VIT1 gene and vitiligo

Sir,

Though extensively studied, the pathophysiology of vitiligo remains an enigma. The striking features of vitiligo, which have to be explained by any hypothesis on its pathogenesis, include its apparent heritability, absence of melanocytes without obvious signs of inflammation, association with ocular abnormalities1 and systemic disorders like thyroid disease, association with stress and trauma2 and segmental distribution in a few cases.

A newly identified gene called VIT13 was found to be associated with vitiligo. A detailed study of the structure of this gene using computational methods revealed features that could explain many of the distinctive features of vitiligo.

The VIT1 gene is located on chromosome 2p16. It has a refseq accession number of NM_018693 and the corresponding protein has an accession number of NP_061163. The genome has four exons and an overlapping region with the tumor marker MSH6. The protein had a single domain, a putative zinc finger in the N-recognition (ZnF-UBR1) with a Pfam accession number 02207 and smart00396.

N-recognition is an ubiquitin-protein ligase, the vital part of the N-end rule pathway.4 The N-end rule pathway is the main initiator of cellular apoptosis by destruction of specific proteins. It has various isoforms recognizing various N-terminal amino acid sequences; hence the name N-end rule pathway. The presence of this ubiquitin domain on vitiligo-associated gene can explain many of the features described above. Ubiquitin expressed by VIT1 may be targeting any of the specific proteins expressed by melanocytes or those responsible for melanocyte activation, thereby leading to melanocyte apoptosis without significant inflammation. Both stress and trauma are known to increase ubiquitin production and worsen vitiligo. Steroids are known to inhibit certain types of cellular apoptosis, especially TNF-a induced apoptosis. This could explain the therapeutic utility of steroids in vitiligo.

Yet another protein sharing the same domain is retinoblastoma-associated factor. This may be a significant finding considering the fact that retinal pigmentary abnormalities are sometimes seen in vitiligo.

The significance of the overlap of VIT1 gene with MSH6 is not known. MSH6 is involved in mismatch repair and mutation in this region leads to various colorectal tumors.5 Pigmentary changes are common in various intestinal polyposis syndromes, and the role of MSH6 remains to be explored.

Hence, genomic evidence suggests a ubiquitin mediated melanocyte specific apoptosis as a possible pathogenic mechanism in vitiligo. Histopathological evidence of inflammation in the normal-appearing skin adjacent to vitiliginous areas may be secondary to the cell injury. However, further research is required to find the probable target protein of this ‘vitiligo associated ubiquitin’. This could have therapeutic applications as synthetic proteins with the same N-terminal sequence can act as a competitive inhibitor of this enzyme.

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REFERENCES

Study of onychomycosis

Sir,

Onychomycosis is one of the commonest nail disorders seen by dermatologists. It describes all fungal infections of the nails and is caused by dermatophytes, yeasts or nondermatophyte moulds.

We undertook this microbiological study of onychomycosis with the aim of determining the prevalence of the various causative agents of onychomycosis in our population. From Jan 1999 to Dec 2001, nail clippings or scrapings were collected from 100 patients clinically suspected of having onychomycosis. They were processed in the Department of Microbiology, Bowring and L. C. Hospital, Bangalore and were studied for the presence of fungi. The nail clippings or scrapings were incubated in 40% potassium hydroxide for 30 minutes and microscopic examination was done for the presence of fungal elements. Culture was done on Sabouraud’s dextrose agar. The isolates were identified by standard techniques. The criteria used to report the moulds as pathogens were direct microscopy positive and isolation of the same fungi in three consecutive samples at intervals of 7 days.

Among the 100 patients, 51 were males and 49 were females. The mean age of the study group was 32.22 (±17.64 SD) years. Table 1 shows the sex distribution and the nails involved. Toe nail infection (78.43%) was commoner in males, while finger nail infection was commoner in females (85.71%) as most affected females were housewives who immersed their hands frequently in water. Two of the male patients with toe nail onychomycosis had HIV infection and three had diabetes mellitus.

Thirty per cent of samples were positive by KOH smears and 40% by culture (Table 2). Out of 40 culture positive samples, one yielded a mixed growth of two fungi. Yeasts predominated (48.78%), followed by dermatophytes (39.02%) and moulds (12.19%). Candida species (90.47%) predominated among yeasts. C. albicans (52.32%) was the commonest species isolated followed by C. tropicalis (37.22%), Trichosporon beigelii (4.76%) and Geotrichum candidum (4.76%) were isolated in one case each. Trichophyton rubrum (68.75%) was the commonest dermatophyte followed by T. mentagrophytes (25%) and Epidermophyton floccosum (6.25%). Fusarium oxysporum, which was isolated from the toe nails of HIV patients in the present study, has been reported as a cause by Jesudanam et al. Curvularia, which was isolated from toe nails of a diabetic patient, has been reported as a cause by Ramani et al. Alternaria and Cephalosporium as causative agents of onychomycosis has been reported by Sehgal et al.

To conclude, Candida species were the most common causes of onychomycosis in the present study. The present study shows that nondermatophyte moulds and yeasts can invade the nail and cause onychomycosis.

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Table 1: Sex distribution and nail involvement in the study group

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Toe nails</th>
<th>Finger nails</th>
<th>Both finger nails and toe nails</th>
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<tbody>
<tr>
<td>Male</td>
<td>51</td>
<td>40</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
<td>49</td>
<td>6</td>
<td>42</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>46</td>
<td>50</td>
<td>4</td>
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</tbody>
</table>

Table 2: Comparison of direct microscopy with culture

<table>
<thead>
<tr>
<th>KOH positive (n = 30)</th>
<th>KOH negative (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture positive</td>
<td>Culture negative</td>
</tr>
<tr>
<td>Culture positive</td>
<td>Culture negative</td>
</tr>
<tr>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>16</td>
<td>54</td>
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