• CASE REPORT •

Acquired Segmental Neuromas

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Neuromas are benign hyperplastic proliferations of normal peripheral nerve components. These can be associated with some genodermatoses, namely Cowden syndrome and multiple endocrine neoplasia (MEN) 2B, especially when numerous lesions are present. Given the potential for malignancy (such as breast cancer, pheochromocytoma, and thyroid cancer) associated with these syndromes, other features indicative of either syndrome should be evaluated in patients presenting with multiple cutaneous neuromas. The evaluation should include a thorough family history and complete physical, dermatologic, and ophthalmologic exams as well as thyroid studies. We report, herein, the case of an 8-year-old female with cutaneous neuromas distributed segmentally with no other associated finding suggestive of an underlying syndrome. [*P R Health Sci J 2013;2:101-103*]

Key words: Cutaneous Neuromas, Multiple Endocrine Neoplasia, Cowden Syndrome

The spectrum of benign nerve sheath tumors includes true neuromas, shwannomas, and neurofibromas. Neuromas are hyperplastic proliferations of the normal components of the peripheral nerve, including axons and Schwann cells. They lack any propensity for recurrence or malignant transformation (1,2). They can be further divided into traumatic neuromas, palisaded and encapsulated neuromas (PEN), and mucosal neuromas associated with multiple endocrine neoplasia (MEN) 2B.

Traumatic neuromas usually follow an injury and have an irregular disorganized architecture consisting of a proliferation of individual nerve fascicles separated by a fibrotic, sometimes inflamed, stroma. Amputation neuromas and rudimentary supernumerary digits are examples of traumatic neuromas.

PENs are benign, solitary neural neoplasms typically seen in adults. They commonly present as small asymptomatic, skin-colored papules on the face. They may also arise in other areas such as the neck, oral cavity, genitalia, trunk, extremities, and acral sites (2). Histopathologically, they are a well-circumscribed, poorly encapsulated, dermal proliferations of peripheral nerve fascicles.

Mucosal neuromas are a variant of PEN usually seen in MEN2B syndrome; they may have a more superficial location histopathologically (usually in the papillary dermis rather than in mid dermis). In immunohistochemistry studies, all three neuroma variants are S100-, neurofilament-, and myelin basic protein-positive.

We report the case of an 8-year-old female with isolated cutaneous neuromas distributed segmentally on the trunk and extremities without any other findings suggestive of MEN2B or Cowden sydrome.

Case Report

An 8-year-old female presented with multiple asymptomatic skin lesions that had manifested 4 years prior. The patient denied any history of prior trauma in the involved areas. Her past medical history was not significant; she denied any history of abdominal pain, nausea, vomiting, or diarrhea. There was no family history of similar lesions, neurofibromatosis or endocrine abnormalities.

On physical examination, there were numerous well-circumscribed, agminated, soft, pink-colored papules on the upper back, right forearm, and dorsum of the left hand (Figure 1). The individual papules measured about 0.5 cm each. Two café au lait macules (measuring 1 and 3cm) were noted on her lower abdomen. There was no axillary freckling or any oral mucosal or conjunctival lesions. No Lisch nodules or astrocytic hamartomas were noted during the ophthalmology exam.

A skin biopsy from one papule revealed a well-circumscribed unencapsulated proliferation of spindled cells separated by prominent clefts, forming round nodules in the papillary and mid dermis (Figure 2). A brain MRI was unremarkable, without evidence of optic glioma. Thyroid studies were normal. Negligible scoliosis was noted on a skeletal survey. Genetic evaluation was negative for the *RET* proto-oncogene and for mutations in the *NF1* gene. Further *NF1* mutation testing from RNA and DNA extracted from cultured Schwann cells from the tissue of one of the histologically-confirmed lesions was also negative.

Our patient was diagnosed with acquired cutaneous neuromas with a segmental distribution. As the lesions were asymptomatic, observation was recommended as the best treatment option for the patient.

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The authors have no conflicts of interest to declare.

