Juvenile Conjunctival Nevus
Clinicopathologic Analysis of 33 Cases

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Abstract: Conjunctival nevi in children and adolescents often have histologic features that can be difficult to differentiate from malignancy. We have identified a subset of childhood nevi displaying a confluent growth pattern and a lack of maturation that we have defined as juvenile conjunctival nevi (JCN), with the aim of further describing the clinicopathologic features of these lesions. Lesions identified as conjunctival nevus in a tertiary referral hospital were reviewed and the subset of lesions identified as JCN were further evaluated. Clinical details including follow-up data were also gathered. Of the 40 conjunctival nevi identified, 33 fit the criteria for JCN. The mean age at time of excision was 10.9 years (range: 4 to 19 y). Thirty-two lesions were of the compound type; one was a junctional nevus. All showed a nested junctional growth pattern. In 17 lesions (61%), the junctional component extended beyond the subepithelial component (shoulder phenomenon). Maturation was absent in 21 of the compound nevi (66%, average age 10.3 y), and incomplete in the remaining 11 lesions (34%, average age 12.1 y). The nuclei of the subepithelial nevus cells were larger than the epithelial nevus cells in 19 nevi (59%) and the same size in 13 (41%). A lymphocytic host response was present in 17 lesions (52%). Mitotic figures were rarely seen. None of the lesions had recurred over an average follow-up period of 34 months. Recognition of JCN as a distinct morphologic variant of a conjunctival nevus with characteristic histologic features may help to distinguish this benign lesion from melanoma.

Key Words: conjunctiva, nevus, melanoma

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Conjunctival melanocytic proliferations comprise 13% to 43% of all conjunctival neoplasms.[9,22,27] They include benign racial melanosis, nevi, melanoma, and a broad group of intraepithelial melanocytic proliferations referred to as primary acquired melanosis (PAM).[3,4–6,9–14,16,17,19,21,24,25,27] Conjunctival nevi are the most common benign acquired melanocytic proliferations. They are seen more frequently in whites than in other races and have an equal sex predilection. Most lesions arise in the first decade or young adulthood but can present at all ages including the elderly.[1,8,13,18,23] Nevi in children and young adults typically present as enlarging lightly pigmented or amelanotic, flat, or raised nodules of the bulbar conjunctiva and are often associated with intralesional clear cysts and prominent blood vessels. Growth of some lesions may accelerate during puberty. With time the growth decreases and the lesions often become more pigmented. The diagnosis can be made by clinical appearance alone in many cases; however, some lesions, in particular nonpigmented nevi, can be difficult to classify by appearance.

Conjunctival nevi are usually biopsied to rule out melanoma or other type of malignancy; in children and adolescents this is often prompted by rapid growth of the lesion. Histologic differentiation between nevi and melanoma in the conjunctiva can be challenging for pathologists unfamiliar with this location,[1] and are the frequent subject of second opinion consultations. As with other so-called nevi of special anatomic sites (acral, genital, intertriginous), benign melanocytic proliferations in conjunctiva can produce "atypical" histologic patterns that in the skin are associated with melanoma. Therefore, such lesions are prone to overinterpretation, either as melanoma or as an atypical lesion, leading to further unnecessary surgery.

Earlier authors on the subject clearly recognized that conjunctival nevi evolve with time and that in childhood they can display extensive junctional activity, nuclear pleomorphism, discohesion of the nevus nests, and a lack of maturation in the subepithelial component.[7,13,15,18,26] Two features in particular, a confluent growth pattern at the epithelial/subepithelial junction with discohesive nevus nests and an apparent lack of maturation, which are worrisome for melanoma in adults, are frequently seen in children. These features may define juvenile conjunctival nevi (JCN) as a histologic variant characteristic for this anatomic site.

To-date, clinicopathologic analysis of conjunctival nevi in children and adolescents has not been systematically performed in large series of lesions with clinical follow-up. The goal of this study was to examine the

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frequency of atypical features in conjunctival nevi in patients ≤20 years old and provide a clinicopathologic description of this group of lesions.

MATERIALS AND METHODS

Patients selected for study were identified by searching the Massachusetts Eye and Ear Infirmary's (MEEI) ophthalmic pathology database between the years 1995 and 2007 for lesions diagnosed as conjunctival nevi in patients aged ≤20 years. Of the 44 cases identified, hematoxylin and eosin-stained sections were available for review in 40 lesions from 39 patients (1 patient had bilateral lesions). All but 2 of the cases were routine cases from the MEEI. The other 2 were sent in consultation from outside sources.

The pathology slides were reviewed and lesions with both a confluent and discohesive growth pattern of nevus nests at the epithelial/subepithelial junction and an apparent lack of maturation were defined as JCN. Maturation of compound nevi was defined as progressive reduction in cellular size and or morphologic type (from A, through B, to C) with depth of the subepithelial component. The lesion was classified as lacking maturation if there was no evidence of maturation across more than 50% of the lesion. If areas lacking maturation were present but involved less than 50% of the lesion, they were recorded as having incomplete maturation. The size of the melanocyte nucleus in the junctional and subepithelial component was expressed as an approximate fraction of the average size of the midlevel epithelial cells. As another measure of histologic maturation the size of nuclei in the intraepithelial component was compared with those in the deep subepithelial component. Lesions without the 2 features characteristic of JCN were classified as ordinary nevi and excluded from the study.

