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Von Recklinghausen Disease with Vitiligo: A Rare Association

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Abstract
Von Recklinghausen disease, also known as neurofibromatosis 1 is one of the commonest neurocutaneous disorders. It is associated with an increased risk of developing benign and malignant tumors. However, only few case reports are mentioned in literature associating neurofibromatosis with autoimmune disorders, vitiligo being one of them. We report a case of 30 years old female, who presented with cutaneous features of neurofibromatosis 1 and vitiligo. Interestingly, she had multiple neurofibromas, which were characteristically depigmented. Only few case reports have been mentioned in literature associating these two disorders. Whether this exists due to some underlying genetic defect of NF1 gene or mere coincidence, it is yet to be found.
Keywords: *neurofibromatosis, vitiligo, coincidence.*

Introduction

Neurofibromatosis type 1 (NF 1) is an autosomal dominant neurocutaneus disorder characterized by presence of cutaneous neurofibromas, café-au-lait macules, axillary and inguinal freckling, lisch nodules in the eyes and skeletal defects including scoliosis, sphenoid wing dysplasia, bony distortion, local cystic and erosive changes. It is a common disorder and various autoimmune diseases have been reported in association with NF1 including multiple sclerosis, systemic lupus erythematosus, membranous glomerulonephritis, IgA nephropathy, mixed connective tissue disease, juvenile arthritis, autoimmune hemolytic anemia, bullous pemphigoid and Graves disease.(1) Another common autoimmune disorder, but reported rarely with NF1 is vitiligo.(2) It is an acquired pigmentary disorder of the skin presenting as depigmented or hypopigmented macules. We present a case of neurofibromatosis 1 and vitiligo with depigmented neurofibromas.

Case Report

A thirty years old female presented to Dermatology OPD with depigmented lesions since past 20 years. There was relapsing and remitting

history. Presently these lesions had been progressing rapidly since past 2 months. She was particularly concerned about depigmented nodules over face and neck. Clinical examination revealed the presenceof multiple depigmented macules and patches and depigmented nodules. She also had twelve café-au-lait macules more than 1.5cm in diameter, axillary and inguinal freckling, plexiform neurofibromas and multiple neurofibromas that were characteristically depigmented. Family history was positive for neurofibromatosis 1 in the mother. Ocular examination was normal with no lisch nodules. We diagnosed her as a case of neurofibromatosis 1 with vitiligo vulgaris. The patient refused for radiological investigation to rule out bony dysplasia, as she had no symptoms pertaining to nervous or musculoskeletal system. Also, her mother had similar disease and she was otherwise healthy. We managed her with oral mini pulse of steroids and azathioprine for vitiligo. For facial depigmented nodules, excision was planned after stabilization of vitiligo.

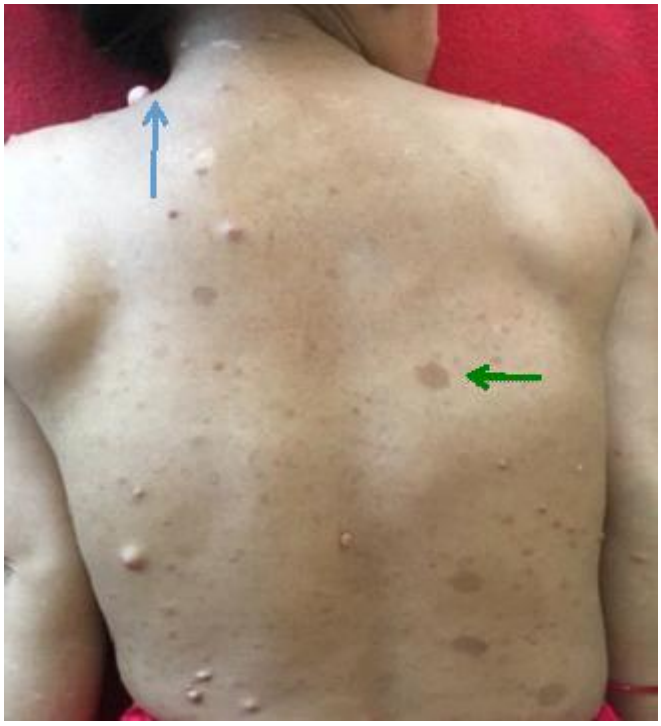

Figure 1: Back of the patient showing depigmeted neurofibromas (blue arrow) and café–au -lait macules (green arrow)

