Original Article

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Pathology Section

Clinical and Microscopic Evaluation of Pediatric Melanocytic Lesions

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ABSTRACT

Introduction: Melanocytic lesions in children are unique challenging propositions both for the dermatologist and the pathologist. The potential for malignant change in melanocytic lesions is a cause for concern and distinction between benign nevus and malignant melanoma is crucial and at times can be extremely difficult.

Aim: To decipher the clinicopathological spectrum of melanocytic lesions in Asian children because of rarity of such studies in our population.

Materials and Methods: A retrospective analysis of all the cases diagnosed as melanocytic lesions in children less than 14 years of age was carried out between 1995 and 2014. The demographic data including the age at diagnosis, gender and site of lesion was compiled from the case files. Histopathological findings and final diagnosis rendered were also studied.

Results: Skin and conjunctival biopsy specimens of melanocytic lesions from 27 pediatric patients formed the study group. The age at presentation ranged from 8 months to 14 years. The mean age at diagnosis was 10.28 years. Twelve (44.44%) lesions were from male children and 15 (55.56%) from female children. Majority, 18 (66.67%) were found in head and neck region. Of 27 childhood melanocytic lesions, 5 (18.52%) were benign pigmented lesions, 20 (74.07%) were benign nevi and 1 (3.70%) case each of non-giant congenital melanocytic nevus and Spitz nevus. No case of malignant melanoma was reported.

Conclusion: Our data highlights the female predominance of pediatric melanocytic lesions, with benign nevi being the most common and head and neck a favored site. Pediatric melanoma although a rarity in Asian children, should not be missed and must be differentiated from atypical spitzoid lesions, the great mimickers of true melanoma.

Keywords: Congenital nevus, Melanoma, Pigmented lesions, Spitz nevus.

INTRODUCTION

Melanocytic lesions in children are unique challenging propositions both for the dermatologist and the pathologist. Melanocytic lesions are common in the pediatric age group and a vast majority of these lesions are benign [1]. They arise from proliferation of one or more of these cells: melanocytes, nevus cells or melanoma cells. Childhood melanocytic lesions comprise a broad spectrum of benign and rarely malignant conditions. They are usually divided into benign pigmented lesions, also known as melanocytoses (freckles, solar lentigines, lentiginosis, Becker's melanosis, Mongolian spot, blue nevus), benign nevi (junctional, compound, intradermal), special variants of nevi (Spitz nevus, spindle cell nevus, non-giant and giant congenital melanocytic nevus, dysplastic nevus) and malignant melanoma [2].

Systemic anomalies like spinal dysraphism and neuro-cutaneous melanosis can also coexist with melanocytic lesions in children [3]. The potential for malignant change in melanocytic lesions is a cause for concern and distinction between benign nevus and malignant melanoma is crucial and at times can be extremely difficult. For instance, the histological features in spitz nevi can closely mimic those of malignant melanoma. It is therefore important for pathologists and clinicians to be aware of the spectrum of melanocytic lesions in children as well as potentially worrisome features of pigmented lesions. Although the incidence of melanoma has increased dramatically over the past three decades, childhood melanoma still remains uncommon [4-6].

A literature search shows the paucity of studies on childhood melanocytic lesions in the Asian region. The aim of the present study was to decipher the clinicopathological spectrum of melanocytic lesions in Asian children because of rarity of such studies in our population.

MATERIALS AND METHODS

Patients

A retrospective analysis of all the cases diagnosed as melanocytic lesions in children (under 14 years of age) between January 1995 and December 2014 from Department of Pathology, Tertiary Care Hospital, North India was undertaken. Patients less than 14 years of age were included based on the availability of the clinicopathological data. The histopathological

reports were reviewed to provide the following: age at diagnosis, gender, site of lesion and histopathological diagnosis. Exclusion criteria were; patients above 14 years of age, non availability of complete clinicopathological data and non melanocytic pediatric lesions. Skin and conjunctival biopsy specimens of melanocytic lesions from 27 pediatric patients formed the study group.

Tissue Samples

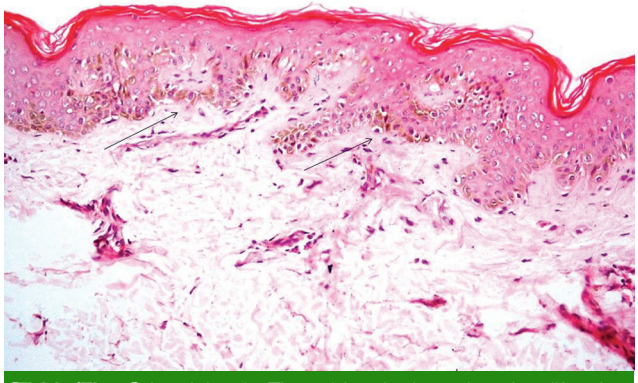
Specimens had been originally fixed in 10% formaldehyde solution for 24 hours and embedded in paraffin blocks. Sections of 3µm thickness were stained with hematoxylin and eosin (H&E) for light microscopy and assessed by a team of pathologists.