Lesions defined as JCN were analyzed further for a number of features usually evaluated in melanocytic proliferations. These included: location (junctional, compound, or subepithelial), average melanocyte nucleus size in the epithelial and subepithelial regions, melanocyte morphologic type (A—epithelioid, B—intermediate/lymphocytelike, C—neurotized/spindle), junctional growth pattern (single cell lentiginous vs. nested), presence or absence of ulceration, conjunctival cysts, mitotic activity, pagetoid spread, and lymphocytic host response. If a second distinct nevic component was observed, the lesion was classified as a combined nevus. The lesion was recorded as having a lateral shoulder if the junctional component extended at least 2.0 mm beyond the subepithelial component.

Clinical data including demographics, size, location, and clinical appearance were also recorded. The follow-up information was gathered by chart review and by contacting the surgeon and/or primary care physician involved. When appropriate, statistical analyses were performed with analysis of variance (SPSS, Inc, Version 10.07, Chicago, IL). Prior approval for this study was obtained from the Institutional Review Board of MEEI.

RESULTS

Out of 40 lesions reviewed 7 (18%) were ordinary compound nevi, with orderly maturation and no areas of confluent growth pattern or at the epithelial/subepithelial junction; these were excluded from the study. One of these lesions was from a 10-year-old boy; the others were from adolescents ranging from 13 to 18 years old. Thirty-three lesions from 32 patients (1 patient had bilateral lesions) showed atypical features, including the 2 characteristics defining JCN: areas of confluent growth pattern at the epithelial/subepithelial junction and incomplete or absent maturation. These included all (96%) but one lesion from children ≤12 years old (total of 23 lesions). The percentage of JCN in patients older than 12 years was lower (65% of 17 lesions). There was a statistically significant difference between these 2 groups ($P = 0.016$, Fisher exact test). Only the JCN were analyzed further.

The clinical characteristics of the 33 JCN are summarized in Table 1. Twenty-one of the patients were male and 11 were female. The mean age at the time of surgery was 10.9 years (range: 4 to 19 y). Twenty-one patients were children ≤12 years old. The lesions were first noticed at an average age of 8.7 years (range: 1 to 19 y) in 28 patients with available data. Ten of the 11 patients with known ethnicity were white. The nevus was located on the bulbar conjunctiva in 28 cases (85%), with 22 (79%) of these in the temporal quadrants. Sixteen lesions were adjacent to the limbus (12 temporal and 3 nasal, 1 unspecified), with 1 extending onto the cornea. In 15 of 30 cases (50%), the nevus was clinically nonpigmented. Sixteen of 26 (55%) lesions with available data were clinically an elevated mass. Follow-up data was available for 27 lesions (82%) with an average of 34 months (range: 1 mo to 11 y) and none of the lesions recurred during this period. Three nevi (IDs 7, 17, 23) were initially noticed after minor trauma to the conjunctiva. Nineteen of 27 (70%) patients reported growth of the nevus before surgery, and 2 noticed an increase in pigmentation. The presence of cysts was recorded in clinical charts in only 5 of 29 lesions (17%). Figure 1A shows a clinical picture of a representative case.

Twenty-nine nevi (88%) were primary excisions and 4 were reexcisions for recurrent lesions. One of these patients, a white boy in whom a pigmented lesion was first noticed at age 8 months underwent excision at 17 months of age and again for a recurrence at 3 years of age; the pathology report of the first excision was cystic nevus, and the second an inflamed conjunctival nevus. When seen at our hospital at age 7 years, in addition to recurrence of the lesion he was noted to have marked scarring of the conjunctiva causing an abnormal eye turn. The other 3 patients with recurrent nevi underwent their initial surgeries at ages 7, 3, and 3 years old, respectively; all 3 were reported as compound nevi.

Histologic features of the series are shown in Table 2 and summarized in the text box . All but one lesion were of the compound type (32 lesions) (Figs. 1B–D); the remaining lesion was a junctional nevus which was

