



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.2538338>Available online at: <http://www.iajps.com>

Review Article

**CONGENITAL MELANOCYTIC NEVUS UPDATED REVIEW
IN MANAGEMENT APPROACHES**

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Abstract:

It is clear that the complexity of the managing concerns enhances with larger CMN, and has higher probability of complication, however management and proper monitoring is important for all cases. This article is intended to provide an information on the managing of congenital melanocytic nevi (CMN). We conducted a search through electronic databases; PubMed, and EMBASE, for studies published in English language thought instant to 2018. The monitoring of patients with CMN is complex. Melanoma risk has historically been overstated. The proof supporting a reduced malignant risk of congenital melanocytic nevi, together with the absence of proof that surgical procedure boosts outcomes, opens a restored argument with regard to the indicators for surgical treatment in addition to the extent of surgery that may be suitable. Nonsurgical management and partial excisions ought to be integrated as a legitimate part of any treatment algorithm. Validated instruments determining both patient-reported and also aesthetic outcomes would likewise be helpful in providing data relating to the result surgical procedure may carry health-related lifestyle.

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Please cite this article in press Ali Ahmed Alabdullah et al., *Congenital Melanocytic Nevus Updated Review In Management Approaches.*, Indo Am. J. P. Sci, 2019; 06(01).

INTRODUCTION:

The term "nevi" is utilized within the field of dermatology to explain different skin lesions of a benign etiology. Melanocytic nevi particularly refer to common moles on the skin. Melanocytes, the skin cells in charge of producing the color or pigment of the skin and also hair, are usually evenly dispersed within the basal layer of the skin. Melanocytic nevi have clusters or nests of modified melanocytes (referred to as "nevocytes") within the epidermis and/or dermis. Both melanocytes and nevocytes originate within the neural crest prior to moving to the skin in early fetal life.

Congenital melanocytic nevi (CMN) are melanocytic nevi defined by their presence at birth or in the first few weeks of life. Frequently their distinct morphology and variation in size can distinguish them from obtained nevi in older youngsters and also adults. Small and also medium-sized CMN are common, whereas huge as well as 'giant' sized CMN are uncommon, seen in 1/20 000- 1/500 000 babies [1]. CMN might be present anywhere on the body as well as can have a more diverse range of colors (various tones of brown, black, pink, and also tan) and also topographical modifications, such as hairiness, superimposed nodules and also papules, and a verrucous or mammillated surface area. Possible complications from CMN include melanoma development and also main nervous system participation termed neurocutaneous melanosis (NCM).

It is clear that the complexity of the managing concerns enhances with larger CMN, and has higher probability of complication, however management and proper monitoring is important for all cases. This article is intended to provide an information on the managing of congenital melanocytic nevi (CMN).

METHODOLOGY:

We conducted a search through electronic databases; PubMed, and EMBASE, for studies published in English language thought instant to 2018. Studies discussing the Congenital Melanocytic nevus were included whether were reviews or control studies. We excluded case reports. Moreover, references of included studies were scanned for more relevant articles.

DISCUSSION:

- **Clinical Presentation and Natural History**

Congenital melanocytic nevi (CMN) are, by definition, present at birth but might not become apparent up until the very first few months of life.

Small melanocytic nevi that appear beyond the neonatal duration and approximately age 2 years often share similar features with CMN and also are frequently referred to as "congenital nevus-like nevi." CMN are classified mainly on the basis of size, with groups defined by maximal projected diameter in adulthood (Table 1). Dimension is established by measuring the maximal size, and after that the axis perpendicular to this; to calculate the projected adult dimension in an infant, the maximal diameter is multiplied by an approximated variable based upon the location of the nevus (head, 1.7-fold; trunk as well as upper extremities, 2.8-fold; lower extremities, 3.4-fold) [2]. Different category plans have been released, with the most current consensus-based system created to promote even more exact recognition and also risk stratification for the growth of considerable complications. This particular schema consists of not only projected adult size but likewise various other morphologic qualities, such as area, existence of nodularity, and number of satellite nevi [2].