Histopathological Findings

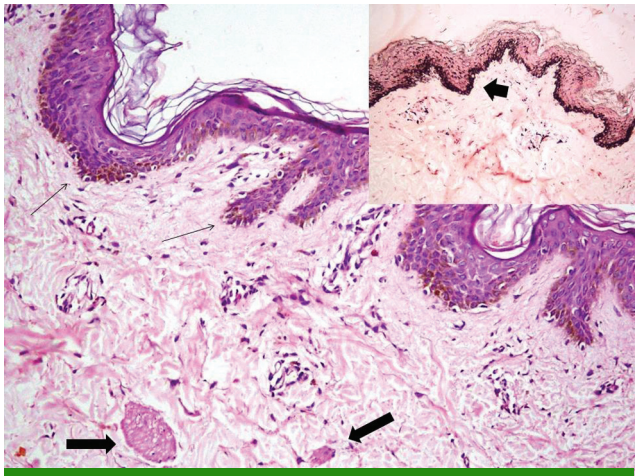
Histopathology of Mongolian spot showed scattered melanin containing melanocytes and melanophages in the dermis. In Becker's melanosis, hyperpigmentation of the basal layer was seen along with few dermal melanophages. Well circumscribed nests of cuboidal nevus cells were seen within the epithelium bulging downward into the subepithelium in the case of junctional nevus of the conjunctiva. Compound nevi showed nests of nevus cells in the dermis with some junctional activity and in intradermal nevi nevus cells were present in dermis with no junctional activity, and few of them showing maturation towards the base. A case of spitz nevus showed hyperkeratosis, irregular acanthosis and nests of variable sized tumor cells in the dermis. Junctional activity was also seen.

RESULTS

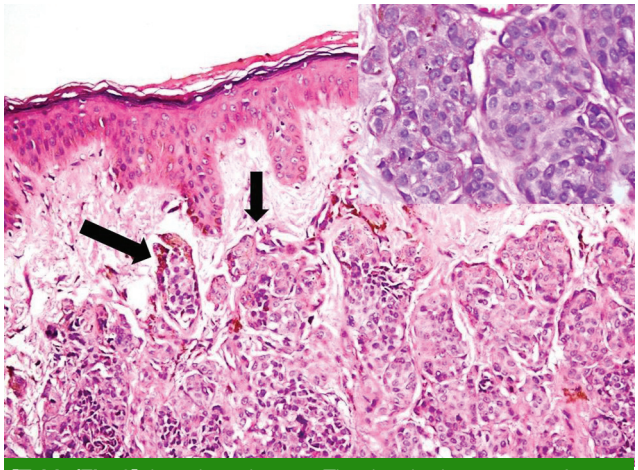
A total of 20,732 pediatric patients below the age of 14 years were screened for melanocytic lesions. Of these 1,248 patients were diagnosed clinically to have melanocytic lesions. Twenty seven cases were confirmed as melanocytic lesions on histopathological examination. Skin and conjunctival biopsy specimens from these 27 pediatric patients formed the study group. Complete spectrum of benign pigmented lesions [Table/Fig-1,2], benign nevi [Table/Fig- 3] and special variants of nevi [Table/Fig-4,5] is shown in [Table/Fig-6]. No case of malignant melanoma was reported.



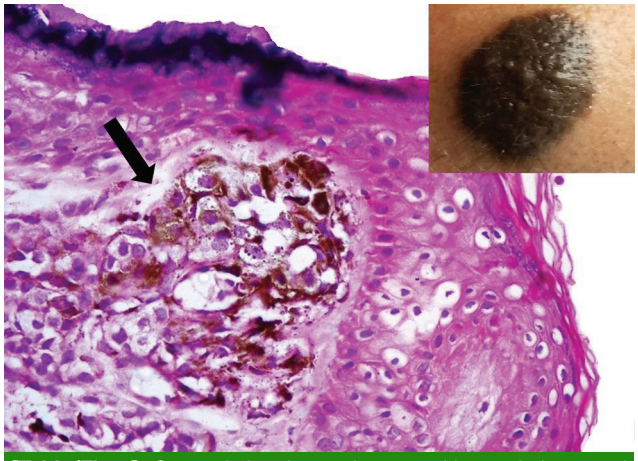
[Table/Fig-1]: Lentiginosis: The epidermis shows basal proliferation of melanocytes (arrows) (H&E, x100).