TABLE 1. Clinical Features of Patients With JCN

ID	Sex	Age*	Eye†	Location	Lesion Thickness	Pigment‡	Vessels‡	Cysts‡	Growth§	Follow-up
1	M	15	OD	Bulbar, temporal	Elevated	No	Yes	No	Yes	11 y
2	M	13	OS	Limbus, temporal	Elevated	ND	Yes	ND	No	6 y
3	F	8	OD	Bulbar, nasal	Elevated	Yes	Yes	No	ND	7 y
4	F	15	OS	Bulbar, nasal	Flat	No	Yes	Yes	No	11 mo
5	M	10	OD	Limbus, temporal	Elevated	No	Yes	No	Yes	10 y
6	F	6	OS	Limbus	ND	ND	ND	ND	Yes	—
7	M	10	OS	Bulbar, temporal	Elevated	No	Yes	Yes	No	7 y
8	F	8	OS	Limbus, temporal	Elevated	Yes	Yes	No	Yes	7 y
9	M	7	OD	Bulbar, nasal	Elevated	Yes	No	No	Yes	6 mo
10	M	11	OS	Bulbar, temporal	Flat	Yes	No	No	Yes	5 y
11	M	9	OD	Limbus, temporal	Flat	Yes	No	Yes	Yes	—
12	F	7	OD	Limbus, temporal	Elevated	No	Yes	No	Yes	4 y
13	F	9	OS	Caruncle	Elevated	Yes	No	No	ND	5 y
14	M	11	OD	Limbus, temporal	Elevated	Yes	No	No	Yes	—
15	M	15	OS	Bulbar, temporal	Flat	Yes	Yes	No	Yes	3 y
16	F	13	OD	Limbus, nasal	ND	No	Yes	No	Yes	1 y
17	M	17	OS	Limbus, temporal	Flat	No	Yes	No	No	2 wk
18	M	15	OD	Bulbar, temporal	ND	Yes	No	No	Yes	1.5 y
19	M	19	OD	Limbus, temporal	Flat	Yes	No	No	Yes	2 mo
20	M	5	OD	Limbus, nasal	Elevated	No	Yes	No	Yes	2 y
21	M	13	OS	Caruncle	Elevated	Yes	No	Yes	Yes	1.5 y
22	F	8	OS	Plica	Flat	Yes	No	No	Yes	1 y
23	M	14	OS	Limbus, temporal	Flat	Yes	No	Yes	No	1 y
24	F	8	OS	Limbus, temporal	Elevated	No	Yes	No	No	8 mo
25	M	13	OD	Bulbar, temporal	Elevated	Yes	Yes	No	No	1 y
26	M	4	OD	Bulbar, temporal	Elevated	No	Yes	Yes	Yes	11 mo
27	M	9	OS	Bulbar, temporal	ND	No	Yes	No	Yes	9 mo
28	F	8	OD	Limbus, temporal	Flat	No	Yes	No	Yes	7 mo
29	M	12	OS	Limbus, temporal	Flat	Yes	Yes	No	No	4 mo
30‖	F	11	OD	Bulbar, temporal	Flat	No	Yes	No	No	4 mo
31‖			OS	Bulbar, temporal	Flat	No	Yes	No	No	4 mo
32	M	12	OS	ND	ND	No	ND	ND	ND	—
33	M	12	OD	ND	ND	ND	ND	ND	ND	—

*Age in years at time of surgery.
‡Pigmentation, vessels, or cysts associated with lesion.
†Eye: OD = right eye, OS = left eye.
§Apparent clinical growth of lesion before excision.
‖Bilateral nevi in the same patient excised on same date.
F indicates female; M, male, ND, no data available.

included in the JCN group as it had confluence of the junctional nests, although it could not be assessed for maturation. Conjunctival cysts were present in 29 nevi (88%) (Fig. 2A). A separate epithelioid clonal (inverted A) component was present in 3 combined nevi (Fig. 2B); 2 of these were recurrent lesions. None of the lesions were ulcerated. All showed a nested junctional growth pattern with a confluent growth pattern at the epithelial/subepithelial junction where the junctional nests were closely apposed or coalesced (Fig. 3). Discohesion of the cells forming junctional nests or clefts between the nests and the epithelium were present in 22 lesions (67%). In 17 lesions (61%), the junctional component extended beyond the subepithelial component (shoulder phenomenon) (Fig. 4A). In 5 cases, the confluent growth pattern involved the lateral shoulder. Pagetoid spread was difficult to assess in the thin conjunctival epithelium and only 1 lesion showed a small focus of pagetoid spread. Single cell lentiginous growth pattern was observed focally in 3 lesions (Fig. 4B). A lymphocytic host response was present in 17 lesions (52%) and was brisk in 3 of them.

Type A epithelioid melanocytes were the predominant cell type in 8 lesions (24%) and type B lymphocyte-like in a further 8 lesions; both types were present in approximately similar proportions in 17 (52%) lesions. A single mitotic figure was observed in 2 lesions. Maturation was recorded as absent in 21 of the 32 compound nevi (66%, average age 10.3 y) and in 11 lesions (34%, average age 12.1 y) only a portion of the lesion showed maturation (Fig. 5). The nuclei of the junctional nevus cells were approximately the same size as those of the adjacent uninvolved epithelium in 20 nevi (61%) and larger in 13 nevi (39%); in the subepithelial nests the nuclei were the same size as the epithelial cells in 5 nevi (16%) and larger in the remaining 27 (84%) compound nevi. The nuclei of the subepithelial nevus cells were larger than the epithelial nevus cells in 19 nevi (59%) and the same size in 13 (41%).

Statistical analysis revealed no significant correlation between age and (1) the histologic presence of cysts, (2) the presence or absence of inflammation, and (3) incomplete versus no maturation.

