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Received 4 March 2018; accepted 23 October 2018

https://doi.org/10.1016/j.abd.2019.09.001
0365-0596/

Neurofibromatosis with vitiligo: an uncommon association rather than coexistence?☆,☆☆

Dear Editor,

Type 1 neurofibromatosis (NF1) is an autosomal dominant multisystem disease caused by a mutation in the neurofibromin 1 gene which affects tissues derived from the neural crest.[1] Clinically, it is characterized by a spectrum of defects comprising of neural tumors, *cafe-au-lait* spots, intertriginous freckling, and skeletal defects. Generalized vitiligo has rarely been reported with neurofibromatosis. Here, we present two cases of NF1 associated with vitiligo and showing the halo phenomenon in neurofibromas.

A 28-year-old male patient who was a known case of NF1 presented with multiple depigmented patches on the skin, which had started developing in the last four years. His family history revealed that his mother also had neurofibromatosis, with no history of any depigmented lesions. Dermatological examination revealed multiple well-demarcated, light-brown macules of size varying from 5 to 50 mm present over the trunk, back, and upper limbs. Numerous sessile as well as pedunculated dome-shaped papulonodular lesions of varying sizes, suggestive of neurofibromas, were present over the face, trunk, back, and upper limbs. Some of these lesions were encircled by a depigmented halo. Sharply defined depigmented patches, consistent with a diagnosis of vitiligo and varying between 2 and 7 cm in size, were present over back, elbows, and dorsum of hands and feet (Fig. 1). Bilateral axillary freckling was also seen. Slit lamp examination of iris showed the presence of Lisch nodules. Dermoscopy of the vitiligo lesion showed reduced pigmentary network as compared to normal skin (Fig. 2).

The second case was a 35-year-old male patient; a known case of neurofibromatosis presented with depigmented patches involving the normal skin and the skin surrounding the neurofibromas over the previous year. There was a family history of neurofibromatosis in his father and brother. On cutaneous examination, multiple dome-shaped, skin colored papulonodular lesions of variable sizes and soft in consistency were present over the face, trunk, back, and extremities. Some nodules had depigmented halo around them. Multiple well-demarcated, light brown colored patches, 5–20 mm in size, were present over back, chest and upper extremities. Sharply demarcated patches of depigmentation suggestive of vitiligo, along with freckles, were present in both the axilla and over the trunk and

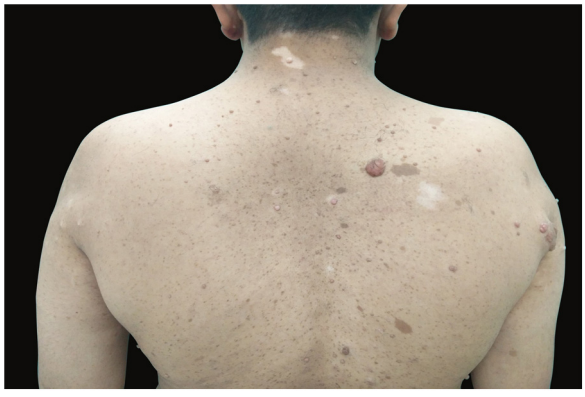

Figure 1 *Café-au-lait* macules, neurofibromas with perilesional halo, and vitiligo patches over the back.

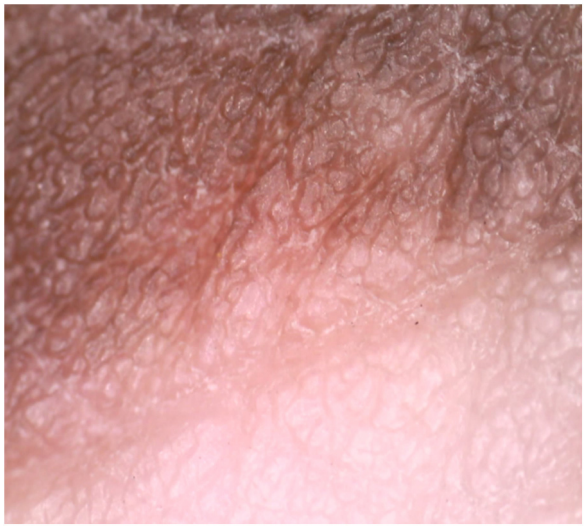

Figure 2 Border of a lesion on dermoscopy, showing reduced pigmentary network in the lesion compared to normal skin.