CMN look like pigmented lesions varying in color from tan to black, with borders that are usually well specified. In addition to proportional enlargement with the kid's growth, CMN might undergo various other morphologic transformations with time. Although CMN are normally initially soft and also smooth, they may develop a grown density of coarse dark hair within the lesion, called hypertrichosis. They can end up being more elevated, with the surface appearing pebbly, verrucous, and even cerebriform [3]. Dermal melanocytes within CMN can likewise undertake neurotization (ie, the differentiation to peripheral nerve sheath cells) leading to plaques similar in look to plexiform neurofibromas [3]. Transient ulcer within the lesion might take place in the neonatal duration as a result of boosted skin fragility in this age. Ulceration and also, a lot more particularly, nonhealing locations within the nevus past the neonatal period may indicate malignant makeover as well as call for punctual clinical assessment. Occasionally, proliferative nodules might show up within the lesion and also can increase problem for malignant transformation; dermatologic examination is warranted for these patients [3]. Alternatively, CMN might sometimes regress in time; this has been reported specifically in CMN located on the scalp [4]. This process might take place, nevertheless, at any type of site, as well as might be preceded by the growth of local dermatitis and/or a depigmented "halo" bordering the sore [4].

- **Complications and Associations**

Neurologic sequelae. Neurologic difficulties of CMN include both neurocutaneous melanosis (NCM) and also spine dysraphism (connected with large CMN in the lumbosacral area). NCM is an entity special to children with CMN, and consists of proliferation of nevocytes within the central nervous system, a reminder of the neural embryologic origin of these cells. The threat of NCM is largest in those with numerous CMN sores, regardless of size [5]. Regularly, this appears as a large "mothership" CMN (forecasted adult dimension > 20 centimeters) accompanied by multiple satellite nevi. Threat is highest for NCM when more than 20 satellites exist. Nevertheless, approximately onethird of patients with NCM will certainly have numerous small to medium CMN without a larger sore [5]. Large CMN in a posterior axial area have additionally been cited as a threat factor for NCM [5].

NCM may be symptomatic in a small percentage of patients, with estimates of prevalence ranging from 4.5% to 11% of patients with this problem [6]. It can materialize as a range of neurologic signs, such as developmental delay, seizures, or hydrocephalus. Prognosis in such cases is usually poor, with high death rates in the first year of life [6]. NCM may additionally be seen on gadolinium enhanced magnetic resonance imaging (MRI) in the absence of symptoms. Results are diverse and might consist of irregular foci within brain parenchyma, diffusely thickened meninges, posterior fossa irregularities, and spinal irregularities. The diagnosis in these cases remains vague, as neurologic symptoms appear to develop in only a portion of youngsters with MRI

problems [7]. Therefore, doing MRI to screen for NCM in asymptomatic but at-risk youngsters remains controversial, especially provided the growing body of literature suggesting that the anesthesia that might be needed for MRI may contribute to adverse neurodevelopmental end results [7]. If a screening MRI is carried out, it needs to ideally be done prior to age 6 months to optimize visualization of melanosis prior to myelination, and when supposed "feed and sleep" studies can be done without anesthetic by bundling the baby after feeding [1]. From a pediatric perspective, frequent neurologic exam, measurement of head circumference, and ongoing developing assessment are important in children with high-risk CMN. Referral to pediatric neurology and/or neurosurgery might be shown.

Melanoma and other neoplasms. Risk variables for the development of melanoma in CMN include large or giant size, with approximated life time danger of 2% to 5% [8]. Moreover, of those patients with large/giant CMN who take place to develop melanoma, approximately 50% do so by age 5 years [9]. Posterior axial area as well as several satellite nevi stand for extra risk aspects for advancement of melanoma within large CMN [1]. In contrast, the danger of melanoma developing within small or mediumsized nevi is estimated at about 1% and also has a tendency to take place postpubertally [9] Of note, melanoma can also rarely develop within the main nervous system of youngsters with NCM. Various other malignancies have actually likewise been reported in kids with big CMN, including rhabdomyosarcoma, liposarcoma, as well as malignant peripheral nerve sheath tumors, but these are likewise unusual [1].

TABLE 1. Classification of Congenital Melanocytic Nevi by Projected Adult Size as Defined by Consensus-Based Classification [2].