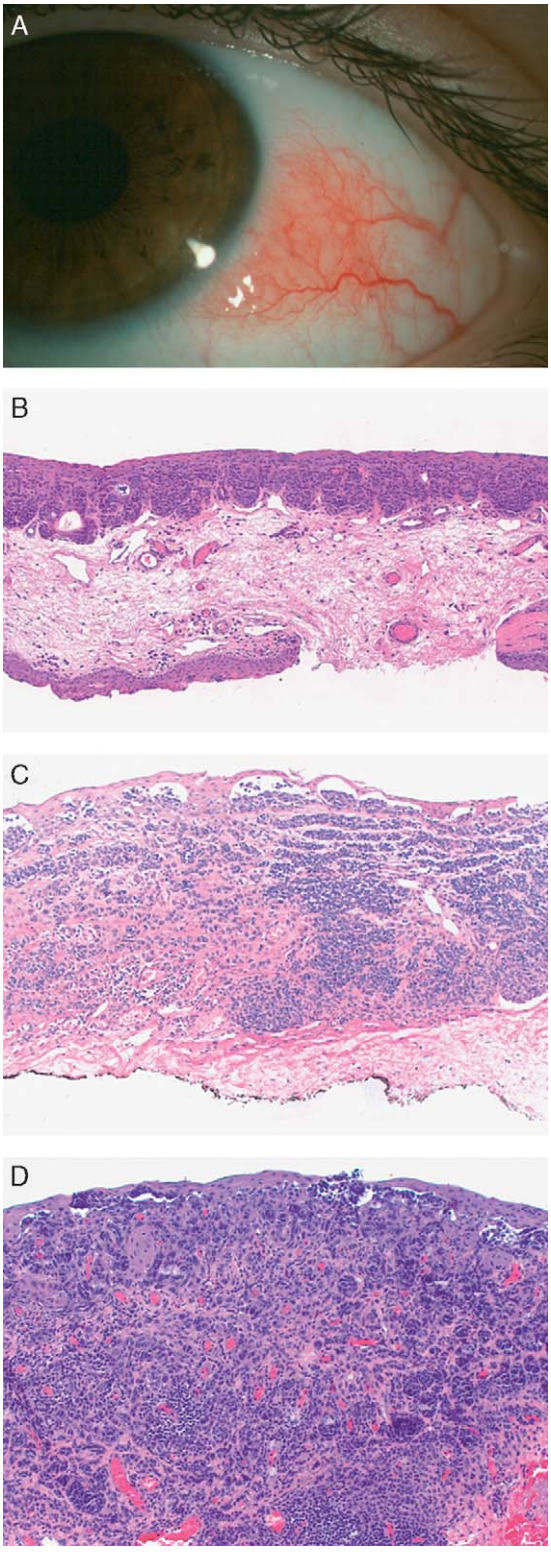

FIGURE 1. A, Photograph of left eye of case 31, showing a temporal bulbar conjunctival nevus that is nonpigmented, vascular, and flat. B to D, Low-power light microscopy of 3 representative compound conjunctival nevi: B = case 25, C = case 10, and D = case 30.

DISCUSSION

Melanocytic nevi are among the most commonly sampled lesions of the conjunctiva yet they are rare specimens in the general surgical pathology or dermatopathology laboratory. Nevi in children and young adults consistently display a lack of maturation with depth and often produce a confluent growth pattern at the epithelial/subepithelial junction. As both features are frequently associated with melanoma in the skin, we used them as the main inclusion criteria for the study, defining JCN. The majority of lesions in our study of patients $\leq$20 years old (83%) fulfilled the criteria for JCN. Patients $\leq$12 years old had a significantly higher proportion of JCN compared with those $>$12 years old (96% vs. 65%).

Our data extends the observations made in earlier articles by Jay[13] and Folberg et al,[7] who commented on atypical features of conjunctival nevi in children. Jay wrote that in contrast to nevi in adults, which show "gradual maturation to fibrillary forms," actively growing nevi in children often contain "epithelioid nevus cells" with "abundant eosinophilic cytoplasm containing large nucleus with prominent eosinophilic nucleolus. Folberg et al[7] noted that conjunctival nevi sometimes show confluent growth patterns reminiscent of PAM with atypia. Our study takes these observations a step further, defining JCN as a morphologic subset of conjunctival nevus. We believe that such an approach will help to differentiate these entirely benign lesions from melanoma in younger patients.

The most important clinical and histologic differential diagnosis of JCN is malignant melanoma. Conjunctival melanomas account for approximately 21% to 25% of biopsied melanocytic conjunctival lesions, however, their incidence is much lower.[9,22] Up to 15% to 40% of melanomas arise in association with a nevus[5,8,16,20,23,24,29]; the remainder arise de novo or in association with PAM. Conjunctival melanomas are very rare in children; however, its classic clinical presentation is of a changing or enlarging lesion on the bulbar conjunctiva. As this description fits many JCN, a biopsy has to be performed to rule out melanoma.