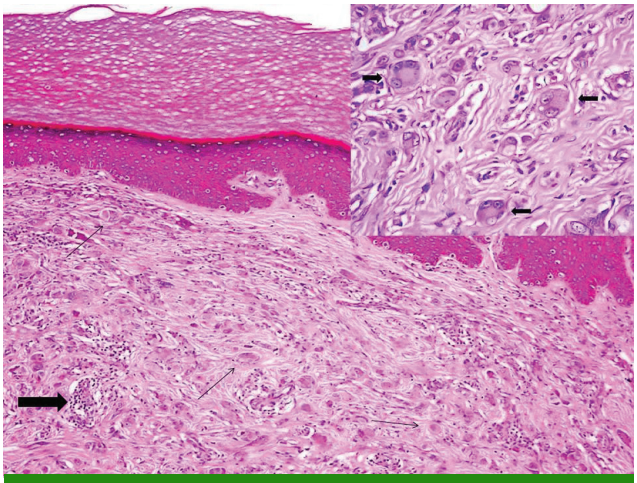
[Table/Fig-2]: Becker's melanosis: Epidermal basal layer hyperpigmentation (arrows), few dermal melanophages and smooth muscle bundles (block arrows) are seen (H&E, x100). Inset shows melanin (arrow) highlighted on Masson Fontana (MF, x100).



[Table/Fig-3]: Intradermal nevus: The dermis shows nests of nevus cells (arrows) (H&E, x200). Inset shows small nuclei without atypia, tiny nucleoli and melanin pigment in the cytoplasm (H&E, x400).



[Table/Fig-4]: Congenital melanocytic nevus: Nests of pigmented nevus cells at the dermal-epidermal junction (arrow) (H&E, x400). Inset shows clinical photograph of slightly raised pigmented nevus with growth of hair.



[Table/Fig-5]: Spitz nevus: Sheets of spindled to polygonal nevus cells (thin arrows) along with patchy inflammatory infiltrate (thick arrow) (H&E, x100). Inset shows bizarre giant cells (arrow) with regular nuclei of similar size containing prominent nucleoli (H&E, x400).

Lesions	Skin	Conjunctiva	n (%)
Benign Pigmented Lesions	**5**	**0**	**5 (18.52%)**
Mongolian spots	1	0	1 (3.70%)
Becker's melanosis	3	0	3 (11.12%)
Lentiginosis	1	0	1 (3.70%)
Benign Nevi	**13**	**7**	**20 (74.07%)**
Junctional nevi	1	1	2 (7.40%)
Compound nevi	2	6	8 (29.6%)
Intradermal nevi	10	0	10 (37.0%)
Special Variants of Nevi	**2**	**0**	**2 (7.41%)**
Spitz nevus	1	0	1 (3.70%)
Congenital melanocytic nevus	1	0	1 (3.70%)
Malignant Melanoma	**0**	**0**	**0**
Total	20	7	27 (100%)

[Table/Fig-6]: Distribution of melanocytic lesions among skin and conjunctival specimens.

The age at presentation ranged from 8 months to 14 years. However, in 7 cases, lesions were present since birth. The mean age in years [mean ± SD] at diagnosis and gender distribution for different lesions is given in [Table/Fig-7]. Distribution of childhood melanocytic lesions in various sites is summarized in [Table/Fig-8].

DISCUSSION

Majority of children do not have visible pigmented cutaneous lesions at birth. Congenital pigmented lesions are seen in less than 2% children only [7]. Congenital melanocytic lesions were seen in 7 cases only in our study. As the age increases the tendency to develop acquired melanocytic lesions increases. In some parts of the world, more than 50%

Lesions	Age at diagnosis (years ± SD)	Gender (%)	
		Male (%)	Female (%)
Benign Pigmented Lesions	**8.73 ± 4.95**	**3 (60)**	**2 (40)**
Mongolian spots	0.66 ± 0	1 (100)	0
Becker's melanosis	11.33 ± 2.49	1 (33.33)	2 (66.66)
Lentiginosis	9 ± 0	1 (100)	0
Benign Nevi	**11.2 ± 3.15**	**9 (45)**	**11(55)**
Junctional nevi	10.5 ± 0.71	2 (100)	0
Compound nevi	10.37 ± 2.61	3 (37.5)	5 (62.5)
Intradermal nevi	12 ± 3.77	4 (40)	6 (60)
Special Variants of Nevi	**5 ± 4.24**	**0**	**2 (100)**
Spitz nevus	2 ± 0	0	1 (100)
Congenital melanocytic nevus	8 ± 0	0	1 (100)
Malignant Melanoma	0	0	0

[Table/Fig-7]: Demographic data of childhood melanocytic lesions (n=27).