Category	Projected Adult Size (cm)
Small	<1.5
Medium	—
M1	1.5-10
M2	>10-20
Large	—
L1	>20-30
L2	>30-40
Giant	—
G1	>40-60
G2	>60

- **Relation between small and medium CMN and genetics**

Although the visibility of CMN is thought to be a sporadic event, small CMN are usually identified in

several relatives within families. CMN rise because of mutations within proteins of the mitogen-activated healthy protein kinase signal transduction pathway (MAPK), in particular NRAS as well as BRAF

hotspots. This pathway plays an important function in gene expression and also cellular development and also survival. Over the last decade, a developing pattern pertaining to the connection between size of the CMN and also corresponding hereditary mutation has actually been defined [10]. Small CMN are more frequently kept in mind to have a BRAF (V600E) mutation compared to their medium, and also large/giant counterparts that much more regularly harbor NRAS (Q61) mutations [10], [11].

- **Relation between Large, giant, and multiple medium CMN and genetics**

Somatic mutations in the NRAS genetics have actually been called the key reoccurring mutation in large/giant/multiple CMN, recategorizing this group of individuals as having a mosaic RASopathy [10], [11] Kinsler et al. [11]. described the hereditary findings in 15 patients with numerous CMN (nine large/giant, four-medium, two-multiple medium CMN), with 12 of 15 patients positive for NRAS (Q61) anomaly existing in their CMN and also absent from the blood and also unaffected tissues, confirming NRAS mosaicism. This mutation was additionally existing in all 11 CNS samples (five people). Main melanoma developed in 3 cases in this cohort, with postmalignant samples readily available for 2. DNA evaluation disclosed a development to loss of heterozygosity with the development of malignancy, along with gains and also losses of chromosomal pieces and whole chromosomal changes. Later on, Salgado et al. explained a BRAF (V600) mutation in a small minority of individuals (n 1/4 5, 7.6%) with large/ gigantic CMN compared with those with NRAS mutations in 77.3% (n 1/4 51) in their cohort, illustrating NRAS is not the special mutation in individuals with larger CMN [12]. Because of these current hereditary discoveries, using targeted treatments to deal with patients has actually been taken into consideration. Ku ¨sters-Vandeveldt et al. described a 13-year-old boy with progressive leptomeningeal illness, with a somatic NRAS (Q61K) mutation in the CMN as well as CNS [13]. Compassionate treatment with a MEK inhibitor was begun, however with the patient's demise 5 days later on. Although the true medical results of the therapy cannot be analyzed due to short therapy span, immunohistochemical evaluation of affected tissue postmortem recommended a possible effect of MEK inhibition. Extra evidence of the energy of specific NRAS inhibitors has actually been received an in-vitro model of nevospheres created from sores of the

spinal cord, brain, and skin from 4 NCM individuals [14].

TREATMENT:

Small and Medium Congenital Melanocytic Nevi management

As CMN can have extra varied, and at times, irregular appearing qualities, a standard skin checkup with a dermatologist or pediatric dermatologist is warranted. For small and also average CMN, as soon as a baseline benign examination is established, individuals may be asked to go back to the dermatologist's office at pubertal age, when the risk of melanoma growth most likely begins. Nonetheless, fast development, topographical changes, and also signs (such as ache, itching, and blood loss) ought to prompt the patient to return for immediate evaluation. Life time melanoma risk in individuals with small and also (single) medium CMN is estimated to be less than 1% and also has a tendency to start at puberty. An organized evaluation of the literature of kids up to age 18 years with fatal or metastasizing melanoma with CMN disclosed 178 cases of youth melanoma (112 cutaneous) from 1887 to 2010 [15]. Just 18 individuals with a small CMN and also 10 patients with a medium CMN developed deadly melanoma over this period. Based on the rarity of melanoma development in small/medium CMN before their adult years, prophylactic excision in childhood years based upon pure melanoma risk is no longer warranted [16].

There are different reasons for elimination of small as well as medium CMN (Table 2). Smaller sized CMN may be removed by key excision, whereas larger sores may call for a presented excision or use of a tissue flap or graft. Alternate modalities (such as dermabrasion and lasers) have been utilized. These methods should not be thought about first-line, and they ought to only be thought about when removal is sought for psychosocial and also cosmetic factors, as well as in cases where surgical excision is not perfect, or the sore is unusable, and also, they ought to not be made use of for CMN that are symptomatic, quickly transforming, and potentially malignant. Considering that these elimination techniques typically use partial elimination of the CMN and also subsequent scarring, life time follow-up after treatment is still needed. A superb table pertaining to elements to think about in the monitoring of small and also moderate CMN can be located in the article by Schaffer [16].