One reason why JCN can appear concerning is the lack of maturation, or even a "reverse maturation," where the subepithelial cells appear larger than those in the junctional nests. We found that in all lesions the size of subepithelial melanocytes was equal to (41%) or greater than the size of the junctional melanocytes (59%). The presence of large epithelioid cells in the subepithelial component added to the impression of atypia in these lesions. These findings are in sharp contrast with the prevailing notion in skin and conjunctival lesions in adults, where lack of maturation and preservation of epithelioid cell morphology are among the cardinal features of melanoma. They are particularly important in recognition of the nevoid variant of melanoma.[28]

A confluent growth pattern is another feature rarely seen in benign nevi in the skin. In adults, this pattern is an expected feature in intraepithelial melanomas and in PAM with atypia.[25] PAM is an acquired multifocal flat

TABLE 2. Histologic Features of JCN

Case	Maturation*	Confluence at Junction†	Shoulder‡	Lentiginous Growth§	Pagetoid Spread	Epithelial Cysts	Nuclear Size (Junctional Component)‖	Nuclear Size (Subepithelial Component)‖	Inflammation
1	Incomplete	Present	Present	Absent	Absent	Present	1-1.5 ×	2 ×	Nonbrisk
2	Absent	Absent	Present	Absent	Absent	Present	1 ×	1 ×	Absent
3	Absent	Present	Present	Absent	Absent	Absent	2 ×	2 ×	Absent
4	Absent	Present	Absent	Absent	Absent	Present	1 ×	1 ×	Absent
5	Incomplete	Present	Absent	Absent	Absent	Present	1 ×	1.5 ×	Nonbrisk
6	Absent	Present	Absent	Absent	Absent	Present	1 ×	1 ×	Absent
7	Absent	Present	Present	Present	Absent	Present	1-2 ×	1.5-2 ×	Nonbrisk
8	Absent	Present	Absent	Absent	Absent	Present	1 ×	2 ×	Absent
9	Present	Present	Present	Absent	Absent	Present	1 ×	1.5-2 ×	Nonbrisk
10	Absent	Present	Absent	Absent	Absent	Present	1.5 ×	2 ×	Nonbrisk
11	Absent	Present	N/A	Absent	Absent	Absent	1 ×	N/A	Absent
12	Incomplete	Present	Present	Absent	Absent	Present	1 ×	1.5 ×	Nonbrisk
13	Absent	Present	Absent	Absent	Absent	Present	1 ×	1.5 ×	Absent
14	Incomplete	Present	Absent	Absent	Absent	Present	1 ×	2 ×	Absent
15	Absent	Present	Absent	Absent	Absent	Absent	1.5 ×	2 ×	Nonbrisk
16	Present	Present	Present	Absent	Absent	Present	1.5 ×	1.5 ×	Brisk
17	Present	Present	Present	Present	Absent	Present	1.5 ×	1.5 ×	Absent
18	Absent	Present	Absent	Absent	Absent	Absent	1 ×	1.5 ×	Absent
19	Incomplete	Present	Present	Absent	Absent	Present	1 ×	1.5 ×	Absent
20	Absent	Present	—	Absent	Absent	Present	1 ×	2 ×	Nonbrisk
21	Incomplete	Present	—	Present	Absent	Present	1 ×	1.5 ×	Absent
22	Absent	Present	—	Absent	Absent	Present	1-1.5 ×	1.5 ×	Nonbrisk
23	Absent	Present	Present	Absent	Absent	Present	1 ×	1.5 ×	Absent
24	Absent	Present	Present	Absent	Absent	Present	1 ×	1.5 ×	Absent
25	Absent	Present	Present	Absent	Absent	Present	1 ×	1 ×	Nonbrisk
26	Absent	Present	Present	Absent	Absent	Present	1 ×	1 ×	Absent
27	Absent	Present	Absent	Absent	Absent	Present	1 ×	1.5 ×	Nonbrisk
28	Incomplete	Present	Present	Absent	Present	Present	1.5 ×	1.5 ×	Absent
29	Absent	Present	Absent	Absent	Absent	Present	1 ×	1.5 ×	Brisk
30	Present	Present	Present	Absent	Absent	Present	1.5 ×	2 ×	Nonbrisk
31	Absent	Present	Present	Absent	Absent	Present	1.5 ×	1.5-2 ×	Nonbrisk
32	Absent	Present	—	Absent	Absent	Present	1-1.5 ×	1.5 ×	Brisk
33	Absent	Present	Present	Absent	Absent	Present	1.5 ×	1.5 ×	Absent

*Progressive reduction in cellular size and or morphologic type (from A, through B, to C) with depth of the subepithelial component.
†Confluent growth pattern of nevus nests at epithelial/subepithelial junction.
‡Extension of junctional component at least 2.0 mm beyond the subepithelial component. Cases marked "—" were unable to be evaluated due to incomplete excision.
§Single cell junctional growth pattern.
‖Nuclear size of the nevus cell as a proportion of the size of a midlevel epithelial cell.