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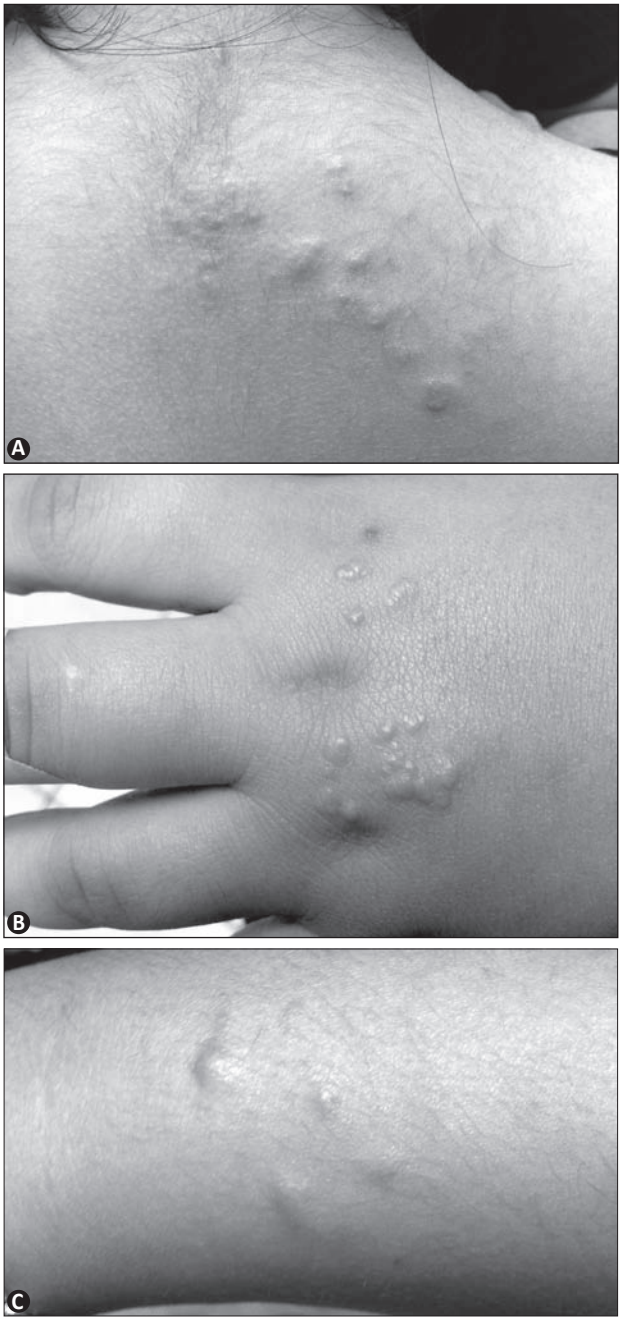

Figure 1. Erythematous soft grouped papules over the upper back (A), left hand dorsum (B), and right dorsal wrist (C).

Discussion

The histopathologic differential diagnosis of a neuroma includes neurofibroma and schwannoma. It is important to distinguish between the two and make an accurate diagnosis, given the potential associations with different syndromes that may accompany either diagnosis. Neurofibromas (NF) consist of less discrete neural bundles, lacking well-formed fascicles separated by clefts. Multiple neurofibromas may be seen in neurofibromatosis (NF1). Our patient had only two café au lait macules and no other features of NF1. Neuromas do not seem to be found more frequently in patients with NF (1).

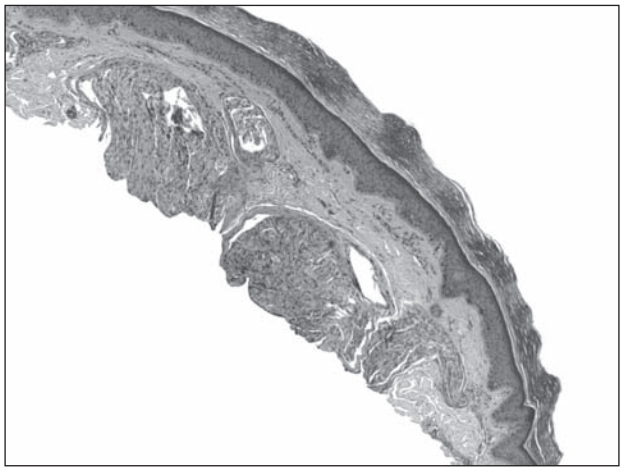

Figure 2. Round, well-delineated, unencapsulated proliferation of spindled cells separated by prominent clefts in the papillary dermis. (Hematoxylin and eosin stain, original magnification, 10X)

Schwannomas are peripheral nerve sheath tumors that, in contrast to neuromas, have thick collagenous capsules, true Verocay bodies, and hypocellular or myxoid (Antoni B) stroma (3). They tend to be deeper and have more palisading without axonal proliferation. Multiple schwannomas are characteristic of Schwannomatosis (Neurofibromatosis 2).