TABLE 2. Reasons for consideration of removal of small and medium CMN [13],[14].

Chronic, unrelenting symptoms, such as itching or irritation
Changes concerning for melanoma development (clinical or histologic)
Locale causing psychosocial distress, usually highly visible sight, such as face and larger lesion - possibly with 'unappealing' surface features such as hair or warty texture
Functional concerns (e.g., bulky or exophytic lesions in the groin or periorbital area)
High level of parental or patient anxiety regarding the lesion
Inability to safely monitor the lesion because of location or topography/coloration
Family/patient unwilling or unable to follow monitoring plan

Giant Congenital Melanocytic Nevi management

The monitoring of GCMNs is debatable and also highly depending on the individual patient. A mostly disputed issue in literature is when and also on whom to perform surgery. Treatment of GCMN varieties from careful waiting to less invasive treatments (dermabrasion, carbon dioxide laser ablation, curettage, chemical peels) to a lot of more extensive procedures (tissue development, en bloc or serial excision with staged direct closure, skin grafting, free tissue transfer, or skin substitutes) [16]. Variables that require to be taken into account when taking into consideration GCMN management include the presence of risky phenotypic features connected to malignant transformation such as size above 20 cm in diameter, trunk area, existence of 3 or more sores, as well as uneven morphology due to the lack of ability to determine morphological transformations [17]. Additional factors to consider unassociated to malignancy danger include the possibility of psychosocial effect and also cosmetic deformity [15].

Historically, treatment goals have centered on total excision of the GCMN before the age of 2 years because of increased risk for melanoma transformation. Arneja and also Gosain offered an algorithm for the treatment of GCMN with surgical excision as the ideal therapy strategy to eliminate pigmented nevus cells as well as lower malignant change [17]. Contrarily, various other studies have actually suggested a much more conservative and also much less invasive method to treating GCMN. De Raeve et al and also Rasmussen et al recommended using curettage to decrease the variety of melanocytic cells as well as potentially reduced the risk for cutaneous melanoma [18], [19]. Current literary works has actually likewise commented that previous literary works overestimated the risk for melanoma as a result of reporting bias and also less

precise histological methods of diagnosis which the true danger lies between 0.7% as well as 2.8% [15-16]. Moreover, a number of research studies have not had the ability to show a decrease in melanoma modification threat with medical administration [20-22]. Granted, these studies have been restricted in both sample dimension as well as follow-up time. Actually, there have actually been 5 instances in the literary works in which melanoma has actually developed in a site of excision and also grafting [23]. As a result of these new data, Arad and also Zuker recently said that therapy ought to focus on esthetics and also out complete excision [24].

Nonetheless, medical excision can be suggested for medical problems outside malignant change including painful ulceration and also bleeding, physical discomfort, worrying dermatologic modifications, several expected surgical procedures, concomitant surgical procedures, and psychosocial distress [25]. Early excision possibly lowers recuperation time and also psychological injury as a result of the patient's lack of recollection of not just the nevus however likewise the surgical procedure [25]. Therefore, in considering the case for prophylactic resection, the nonmalignant sequelae of GCMN have to be factored right into the equation.

CONCLUSION:

The monitoring of patients with CMN is complex. Melanoma risk has historically been overstated. The proof supporting a reduced malignant risk of congenital melanocytic nevi, together with the absence of proof that surgical procedure boosts outcomes, opens a restored argument with regard to the indicators for surgical treatment in addition to the extent of surgery that may be suitable. Nonsurgical management and partial excisions ought to be integrated as a legitimate part of any treatment

algorithm. Validated instruments determining both patient-reported and also aesthetic outcomes would likewise be helpful in providing data relating to the result surgical procedure may carry health-related lifestyle.

The disfigurement as well as painful therapy arising from a GCMN can negatively affect the psychosocial functioning of not just the patients however also their family members. Given the disfiguring nature of both the nevus itself as well as the postoperative scar, the patient's quality of life and also the cosmetic outcome of surgery must be taken into consideration when considering timing of surgical excision.

Neurologic involvement and melanoma continue to be the two most destructive problems in patients with multiple and also larger CMN. Recent advances in molecular techniques have actually revealed that various sorts of CMN are the outcome of unique mutations in NRAS and BRAF. New, genetically targeted treatments for patients with issues might be of value, and research for possible treatments is ongoing

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