Lesions	Head & Neck (%)	Torso (%)	Extremities (%)	Total (%)
Benign Pigmented Lesions	**1 (20)**	**3 (60)**	**1 (20)**	**5 (100)**
Mongolian spots	0	1 (100)	0	1 (100)
Becker's melanosis	0	2 (66.66)	1 (33.33)	3 (100)
Lentiginosis	1 (100)	0	0	1 (100)
Benign Nevi	**17 (85)**	**2 (10)**	**1 (5)**	**20 (100)**
Junctional nevi	2 (100)	0	0	2 (100)
Compound nevi	8 (100)	0	0	8 (100)
Intradermal nevi	7 (70)	2 (20)	1 (10)	10 (100)
Special Variants of Nevi	**0**	**2 (100)**	**0**	**2 (100)**
Spitz nevus	0	1 (100)	0	1 (100)
Congenital melanocytic nevus	0	1 (100)	0	1 (100)
Malignant Melanoma	**0**	**0**	**0**	**0**
Total	18 (66.67)	7 (25.92)	2 (7.41)	27 (100)

[Table/Fig-8]: Site of distribution in childhood melanocytic lesions (n=27).

pediatric population may have melanocytic lesions of skin and conjunctiva [7-9]. Most of the melanocytic lesions in children are benign and melanoma arising before puberty is extremely rare [10]. In the current study no case of malignant melanoma was reported. However, the rising incidence of melanoma in pediatric age group over the past 30 years warrants a prompt and accurate diagnosis [11]. The relevant features to establish the correct diagnosis include; age of presentation, localization and histopathological findings [12]. The distinction between benign nevus and melanoma even on histopathology can be

very challenging in few cases [13].

Benign melanocytic proliferations lesions may be present in the epidermis or dermis. Freckles, solar lentigines, lentiginosis, the melanocytic macules seen in Albright's syndrome and Becker's melanosis constitute the epidermal melanocytoses. Mongolian spot, nevi of Ota and Ito and the blue nevus are categorized under the dermal melanocytosis [2]. Benign proliferations of melanocytes form nevi which can be congenital or acquired. Congenital nevi appear at birth or within first 6 months of life and acquired nevi become clinically apparent in the first or second decade of life. They can be classified as junctional, compound and intradermal on histologic examination. The junctional nevus is only seen in early life and shows nests of nevus cells within the lower epidermis. The nevus cells may bulge into the papillary dermis however the contact with the overlying epidermis is intact. In compound nevus the nevus cells are present at the dermoepidermal junction and may extend into the deep dermis as well. The junctional activity is characteristically absent in the intradermal nevus. The papillary dermis shows nests of nevus cells. Spitz nevus, spindle cell nevus, non-giant and giant congenital melanocytic nevus and dysplastic nevus are special variants of nevi.

In the present study, of 27 melanocytic lesions, 18.52% were melanocytoses, 74.07% were nevi and 7.41% were special variants of nevi including one case of Spitz nevus. These results are similar to previous reports from Aykol et al.,[9] which showed a prevalence of 73.85% for common melanocytic nevi. A comparative analysis of the present results with other studies on childhood melanocytic lesions is done in [Table/Fig-9].

Out of total melanocytic nevi in our study, 7.41% were junctional nevi, 29.63% were compound and 37.04% were intradermal. Novais et al., [12] in their study on conjunctival specimens observed that 4.5% of total nevi were junctional, 63.6% were compound and 31.8% were subepithelial. Shields et al., [16] found preponderance of compound nevi 70%, followed by subepithelial nevi 24%, combined nevi 4%, blue nevi were 3% and junctional nevi 3%. The results in studies by Novais et al., [12] and Shields et al., [16] are not in concordance with the results of our study. This discordance can be explained on the basis of the time gap between the age at the time of appearance of lesion and the age at the time of seeking clinical attention. The reason for this time gap in our study population could be the ignorance towards skin lesions due to lack of awareness and poor health facilities in the country. Junctional and intradermal are different stages of progression of nevi which explains the higher incidence of junctional nevi at an early age. During progression from junctional to