Histological Features of Juvenile Conjunctival Nevi

	(Percentage of Cases)
Common	
Confluent growth pattern*	(100%)
Lack of maturation/"reverse maturation"*	(100%)
Nested growth pattern	(100%)
Compound nevus type	(97%)
Epithelial cysts	(88%)
Often Seen	
Discohesion of intraepithelial nests	(67%)
Shoulder phenomenon	(61%)
Lymphocytic host response	(52%)
Rare	
Combined nevus	(9%)
Lentiginous growth	(9%)
Mitoses	(6%)
Pagetoid spread	(3%)
Ulceration	(0%)

*Features used to define juvenile conjunctival nevus.

proliferation of the conjunctiva with irregular borders. It is rarely seen in children and is clinically distinct from JCN. However, high-risk PAM with atypia can be difficult to distinguish histologically from JCN, as it can display nesting and a confluent growth pattern with discohesion reminiscent of the junctional component in JCN. In PAM with atypia this growth pattern is due to confluence of nests and single lentiginous cell proliferation. In contrast in JNC, the confluence is usually due to close apposition or coalescence of rapidly growing nests. Diagnosis of PAM and differentiation from its mimics requires attention to cytologic features. In high-risk PAM with atypia, best considered as an outright melanoma in situ, the cells are epithelioid and show vesicular nuclei with variable pleomorphism. The nuclear to cytoplasmic ratio is moderate to low. Low-risk PAM with atypia is less likely to be confused with JCN. It features predominantly lentiginous growth of small to medium-size melanocytes with hyperchromatic nuclei, little cytoplasm, and high nuclear to cytoplasmic ratio.

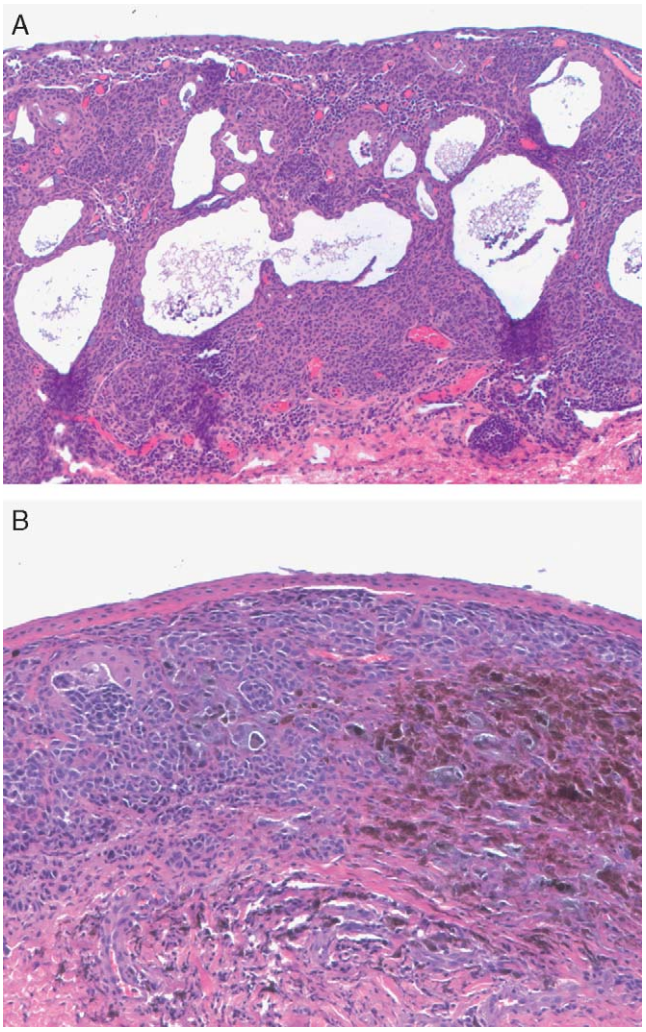

FIGURE 2. A, Nevus showing induction of junctional cysts by the subepithelial component (case 26). B, Combined nevus with distinct ''clonal'' epithelioid component showing type A pigmented epithelioid melanocytes in the subepithelial component on the right (case 14).

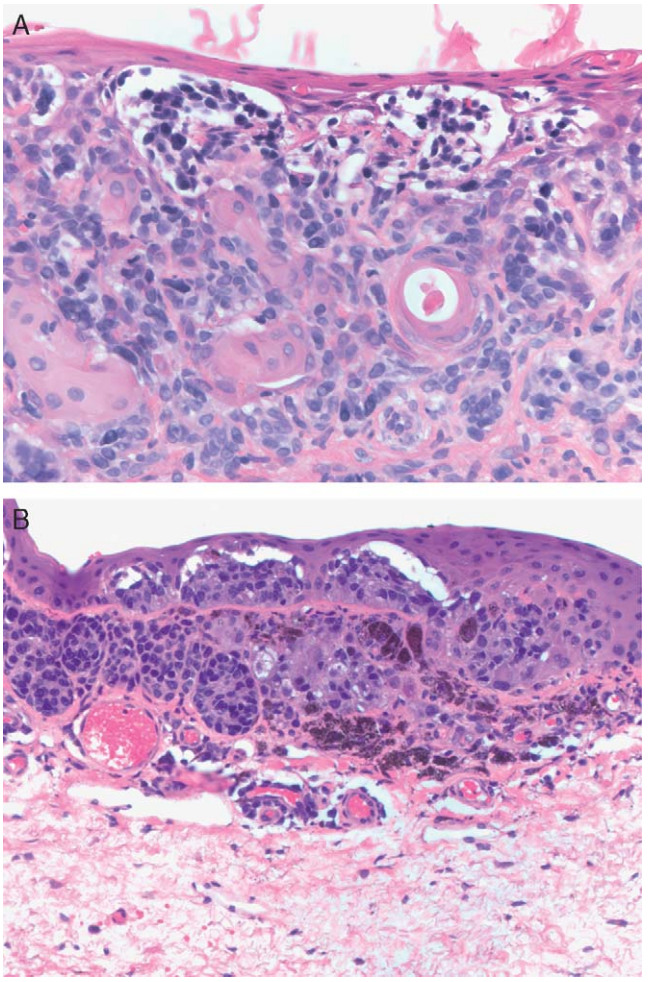

FIGURE 3. Nested and confluent growth pattern of melanocytes in the junctional component. The confluence is due to close apposition of junctional nests. A (case 7) shows discohesion of the nests. B (case 15) shows clefting between the nevus nests and the epithelium.

Additional atypical features seen in JCN include discohesion of nests and a lateral shoulder of the junctional proliferation, which may be particularly worrisome if combined in the single lesion. Folberg et al[7] commented that confluence of nests can be present, but is usually limited to the area directly overlying the subepithelial component; in contrast over half of our cases displayed a shoulder. Admittedly, it may be virtually impossible to unequivocably differentiate between melanoma, PAM with atypia and JNC in a small biopsy of a lateral shoulder showing a confluent growth pattern and cell discohesion. In such lesions, focal features must be interpreted in the context of the entire lesion.

Rare mitotic activity was detected in 2 lesions. This indicates that mitoses are uncommon in JCN, but the number of cases studied is insufficient to make a definitive statement on mitotic activity as a discriminator between a benign nevus and melanoma. In conventional nevi mitotic activity can be found in benign lesions, and as with other characteristics it has to be interpreted in the context of other features. Other features which favor melanoma versus a conjunctival nevus are significant nuclear pleomorphism, hyperchromasia, spindle cell morphology, destructive growth pattern, and invasion of the cornea, none of which were noted in our patients.

Other histologic features of JCN were less distinctive or less frequent. Most (96%) were compound nevi. A focus of single cell lentiginous growth was present in 3 cases. Assessment of pagetoid spread in thin conjunctival epithelium is very difficult and is not a reliable feature. However, 1 lesion showed a focal pattern reminiscent of pagetoid spread in the skin in thickened perilimbal epithelium. All the lesions were composed of epithelioid type A or type B melanocytes. A lymphocytic infiltrate was present in about half of the lesions which is consistent with prior reports in the literature.[26]

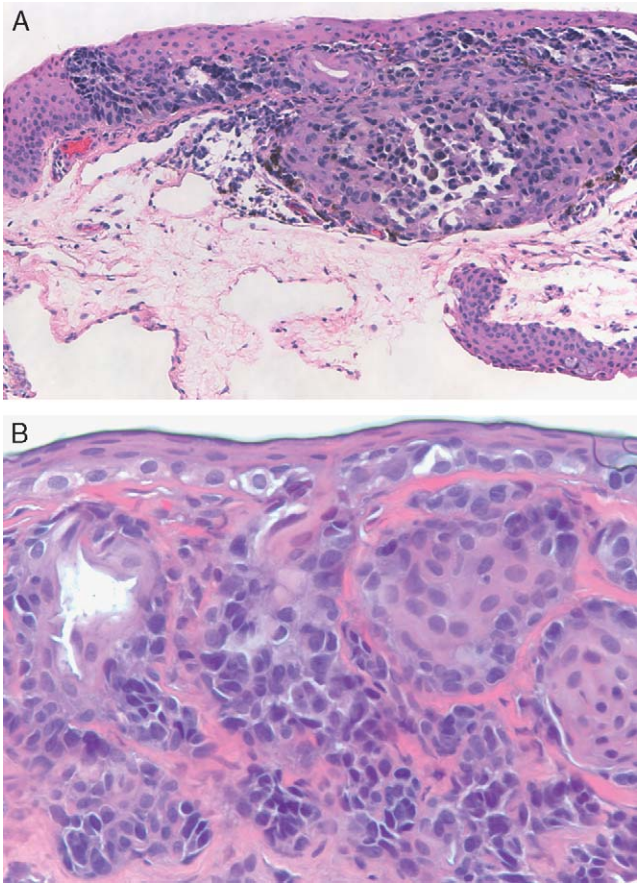

FIGURE 4. A, Shoulder phenomenon showing lateral extension of the junctional component beyond the subepithelial component (case 3). Of note is the confluent growth pattern. B, Single cell confluent (lentiginous) growth pattern (case 17).

