NPY Gene Polymorphism in Vitiligo: A Case-Control Study in Egyptian Patients

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Sir,

Vitiligo is a depigmentary dermatosis in which destruction or loss of function of epidermal melanocytes occurs.[1]

In Egypt, reported prevalence is 1.22% in overall population.[2]

Neuropeptide Y (NPY) is produced either by sympathetic postganglionic nerve fibers or by activated macrophages. It stimulates melanocyte dendricity and regulates cell substrate adhesion, cell motility, and configuration.[3] It regulates catecholamine release[4] which was claimed to participate in the development of vitiligo.[5] The NPY gene contains four exons and is located on chromosome 7p15.1.[6]

Single-nucleotide polymorphisms are genetic changes of one nucleotide and these changes could have functional implications.[7]

The present study aimed to detect the association of NPY gene 399T/C polymorphism and vitiligo to explore if it increased disease risk or influenced clinical presentation in Egyptian patients.

Forty patients with vitiligo were selected and 40 healthy, age and gender-matched unrelated participants were enrolled as a control group. Control participants had no past or family history of vitiligo. A written consent form approved by local ethical research committee was obtained from every participant before study initiation.

Assessment of disease activity was done according to vitiligo disease activity score.[8] Assessment of disease severity was done by vitiligo area severity index score.[9]

Patients with dermatological diseases other than vitiligo, with systemic, neurological, and/or autoimmune diseases or malignancy were excluded from the study.

Detection of NPY gene polymorphism was done by restriction fragment length polymorphism-polymerase chain reaction.

Clinical data of selected cases are summarized in Table 1. CC genotype and C allele were significantly associated with cases compared with controls. They increased vitiligo risk by 3.75 and 7 folds, respectively.

Table 1: General characteristics of vitiligo patients

| Variable                        | Vitiligo patients (n=40), n (%) |
|---------------------------------|-------------------------------|
| Age of onset (years)            |                               |
| Mean±SD                        | 22.88±16.1                    |
| Range                          | 5-55                          |
| Age (years)                     |                               |
| Mean±SD                        | 25.93±17.2                    |
| Range                          | 7-62                          |
| Duration (months)               |                               |
| Mean±SD                        | 39.43±40.2                    |
| Range                          | 2-204                         |
| Gender                         |                               |
| Male                            | 16                            |
| Female                         | 24                            |
| Age group                      |                               |
| Child                           | 19 (47.5)                     |
| Adult                          | 21 (52.5)                     |
| Site of lesions                |                               |
| Trunk                          | 13 (32.5)                     |
| Extremities                    | 22 (55.0)                     |
| Head and neck                  | 5 (12.5)                      |
| Family history                 |                               |
| Positive                       | 3 (7.5)                       |
| Negative                       | 37 (92.5)                     |
| Type of vitiligo               |                               |
| Segmental                      | 20 (50.0)                     |
| Nonsegmental                   | 20 (50.0)                     |
| Spontaneous repigmentation     |                               |
| Absent                         | 40 (100.0)                    |
| Leukoplakia                    |                               |
| Present                        | 5 (12.5)                      |
| Absent                         | 35 (87.5)                     |
| VIDA score                     |                               |
| 0                              | 21 (52.5)                     |
| 1                              | 5 (12.5)                      |
| 2                              | 4 (10.0)                      |
| 3                              | 7 (17.5)                      |
| 4                              | 3 (7.5)                       |
| Mean±SD                        | 1.15±1.4                      |
| Activity of disease            |                               |
| Stable                         | 21 (52.5)                     |
| Active                         | 19 (47.5)                     |
| VASI score                     |                               |
| Mean±SD                        | 3.57±1.13                     |
| Range                          | 2.20-5.9                      |

SD: Standard deviation, VASI: Vitiligo Area Severity Index, VIDA: Vitiligo Disease Activity
The -399T/C polymorphism (T/C) is associated with the initiation of transcription and can change NPY transcription activity. When the -399 locus contains the C nucleotide, plasma NPY levels are higher, leading to increased catecholamine production. Catecholamines contribute to melanocyte damage by free radical release or immune-mediated cytotoxicity. They stimulate the release of heat shock proteins by melanocytes and activate antigen-presenting cells such as dendritic cells and Langerhans cells.

In the current work, a significant association was found between T/C genotype and vitiligo lesions on extremities [Figure 1c]. This was not reported before and needs further investigation to be clarified.

The present work revealed lack of association between genotypes and disease activity. This was against the previous report of Laddha et al.[1] This controversy can be explained by different clinical criteria and ethnic backgrounds of selected populations.

Therefore, based on the current finding, NPY antagonists may be used in future for vitiligo treatment. However, as vitiligo is a complex disease with multiple genes and immunological and environmental factors, single genetic study is not enough and studying other genes, gene–gene, and gene–environment interactions are needed.

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Conflicts of interest
There are no conflicts of interest.
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