Place	Author, year	Study period	No. of cases	Median age	Sex predilection	Common site	Morphologic spectrum
Rio de Janeiro	Bomm et al., [4] 2014	2000-2010	63	7.7 years	M=F	Trunk	Compound nevi: 13 Junctional nevi: 4 Intradermal nevi: 3 Spitz nevi: 12 Atypical & Congenital nevi: 4 each Blue nevus: 1 Melanoma: 22
Lithuania	Valiukeviciene et al.,[7] 2005	2005	445	NA	M>F	Trunk	Melanocytic nevi: 86% Atypical melanocytic nevi: 7% & CMN: 3%
Austria	Moscarella et al., [10] 2012	1998-2007	22564	NA	F>M	Trunk	Nevi: 22526 (Dermal 33.2%, Compound 33.2%, Clark 21.3%, Congenital 7.9%, Spitz/Reed 1.9%) & Melanoma: 38
Stanford	Berk et al.,[11] 2010	1995-2008	25	Melanoma: 17 years MelTUMP: 10 years SNAF: 6 years	F>M	Melanoma: Trunk MelTUMP: Head/ neck SNAF: Extremities	Melanoma: 13 MelTUMP: 7 SNAF: 5
Ankara, Turkey	Akbas et al.,[14] 2015	NA	64	NA	F>M	Head and trunk	Benign melanocytic nevi: 58 & Becker nevus: 6
Puducherry, India	Senthilkumar et al.,[15] 2006	2002-2004	41	1.4 years	F>M	Back	Mongolian spots: 30 CMN: 8 Giant CMN: 1 Nevus spilus: 1 Nevus of Ota: 1
North India	Present study	1995-2014	27	10.3 years	F>M	Head and neck	Benign pigmented lesions: 5 (18.52%) Benign nevi: 20 (74.07%) CMN: 1 (3.70%) Spitz nevus: 1 (3.70%)

[Table/Fig-9]: Comparative studies on childhood melanocytic lesions.
*M: Male; F: Female; CMN: Congenital melanocytic nevus; MelTUMP: Melanocytic tumor of uncertain malignant potential; SNAF: Spitz nevus with atypical features.

intradermal, the nevus cell nests migrate from the epidermis to the dermis. The median age of our patients with junctional nevus was 10.5 years and with intradermal nevi was 12 years. All moles undergo changes as part of their natural course, and most changing moles do not represent melanomas [17]. These may increase or decrease in size, become darker or lighter as the time progresses [16]. Changes may occur as a result of involution, irritation or hair follicle rupture.

Studies have found that prevalence of melanocytic lesions shows a rise with increasing age [7]. However, some researchers believe that the number of nevi per unit of skin area show an increase only till 9 years of age [8]. Our study has also shown similar results. 11.11% lesions were noted in children aged 0-5 years, 33.33% lesions were noted in children aged 6-10 years and 55.56% lesions were noted in children aged 11-14 years.

The present study shows a gender distribution of melanocytic lesions as: 44.44% in males versus 55.56% lesions in females. Most researchers have found a higher number and density of melanocytic nevi in boys compared with girls [8,18,19]. The reasons for this discordance can be a small sample size and frequent reporting to the dermatology clinic by females because of the cosmetic reasons.

In our study 66.67% lesions were noted in face and neck region including conjunctiva, 25.92% lesions were in torso region and 7.41% lesions were over extremities. In males, 66.67% lesions and in females, 55.55% lesions were in face and neck region. These observations are in concordance with various studies done worldwide according to which median densities of nevi were highest on the face [20-22]. When taken together, nevus densities were highest on exposed body sites [23]. Besides skin and conjunctiva, melanocytic lesions may also be found in choroid [24], gastrointestinal tract [25], cervix and vagina [26,27]. However, in our study, we did not come across such sites, as most of these sites are rarely sampled in pediatric age group because of the asymptomatic nature of these lesions. Differences in pattern of sun exposure may be responsible for the gender variation in the anatomic site distribution of melanocytic lesions [21].

LIMITATIONS

The limitations of our study are its unicentricity and a relatively small sample size over a considerably long time period, which could be due to infrequent sampling of majority of pediatric melanocytic lesions which appear clinically benign where only reassurance is given and lesions are not biopsied.

CONCLUSION

Our experience is a single-centre clinical and histopathological study of pediatric melanocytic lesions. To the best of our knowledge, this is the first study of its type from Asia spanning over 20 years in which histopathological specimens of skin and conjunctiva were analyzed to comment upon the age at diagnosis, gender, site of lesion, and histopathological diagnosis. Our results indicate that mean age at diagnosis is 10.28 years, melanocytic lesions are more common in females as compared to males, the most common site of these lesions is head and neck and benign nevi are the most common melanocytic lesions in the pediatric age group.

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