Case Report **Open Access**

Late Onset neurofibromatosis (NF-VII) presenting with segmental distribution of lesions: A novel case report.

Muhammad Amer Saleem, Naveed Akhtar Malik, Maham Amin, Wajahat Sultan Baiga

Abstract:

Neurofibromatosis (NF) is a hemartoneoplastic syndrome with up to eight possible variants. By far NF Type I is the most common presentation. A 74 years old gentleman present at our dermatology OPD with history of asymptomatic progressive nodular lesions appearing on his left arm only for past 4 years. The family history was insignificant and examination revealed soft pedunculated skin-colored nodules of varying sizes distributed primarily over flexor aspect of left arm. There were no associated pigmentary changes or lisch nodules. Excisional biopsy reveled a well-circumscribed nodular lesion in dermis composed of multiple spindle cells packed loosely in myxoid stroma with scattered mast cells. Late onset NF (NF-VII) and segmental NF (NF-V) are rare variants of this genetic disorder. We present a very unique case of late onset NF which presented with segmental distribution in his 7th decade of life representing an overlap of Type VII and type V sub-types.

Keywords: Late onset, Neurofibromatosis, Segmental.

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INTRODUCTION:

Neurofibromatosis (NF) is an autosomal dominant (AD) disorder characterized by dysfunction of gene that acts as a tumor suppressor.[1] This disorder encompasses a group of related disease in which tumors arise from nerves and can affect the skin and bones too. The more common and widely recognized sub-types of the disorder include type I and II NF.[2] By far the most common presentation is NF type I. It is characterized by multiple neurofibromas affecting the skin and tumors of the nervous system. Additionally, skin pigmentary changes such as café au lait macules (CALMs) and/or axillary freckling, positive family history, bones and ocular changes may also be present. The type II NF is less common, however, it is predominantly characterized by tumors of the central nervous system which can result in hearing, balance and vision abnormalities along with muscle weakness in various parts of the body. Apart from these common sub-types, Ricarrdi et al. classified this genetic disorder into six more variants denoted by NF type I to VIII.[3] Keeping in view the heterogeneity for neurofibromatosis, this classification has played a pivotal role in diagnosing and managing patients of neurofibromatosis. NF type V is characterized by neurofibromas and CALMs limited to one side of the body in a segmental distribution. It is caused by a somatic mutation during embryonic development and therefore, it is not hereditary and affects only a specific area of the body.[4] The mean age of onset of segmental neurofibromatosis is 28 years.[5] NF VII on the other hand is a variant which appears late in adulthood mainly after the 3rd decade of life and has neurofibromas only distributed over whole body. It is extremely rare entity and is characterized by absence of common features of other types of neurofibromatosis such as pigmentary changes (CALMs, Axillary freckling) and eye changes (Lisch nodules).[5] But it is very important to recognize this condition as the risks of malignant transformation of neurofibromas and internal malignancies is markedly high as compared to other types.[7] These types are only occasionally encountered in dermatology clinics. We present a very unique case of late onset NF with no associated pigmentary or eye changes which presented with segmental distribution in the 7th decade of his life representing an overlap of Type VII and type V sub-types.

Muhammad Amer Saleem,
Senior Registrar, Department of Dermatology,
Wah Medical College (POF Hospital), Wah Cantt.
Email: dr_amer@outlook.com

Naveed Akhtar Malik,
Professor, Department of Dermatology,
Wah Medical College (POF Hospital), Wah Cantt.
Email: naveedmalik467@hotmail.com

Maham Amin,
Senior Registrar, Department of Dermatology,
Wah Medical College (POF Hospital), Wah Cantt.
Email drmahamsyed@gmail.com

Wajahat Sultan Baig,
Assistant Professor, Department of Medicine,
Wah medical College (POF Hospital), Wah Cantt.
Email: wajahat_sultan@yahoo.com.

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Case Report:

A 74 years old gentleman with no known co-morbids presented to our outpatient dermatology department with complain of multiple asymptomatic raised lesions present on the left arm (Figure 1). The family history was insignificant. The first lesion developed about 4 years back just above the left cubital fossa and since then multiple lesions appeared over due course of time. The lesions increased both in size and number involving whole of the left upper limb prompting patient for dermatology consultation.

On cutaneous examination there were multiple, soft, non-tender and skin colored nodules with no temperature gradient were present involving the left arm with a flexor predominance. The nodules were of varying sizes and button-hole sign was negative. There were no associated pigmentary changes on the background skin which appeared completely normal. Rest of the cutaneous and systemic examination was completely unremarkable. Ophthalmology consultation was taken for slit lamp examination but lisch nodules were absent.

Therefore, excisional biopsy of one of the larger nodules was taken and sent for histopathology that revealed a well-circumscribed nodular lesion in dermis (Figure 2A) composed of multiple spindle cells having serpentine nuclei with pointed ends packed loosely in myxoid stroma and scattered mast cells were also seen (Figure 2B).

Patient was counselled about the disease in detail. He was advised to get only those neurofibromas removed which are very large or cosmetically unappealing to him. He was also advised to keep a check on these nodules with careful periodic examination and immediately visit the dermatology OPD if any of the lesion becomes itchy or painful, increases rapidly in size, hardens or ulcerates and if he develops and neurological complains like tingling, weakness or numbness in the arm. Patient requested to remove two more lesions near the cubital fossa that were excised by electrocauterization. Patient is now on regular follow up with our department once a year.

