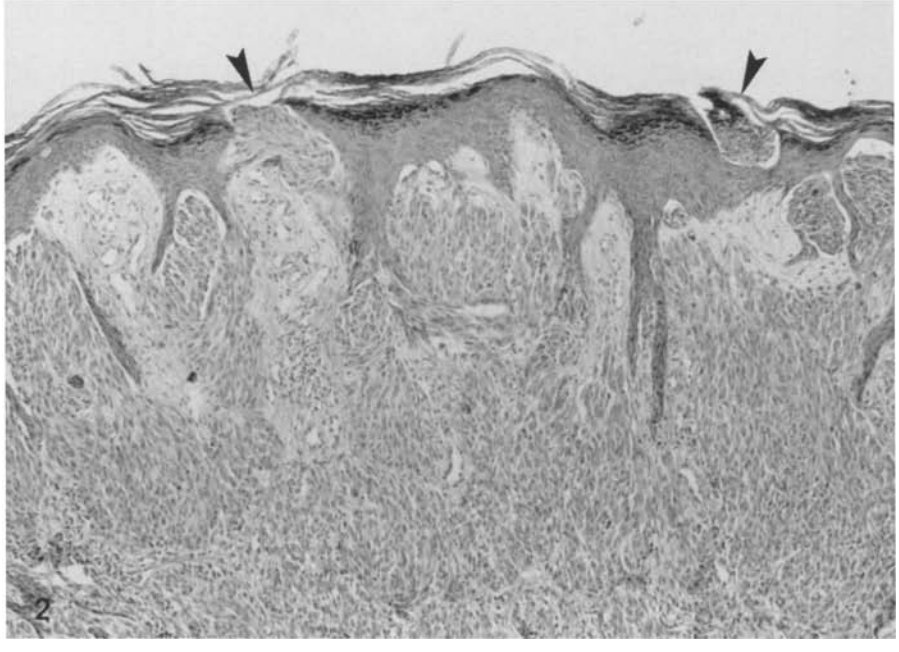

Fig. 2. Spitz nevus: transepidermal elimination of nevus cell nests

Their age ranged from 2 to 53 years (mean 14.56 ± 11.18). The distribution of 88 lesions was as follows: head and neck 42,0%, upper extremities 18.2%, trunk 12.5% and lower extremities 27.3%. Of the 89 cases, 75 (83.3%) were of the compound nevus type, among which 19 (21.1%) showed evidence of intraepidermal involvement and 14 (16.7%) of the pure dermal nevus type. As previously mentioned, we did not include the junctional nevi composed predominantly of spindle cells. No case of the rare junctional predominantly epithelioid cell type was observed. Nineteen cases showed evidence of intraepidermal involvement. There were 10 cases with small nevus cell nests just above the epidermal basal cell layer, but without involvement of the uppermost Malpighian cell layers (Fig. 1) and 9 other cases with evidence of true transepidermal elimination (10% of all the cases) (Fig. 2). None of our 89 cases showed prominent upward spread (pagetoid spread) of single melanocytes, although single melanocytes could sometimes be observed just above the epidermal

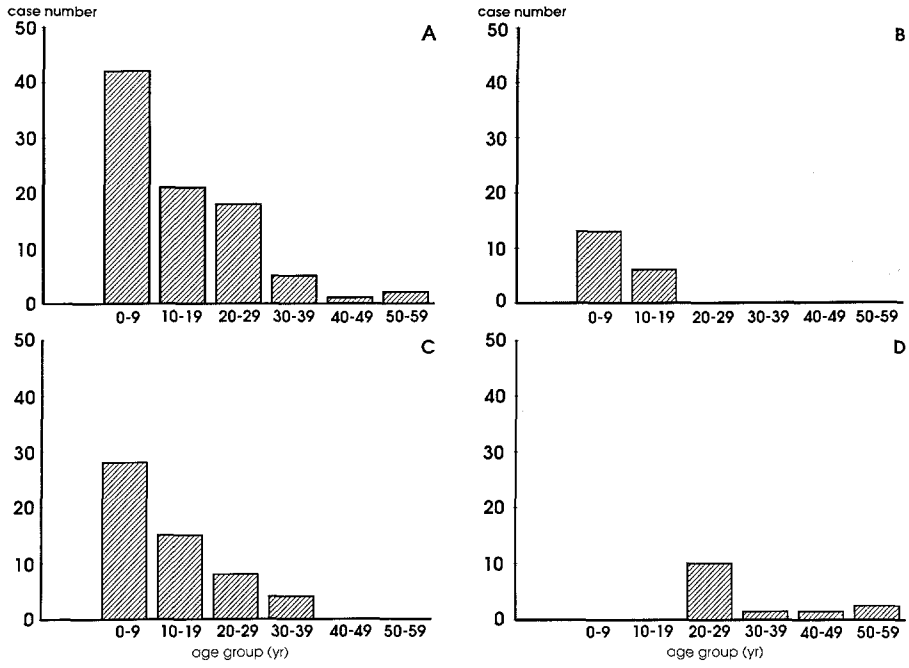

Fig. 3. Histogram: age distribution of Spitz nevi according to their epidermal and/or dermal involvement. **(A)** all cases **(B)** compound nevi with suprabasal epidermal involvement, including cases with transepidermal elimination. **(C)** compound nevi without suprabasal epidermal involvement **(D)** dermal nevi

Table 1. Age distribution of Spitz nevi ($n=89$) according to architectural patterns

Group	Architectural pattern	Number (%)	Mean age (+SD)
1	Compound nevi with suprabasal epidermal involvement	19 (21)	7.16± 4.52
2	Compound nevi without suprabasal epidermal involvement	56 (63)	13.18± 8.88
3	Dermal nevi	14 (16)	30.14±11.25

Student's t-test for small populations: $p<0.001$ between groups 1 and 3, and 2 and 3: $p<0.01$ between groups 1 and 2

basal cell layer. These suprabasal melanocytes were always seen in association with either intraepidermal nesting or transepidermal elimination. Of particular interest was the age distribution of the different architectural patterns, as summarized in Table 1 and on histograms (Fig. 3). The mean age for all patients with Spitz nevi was 14.56±11.18 years, whereas the mean age was 5.67±3.77 years for patients with compound nevi with transepidermal elimination, 7.16±4.52 years for patients with compound nevi and suprabasal epidermal involvement, 13.18±8.88 years for patients with compound nevi without suprabasal epidermal extension and 30.14±11.25 years for patients with dermal nevi. Using the Student's t-test for small populations, the mean age of the dermal nevus group differed significatively ($p<0.001$) with all the groups of compound nevi. The difference was also significant, although to a lesser degree ($p<0.01$) between compound nevi with epidermal involvement and compound nevi without epidermal involvement. There was no significant difference between the mean age of patients with compound nevi and transepidermal elimination and patients with compound nevi and overall intraepidermal involvement.

Beside the architectural pattern, no particular histological features seen in any one of these groups were absent in others.

Discussion

In their review of 211 cases of Spitz nevus, Weedon and Little (1977) quoted that they found no noteworthy histological differences between Spitz nevi in children and adults. In contrast, Paniago-Pereira et al. (1978) affirm that Spitz nevi from children are characterized by papillomatosis, severe oedema of the papillary dermis, striking telangectases, a low melanin content, mostly epithelioid nevus cells, and "acantholytic" nevus cells, whereas desmoplastic intradermal types of Spitz nevi are usually from adults. These two reviewers do not evaluate the incidence of epidermal involvement in children and adults although its existence is well known. It was reported to occur in 36% of the 211 cases described by Weedon and Little (1977) and in 33% of the 33 cases studied by Peters and Goellner

(1986). This is even higher than the 21% (19/90) found in the present series. However, the intraepidermal component usually remains minimal without or with little upward spread of individual atypical melanocytes (Paniago-Pereira et al. 1978; Peters and Goellner 1986; Weedon and Little 1977). Transepidermal elimination of nevus cell nests, – a mechanism by which a substance is eliminated through the epidermis (Goette 1987; Mehregan 1970) – was seldom observed (Kantor and Wheeland 1987; Yuki and Shitara 1984). In 4 of the 76 cases of Spitz nevus with upward migration of nevus cells reported by Weedon and Little (1977), the epidermal invasion was described as being prominent with nests of nevus cells extending almost to the stratum corneum. These cases may represent the process of transepithelial elimination. In the present series, 9 cases (10%) showed evidence of such a phenomenon. All of our cases were under 14 years of age (mean age 5.67 ± 3.77; range 2–14 years) and also showed evidence of intraepidermal nesting. This is in disagreement with Gartmann (1982) who did not observe transepithelial elimination in 491 cases of Spitz nevus. Transepidermal elimination of nevus cell nests also occurs in common junctional melanocytic nevi, its frequency varies from 0.13% (Gartmann, 1982) to 2% (Yuki et al. 1984). It has been suggested that it may represent a mechanism of involution (Kantor and Wheeland 1987).

Of particular interest is the age distribution of Spitz nevi according to the different architectural patterns. The mean age of the patients was significantly lower in the group of compound nevi with intraepidermal involvement (7.16 ± 4.52 years) than in the group of compound nevi without intraepidermal involvement (13.18 ± 8.88 years); it was still significantly lower than in the group of pure intraepidermal nevi (30.14 ± 11.25 years).

These data reflect the progressive decrease with age of the compound Spitz nevus (no case from the fifth decade onwards) and the absence of the dermal variety in early life (no case before the third decade). Our observations are in accordance with the hypothesis that Spitz nevi have a life history that is comparable to that of common acquired melanocytic nevi; the lesions appear at the dermoepidermal junction where the cells proliferate actively, progressive extension to the papillary and reticular dermis occurs, followed by the disappearance of the junctional component. Ultimately, the dermal component may also disappear (Reed et al. 1978). Because Spitz nevi and malignant melanomas have so many histological features in common, details that can help in their differential diagnosis are particulary welcome. This seems to be the case for the involvement of the epidermis. If this feature does not help in differentiating Spitz nevus from malignant melanoma in children, epidermal involvement in an adult Spitz-like nevus should be considered as an argument for malignancy.

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