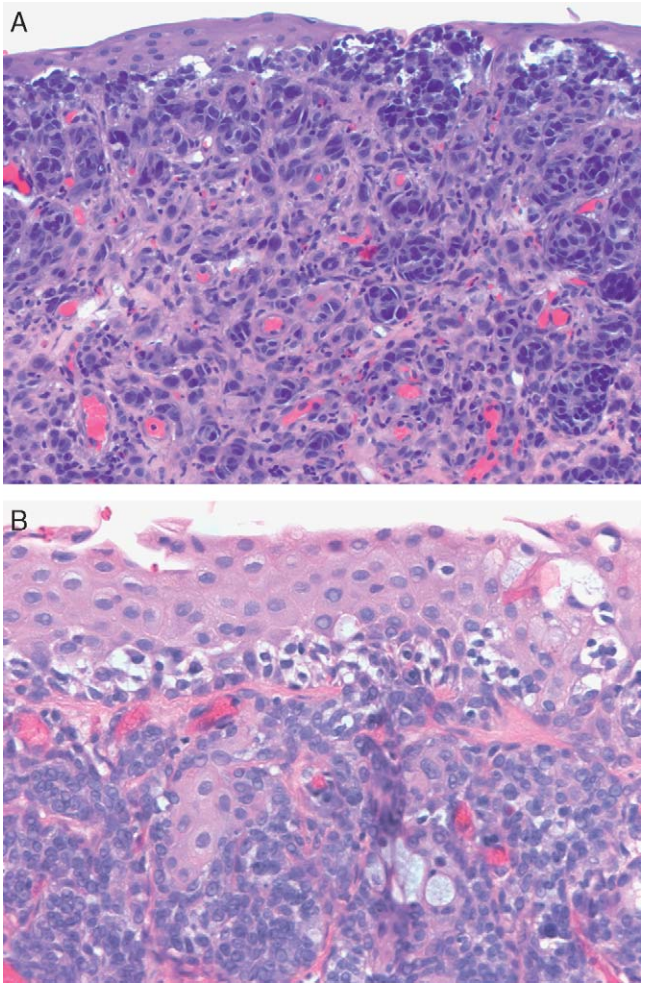

FIGURE 5. Lack of maturation and epithelioid cell atypia of the subepithelial component. A shows a typical JCN with preserved cell and nuclear size through the depth of the lesion (case 21). B illustrates that the nuclear size of the subepithelial melanocytes are larger than those forming the junctional nests (case 30).

The presence of cysts is one of the clinical features which helps one differentiate between conjunctival nevi and melanoma as cysts are rarely seen in melanoma.[21] In our series, the presence of conjunctival cysts was recorded in patient's charts in only 4 cases, however, it was histologically seen in the majority (88%) of cases. It is not clear if the presence of cysts has low sensitivity for JCN or merely represents incomplete documentation.

The clinical findings in our series are generally in keeping with the literature.[8,18,19,23] The majority of patients with known ethnicity were white. The average age at surgery (10.9 y) was comparable with the series reported by Zamir et al[26] (12.2 y). In many cases the lesion had been present for years before excision. This observation is also consistent with findings of Jay[13] who found that conjunctival nevi were most commonly initially noticed in the first decade. All but 3 lesions were located in the bulbar conjunctiva. Thus, as previously suggested, palpebral or forniceal melanocytic conjunctival proliferations should be evaluated for possible melanoma.[7,11] Almost half of the nevi in our series were clinically nonpigmented. This figure is similar to that reported by Zamir et al.[26] In contrast, the surveys of nevi of all ages by Shields et al[23] and Gerner et al[8] showed that the majority were pigmented. This discrepancy can be explained by the different reasons for sampling in children and adults. The growth of a lesion seems to be the most common reason for biopsy in children (our study and Zamir et al[26]) whereas lesions in adults are usually clinically stable and are often sampled because of increasing pigmentation and/or growth.[26]

Although none of the patients developed a recurrence during the follow-up period, 4 of the nevi studied were recurrent lesions suggesting that a longer follow-up time may be needed to more accurately evaluate this outcome. As the recurrent lesions did not display any clinical features distinctive from the other JCN, this may represent another atypical but benign feature of these lesions, however, each case should be individually assessed. Interestingly, 2 of the 4 recurrent lesions were combined nevi with a separate epithelioid clonal

component in addition to the features of JCN. This may indicate that this subtype of nevi behave differently to other JCN, or are evolving melanomas, however, this is unlikely as neither lesion recurred after reexcision. In support of the benign nature of these nevi a review of 30 combined nevi in patients of all ages by Crawford et al[2] stated that none recurred or underwent malignant change.

JCN characterized by at least a focal absence of maturation with depth and a confluent growth pattern represent the majority of conjunctival nevi in children less than 12 years old, but are not limited to this age group. Recognition of JCN as a distinct morphologic variant of a nevus characteristic for this anatomic site may help to distinguish this benign lesion from melanoma.

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