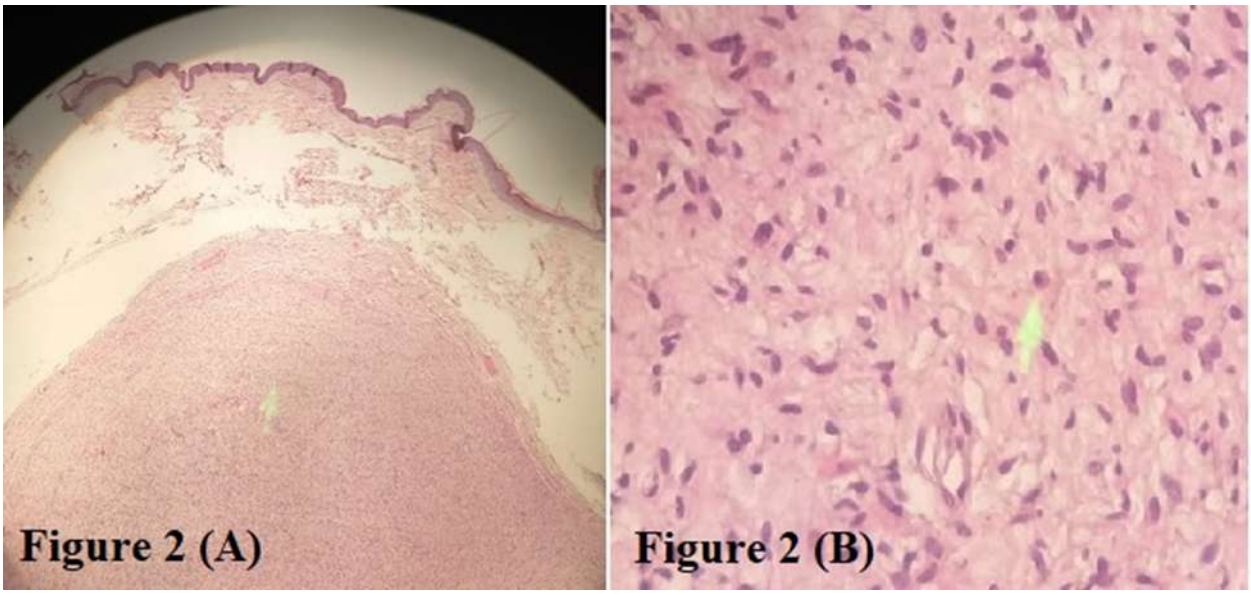
DISCUSSION:

NF is a hemartoneoplastic syndrome that is generally known to follow autosomal dominant pattern of inheritance.[8] Neurofibromatosis type I and type II are caused by a genetic mutation on long arms of chromosome 17 and 22 respectively.[9] However, some of its variants are not inheritable and yet the hereditary pattern of others still remain unknown. The most common presentation of the disorder is type I accounting for 96% of presentations followed but NF type II (3%).[1] The other six variants of NF as classified by Riccardi are encountered <1% in dermatology clinics.

The varying presentation of neurofibromatosis makes it difficult to classify it into a couple of variants and therefore, classification proposed by Riccardi has reduced the likelihood of missing the diagnosis in case the presentation of neurofibromatosis is unusual. One of the rare variants of NF is the late-onset NF (type VII) which is characterized by development of only neurofibromas of the skin and lack CALMs.[10] The inheritance pattern of this type remains unknown and the patient can exhibit malignant transformation of neurofibromas or tumors of nervous system. This variant has a diffuse cutaneous pattern and lesions are not confined

Figure 1: Multiple nodular lesions scattered only over the left arm of the patient (A) with sparing of the other body parts (B).

Figure 2: (A) Low power microscopic view of the biopsy specimen. (B) High power microscopic view of the biopsy specimen (arrow pointing towards a mast cell).



to a specific body part. It is very important to recognize this entity as patient has to remain on yearly follow-ups for monitoring of any malignant transformation. On the other hand, Type V (segmental) NF is a result of somatic mutation and is not inheritable. It is characterized by presence of neurofibromas and CALMs limited to one specific region of the body. The risk of malignant transformation and other complications in this variety is very low as compared to other sub types.[10]

Our patient had onset of neurofibromas in the 7th decade of life with complete absence of any related pigmentary changes. He did not have any active complains or family history and systemic examination was completely unremarkable. Ophthalmology consultation also failed to reveal any additional signs of NF such as lisch nodules on iris. Late onset NF has rarely been reported in literature and same is the case with segmental variant. However, the novel finding in our patient was that the features were limited to left arm only representing a possible overlap with segmental variant. We are classifying it as an overlap because the age of presentation is 74 years and the patient had neurofibromas with lacking evidence of other changes associated with neurofibromatosis which prompts the diagnosis of late onset neurofibromatosis, however, in late onset neurofibromatosis the neurofibromas are generalized and in our case at such advanced age patient presented with condition confined to a specific body area. We would like to classify this as an overlap and suggest long term follow up to patient in order to keep a check on malignant transformation.

CONCLUSION:

Apart from NF-I and NF-II, the other forms of NF are very rare. The late onset and segmental forms of NF are well recognized entities despite their rarity. After extensive search of the literature and to the best of our knowledge, we have classified this case as an overlap of these two variants and suggested long term follow up to patient on annual basis to monitor any malignant change.

Authors Contribution:
Muhammad Amer Saleem: Acquisition of data and drafting the article
Naveed Akhtar Malik: Conception and design plus final approval of the version to be published
Maham Amin: drafting the article literature review
Wajahat Sultan Baig: revised it critically and final approval of the version to be published

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