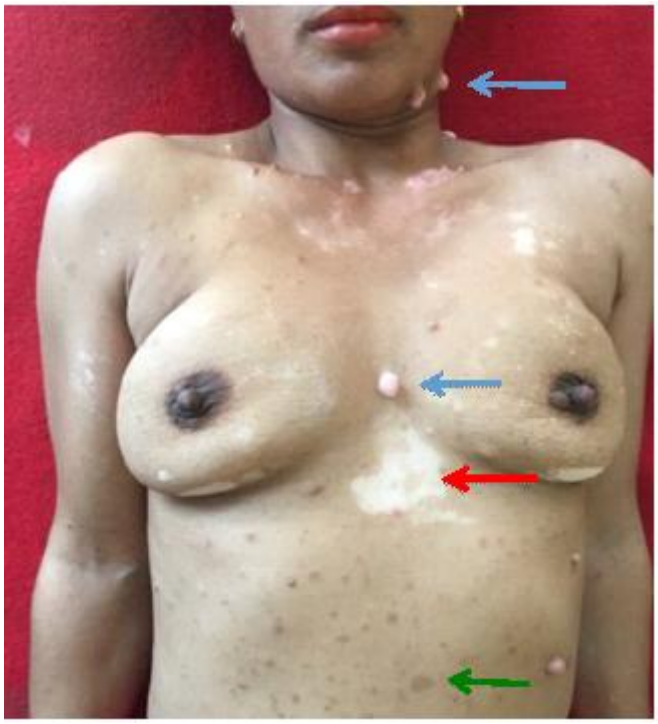

Figure 2: Blue arrows showing depigmeted neurofibromas; red showing vitiligo patches; green showing café-au -lait macules

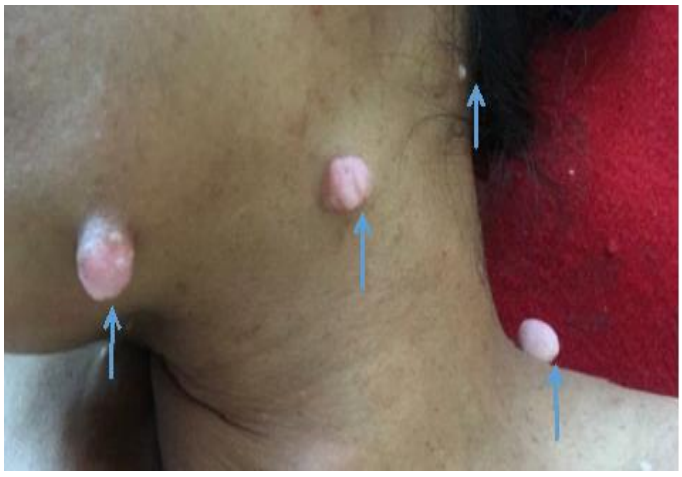

Figure 3: Characteristic depigmented neurofibromas (blue arrows) with surrounding normally pigmented skin

Discussion

Neurofibromatosis 1 is a relatively common hamartoneoplastic disorder with a prevalence of 1 in 3500 individuals. The diagnosis is based on meeting any two of the seven criterias that were established in 1987. These include (1) two or more neurofibromas on or under the skin or one plexiform neurofibroma, (2) freckling of the groin or the axilla, (3) six or more cafe´-au-lait spots

measuring 5 mm in the greatest diameter in prepubescent individuals and over 15 mm in the greatest diameter in post- pubertal individuals, (4) skeletal abnormalities such as sphenoid dysplasia or thinning of the cortex of the long bones of the body, (5) two or more lisch nodules in eyes, (6) optic glioma, or (7) a first-degree relative with NF1. These diagnostic criteria are highly specific to adults with NF1.[3] Vitiligo is a common pigmentary disorder affecting 0.1-2% population worldwideand about 0.5-2.5% population in India.[4] NF1 and vitiligo are hence common and easily diagnosed disorders, but literature review reveals very rare reports of this association. As seen in our patient, is it a mere coincidence, or some definite link is present between these two disorders is yet to be known. Our patient had lesions of both these diseases with depigmented neurofibromas over a normal skin. The pigmentary change is our interest in this case.

Is it a mere coincidence?

Bukhari et al suggested that since the pigment producing melanocyte originates in the neural crest, the presence of pigmentary lesions is expected due to changes in melanocyte cell growth and differentiation. They also stated that cell culture studies have shown that the NF1 gene defect affects melanogenesis in epidermal melanocytes of NF1 patientsresulting in the various hyperpigmentary changes seen in NF1.[5] Hence, hyperpigmented lesions like freckling and café -au -lait macules are observed in neurofibromatosis and presence of depigmented lesions is a mere coincidence.

Is there a possible link?

Singh et al stated that chemical mediators produced from the nerve endings might be responsible for destruction of melanocytes or inhibition of melanin synthesis leading to depigmentation.[6] Hence, there may be some possible link, which affects pigment production and lead to vitiligo lesions.

Neurofibromatosis 1 is due to mutation in NF1 gene, which maps to chromosome 17q11.2 and is a ‘‘suppressor gene.’’ Mutations affecting this gene might explain the various benign and malignant tumors arising in NF1 patients. Another author stated that loss of suppressor effect on immune system might be responsible for the association of autoimmune diseases like vitiligo with neurofibromatosis 1.[1]

This association is being reported so as to encourage similar case reports and further studies to unravel this association. Whenever a diagnosis of neurofibromatosis type 1 is made, one should be aware of the possibility of coexisting autoimmune diseases owing to increased reports of such association.

Conclusion

Neurofibromatosis 1 and vitiligo despite being common disorders are very rarely reported together in the same patient. Our case also highlights the characteristic depigmented neurofibromas with surrounding normally pigmented skin. Whether this exists due to some underlying genetic defect of NF1 gene or mere coincidental presence of two separate diseases in the same patient is yet to be found. We are reporting this association due to rarity of occurrence and to encourage extensive studies in this association.

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Conflicts of Interest: There are no conflicts of interest.

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