Recently, cutaneous neuromatosis has been described as an early manifestation of Cowden syndrome (CS), often appearing in early childhood, in contrast to the classic cutaneous manifestations of CS that often do not develop until late adolescence (4,5). CS and Bannayan–Riley–Ruvalcaba syndrome are part of the PTEN hamartoma tumor syndrome (PHTS), an autosomal dominant genodermatosis characterized by hamartomatous lesions involving tissues of ectodermal, mesodermal, and endodermal origin. A high risk of thyroid and breast cancer has been associated with CS. Patients with CS often develop multiple cutaneous hamartomas, such as trichilemmomas, oral papillomas, acral keratoses, sclerotic fibromas, and lipomas. Cutaneous neuromas are estimated to be present in 5 to 10% of all patients with CS (4). These are usually observed on the extremities or face (4). The lack of a family history of PHTS and the absence of characteristic CS findings (such as macrocephaly or any of the mucocutaneous lesions described above) makes this diagnosis unlikely in our patient.

Multiple mucosal neuromas are pathognomonic for MEN2B (Mucosal Neuroma Syndrome), an autosomal dominant disease characterized by medullary thyroid carcinoma, pheochromoctyoma, and gastrointestinal ganglioneuromatosis. A marfanoid body habitus and peculiar facies with everted eyelids, flat nasal bridge, and enlarged nodular lips are

characteristic. Mucosal neuromas typically present at birth or in early childhood (6). Cutaneous neuromas have been observed on the perinasal region, pinna, face, and trunk; however, these are rarely part of the syndrome (7,8,9,10). MEN2B without mucosal neuromas has not been reported in the literature (7).

Multiple cutaneous neuromas have been reported in 7 patients, some with features of MEN2B (11). For example, 1 had a marfanoid habitus (12) and another had medullary thyroid carcinoma (7). A RET mutation in exon 13 was confirmed in the latter; thus, it is unclear whether this patient had an unusual presentation of MEN2B or an overlap of MEN2A/2B, as the patient also had macular amyloidosis. Multiple cutaneous neuromas without systemic abnormalities have been reported in 5 patients (2,11,13,14,15). Two of these also had mucosal lesions (13,14).

Multiple cutaneous neuromas usually develop in adulthood, although they have been reported in 2 young patients, one who was 7 years of age, and the other who was 13 years of age (2,11). In the case of our patient, the lesions started when she was age 4. Linear arrangements have been observed (2,7,12,15). The distribution of our patient's cutaneous neuromas presented in a segmented fashion. To our knowledge, this presentation has not been described before.

Conclusion

We report a case of segmental cutaneous neuromas. A careful family history, a physical exam that includes a thorough dermatologic and ophthalmologic evaluation, and thyroid studies are of utmost importance given the potential association of multiple neuromas with MEN2B and PHTS. Long-term follow-up is warranted in these patients as the potential for developing a malignancy associated with these syndromes later in life remains.

Resumen

Los neuromas son proliferaciones benignas de componentes normales del nervio periférico. Éstos pueden estar asociados a algunas genodermatosis, como Síndrome de Cowden y Neoplasia Endocrina Múltiple 2B. Debido a la posibilidad de desarrollar cáncer (de mama, feocromocitoma y de tiroide), otras características indicativas de estos síndromes deben ser evaluadas en pacientes con múltiples neuromas cutáneos. La evaluación debe incluir un historial familiar detallado, examen físico, dermatológico y oftalmológico, así como estudios de tiroide. Presentamos el caso de una niña de 8 años de edad con múltiples neuromas cutáneos en una distribución segmental con ningún otro hallazgo indicativo de la presencia de un síndrome subyacente.

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