Large or multiple congenital melanocytic nevi: Occurrence of neurocutaneous melanocytosis in 1008 persons

Bari Joan Bett, MD
West Salem, Ohio

Background: There is a dearth of information regarding the occurrence of neurocutaneous melanocytosis (NCM) in a large cohort of persons with large congenital melanocytic nevi (LMCN) or multiple congenital melanocytic nevi (MCMN).

Objective: The purpose of this article is to report occurrence of NCM and other complications in 1008 persons having LCMN or MCMN.

Methods: Evaluation of information obtained from a database of persons with LCMN or MCMN voluntarily submitted by the affected persons to a nevus support group, the Nevus Network.

Results: Of those with truncal LCMN, 6.8% developed significant complications, 4.8% developed symptomatic NCM, and 2.3% died from either benign or malignant NCM or cutaneous melanoma. Of the 4.8% of persons with a truncal nevus who developed symptomatic NCM, 34% died. Of those with head or extremity LCMN, 0.8% developed symptomatic NCM, and, to date, none have died from any cause. Of the small number with MCMN without a giant nevus, 71% developed symptomatic NCM, and 41% died of it.

Limitations: Attending physician confirmation of submitted information was unavailable.

Conclusions: LCMN of the trunk were associated with a relatively low occurrence of medical complications and death in our group, considering the large nevomelanocytic burden present. If symptomatic NCM developed in those with truncal nevi, the occurrence of death rose to a third. LCMN of the head or extremity were associated with minimal medical complications and no deaths. In contrast, most of the rare persons (N = 17) with MCMN developed symptomatic NCM, and more than a third died. (J Am Acad Dermatol 2006;54:767-77.)

The term *neurocutaneous melanosis* was first used by Van Bogaert[1] in 1948 and is now more accurately characterized as neurocutaneous melanocytosis (NCM). NCM is defined as large or multiple congenital cutaneous nevi with benign or malignant leptomeningeal melanocytosis.[2,3] NCM is a rare syndrome first reported by Rokitansky[4] in 1861. Reports of other cases[5-9] have since been published, but reliable information regarding occurrence of NCM in large numbers of at-risk persons has been sparse. We describe the occurrence of NCM in a database of 1008 persons with large or multiple congenital cutaneous nevi in this article. The occurrence of cutaneous melanoma among the members of this database has previously been published.[10]

Large congenital melanocytic nevi (LCMN) are generally defined as nevi that have or are predicted

Abbreviations used:

BTN:	bathing trunk nevus
CALM:	café au lait macule
LCMN:	large congenital melanocytic nevi
MCMN:	melanocytic nevi
MRI:	magnetic resonance imaging
NCM:	neurocutaneous melanocytosis

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Correspondence to: Bari Joan Bett, MD, PO Box 305, West Salem, OH 44287-0305. E-mail: info@nevusnetwork.org.
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to have a largest diameter of at least 20 cm in adulthood. In our database, truncal nevi are defined as large (>20 cm) or giant (>40 cm) congenital melanocytic nevi in a torso or bathing trunk location. Stratification of nevi by size is not yet standardized, and a new classification has recently been proposed.[11] Infants with a nevus at least 9 cm in diameter on the skull or 6 cm in diameter on the body, and persons with a nevus covering a substantial portion of a small body area such as the face, hand, or foot were included.[7,12,13] The size of large congenital nevi in persons ages 1 to 18 years was estimated with the use of skin surface approximation charts.[5] Several persons with tardive large or giant nevi, nevi that slowly appear months to, rarely, years after birth, were included. One person with a giant café au lait macule (CALM), the brother of a person with an LCMN, was also included in the database. Satellite nevi are generally defined as excess deposits of nevomelanocytes in the skin manifesting clinically as scattered, small (<1.5 cm diameter) to medium (1.5-19.9 cm diameter) moles in the presence of a large or giant congenital nevus.[7,14] In addition, the very few persons born with only multiple (greater than or equal to 3, the least number of nevi reported in a patient with NCM[15]) congenital melanocytic nevi (MCMN), also small to medium, scattered, and without an accompanying giant nevus, were included.[2]

METHODS

Information obtained from 1072 persons by voluntary report through a nevus support group, the Nevus Network, was compiled. Initial and follow-up information was obtained via letter, telephone, or E-mail. Information in the database was entered by hand and is updated manually on a continual basis. Anonymity for entrants was offered and confidentiality is provided. Each person or guardian was asked to submit the following information: date of birth; gender; race; geographic location; location and size of the LCMN or MCMN; presence/absence/number of satellites; accompanying medical/psychosocial conditions; presence/absence/type/results of treatment; magnetic resonance imaging (MRI) dates and results; and presence of melanoma, NCM, hydrocephalus, seizures or other complications. The size of the nevus was estimated by actual measurement, photograph, paper drawing, or verbal/written description of the body surface involved. Our database does not yet distinguish between large or giant nevi. Data were incomplete on some entries, generally involving presence/absence/number of satellites, race, MRI results, and treatment. Independent verification of the submitted material by attending physicians was not available. However, the number of persons or guardians providing inaccurate information would most likely be low. Satellite nevi were distinguished from normal acquired melanocytic nevi by clinical history. The presence/absence of satellites was treated as a dichotomous variable as our database does not yet record the number of satellites for all entries. Follow-up ranged from several days to many years with a mean of 5.6 years. There were 5142 person-years of observation, with a person-year being 1 year of observation for 1 person. Database members were considered lost to contact if no current postal address, telephone number, or E-mail address was available.

RESULTS

There were 1072 persons in the database. Sixty-four were excluded, leaving 1008 persons. Those excluded were persons who were unwilling to share any information except that they had a family member with a nevus or who refused permission for inclusion of their information. Of the 1008 persons, 59.4%, including the author, had a truncal LCMN, either a bathing trunk nevus (BTN), torso (back and/or chest and/or abdomen) nevus, or torso with head (neck and/or scalp and/or facial) nevus. Of the remaining persons, 29.0% had a nevus of the head, 9.9% had an extremity nevus, and 1.7% had MCMN without a giant nevus.

Truncal LCMN and NCM

NCM was diagnosed in 35 of 599 persons with large or giant truncal nevi, as shown in Tables I and II. Persons with NCM were considered symptomatic if they had neurologic signs or symptoms that could reasonably accompany leptomeningeal melanocytosis such as hydrocephalus, seizures, tremors, cranial nerve palsies, developmental delay, or motor delay. Ten persons also developed hydrocephalus and/or seizures without having known evidence of NCM on MRI, as shown in Table III. The incidence of epilepsy (recurrent unprovoked seizures) in the general population is not well defined. Published figures vary from 0.001%[16] to approximately 1% from birth to age 20 years, rising to about 3% by age 75 years.[17] The incidence of hydrocephalus in the general population is thought to be approximately 1 in every 500 children (0.002%).[18] Although persons with LCMN can develop hydrocephalus or seizures for other reasons, the most common reason in our cohort would be NCM, especially as MRI scanning is not 100% sensitive. Therefore, these 10 persons also were classified as having presumptive symptomatic NCM, giving a total of 45 of 599 (7.5%) persons with NCM. This approach would overestimate the actual risk slightly. Age at diagnosis of NCM ranged from