☆ How to cite this article: Tandon S, Singh A, Arora P, Gautam RK. Neurofibromatosis with vitiligo: an uncommon association rather than coexistence? An Bras Dermatol. 2019;94:624–6.

☆☆ Study conducted at the Dermatology Department, Dr. Ram Manohar Lohia Hospital, New Delhi, India.

Table 1 Previously reported cases of type 1 neurofibromatosis (NF1) associated with vitiligo.

Year	Author	Type of NF	Type of vitiligo	Associated halo phenomenon	Other associated features
1992	Singh et al.	NF1	Generalized	Absent	
2006	Oiso et al.	NF1	Generalized	Present	
2006	Bukhari et al.	NF1	Generalized	Absent	Left occipital bone defect
2006	Yalccin et al.	NF1	Generalized	Absent	Hashimoto's thyroiditis, Noonan syndrome
2008	Nanda	NF1	Generalized	Absent	
2016	Duman et al.	NF1	Generalized	Absent	Inferior chorioretinal coloboma and optic disc pseudo-doubling in the right eye
2016	Reinehr et al.	NF1	Acral	Absent	
2018	Present	NF1	Generalized	Present	

back. Dermoscopy of the lesion showed reduced pigmentary network.

NF1 is one of the most common autosomal dominant neurocutaneous disorder, with an estimated prevalence of around 1 in 3500 individuals. It has a highly variable clinical expression and approximately 30–50% of all patients lack a family history of the disease, representing *de novo* mutations of the NF1 gene.

Friedrich Von Recklinghausen was the first to describe the classical features of the disease and pointed out that the origin of the skin tumor was from peripheral nerves. *Café-au-lait* macules (CALMs) which are the first sign of NF1, signify the collection of heavily pigmented melanocytes originating from the neural crest in the epidermis. Ninety-five percent of patients of NF1 have CALMs by the time they reach the adulthood. Regarding the pigmentary changes, it was suggested that since the pigment producing melanocyte originates in the neural crest, the presence of pigmentary lesions due to changes in melanocyte cell growth and differentiation can be expected. Cell culture studies have shown that the NF1 gene defect affects melanogenesis in the epidermal melanocytes of NF1 patients, resulting in the various hyperpigmentary changes seen in NF1.[2]

The halo phenomenon signifies the sudden development of a depigmented halo around a congenital nevus, Spitz nevus, blue nevus, neurofibromas, and malignant melanomas. Shin et al.[3] described a case of naevus combined with vitiliginous changes and speculated that the immunological process involved in vitiligo simultaneously affected the underlying dermal naevus cells, causing their degeneration. Gach et al.[4] pointed out that clinical and histological similarity between the congenital melanocytic nevi and neurofibromas was because of the fact that both melanocytes and Schwann cells originate from the neural crest (Table 1). The levels of chronically activated $CD8^+$ T-cells are increased in NF1 patients, which provides further evidence that the halo phenomenon in neurofibromas in the presence of generalized vitiligo develops as an immunological response.[5]

A thorough review of the literature yielded the following cases of neurofibromatosis associated with vitiligo as described in table 1. The sudden appearance of the halo phenomenon in patients of neurofibromatosis should not be treated as a mere co-existence, but as a marker of a much more sinister association between neurofibromatosis and vitiligo. We recommend that further studies should be carried out to provide a greater insight into this complex association.

Financial support

None declared.

Author's contribution

Sidharth Tandon and Pooja Arora: Approval of the final version of the manuscript; elaboration and writing of the manuscript; critical review of the literature; critical review of the manuscript.

Ajeet Singh: Approval of the final version of the manuscript; conception and planning of the study; elaboration and writing of the manuscript; obtaining, analyzing and interpreting the data; effective participation in research orientation; critical review of the literature; critical review of the manuscript.

Ram Krishan Gautam: Critical review of the literature; critical review of the manuscript.

Conflicts of interest

None declared.

References

1. Theos A, Korf BR, American College of Physicians; American Physiological Society. Pathophysiology of neurofibromatosis type 1. Ann Intern Med. 2006;144:842–9.
2. Kaufmann D, Wiandt S, Veser J, Krone W. Increased melanogenesis in cultured epidermal melanocytes from patients with neurofibromatosis 1 (NF1). Hum Genet. 1991;87:144–50.
3. Shin JH, Kim MJ, Cho S, Whang KK, Hahm JH. A case of giant congenital nevocytic nevus with neurotization and onset of vitiligo. J Eur Acad Dermatol Venereol. 2002;16:384–6.
4. Gach JE, Carr RA, Charles-Holmes R, Harris S. Multiple congenital melanocytic naevi presenting with neurofibroma-like lesions complicated by malignant melanoma. Clin Exp Dermatol. 2004;29:473–6.
5. Karmakar S, Reilly KM. The role of the immune system in neurofibromatosis type 1-associated nervous system tumors. CNS Oncol. 2017;6:45–60.

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Received 9 March 2018; accepted 25 October 2018

https://doi.org/10.1016/j.abd.2019.09.003
0365-0596/

Hibernoma: case report of a rare lipomatous tumor☆,☆☆

Dear Editor,

We report the case of a 24-year-old female, Fitzpatrick phototype V, referred to our Dermatology Department for an asymptomatic mass in her left dorsal region. The patient reported a slow growth of this mass over several years. Physical examination revealed a palpable, soft, subcutaneous tumor in the left dorsal region, without apparent involvement of the superjacent skin, which was painless on palpation. The remainder of the examination was otherwise normal.

A high-resolution thoracic computed tomography performed one year before, in the context of an episode of asthma exacerbation, had revealed a large, low-density, subcutaneous nodularity in the referred topography (Fig. 1A). Also, an ultrasound-guided core needle biopsy (Fig. 1B)of this well-defined, slightly hyperechoic, subcutaneous mass identified a neoplasm of globular cells, some with multi-vacuolated cytoplasm and others with granular, eosinophilic cytoplasm, without nuclear atypia.

Considering this, we performed a complete surgical tumor resection, under local anesthesia, in an uneventful procedure (Fig. 2A). The tumor measured approximately $60 \times 50 \times 20$ mm, had a gelatinous external surface and, on section, showed a soft consistency and a brownish coloration (Fig. 2A and B). The histopathological examination revealed a hypodermic tumor, involved by a thin fibrous capsule, constituted by adipocytes with granular, eosinophilic cytoplasm, without cytologic atypia, numerous multi-vacuolated adipocytes and some uni-vacuolated cells, establishing the definite diagnosis of a hibernoma (Fig. 3). The patient recovered fully after surgery, without tumor recurrence after six months of follow-up.

Hibernomas are rare, benign soft-tissue tumors arising from vestigial brown fat, which can be located in the subcutaneous tissue, the skeletal muscle, or the intermuscular fascia.[1,2] There are four histological variants of hibernoma: typical (82%), myxoid (9%), lipoma-like (7%), and spindle-cell (2%).[1] Hibernomas vary in size (1–24 cm, average dimension 9.3 cm) and location, occurring most commonly in the thigh, peri- and interscapular region, neck, arm, abdominal cavity, and retroperitoneum, and they are typically highly vascularized.[1,3–5] They are most often diagnosed in adults (mean age 38 years).[1]

These lipomatous tumors generally present either as slow-growing, painless, soft, palpable and mobile masses, or as incidentalomas in imaging studies.[1,3–5] Symptoms secondary to compression of adjacent structures can also develop due to their growth.[1,3,4] Differential diagnosis is not always straightforward, and includes not only benign soft-tissue neoplasms (like atypical lipomas, hemangiomas, and angiolipomas) but also malignant, aggressive tumors (namely well-differentiated liposarcomas, myxoid liposarcomas, and rhabdomyosarcomas).[1,2] In fact, hibernomas can mimic these other tumors clinically, imagiologically, and even histologically, considering some similar features in biopsy specimens.[1–5]

Histopathological examination of the tumor following complete surgical excision, which is curative, is essential for confirming the diagnosis.[1,4,5]

Financial support

None declared.

Author's contribution

Margarida Moura Valejo Coelho: Approval of the final version of the manuscript; elaboration and writing of the manuscript; obtaining, analyzing and interpreting the data; effective participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct

☆ How to cite this article: Valejo Coelho MM, João A, Fernandes C. Hibernoma: case report of a rare lipomatous tumor. An Bras Dermatol. 2019;94:626–8.

☆☆ Study conducted at the Department of Dermatology and Venereology, Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal.