Letter in Response to Previously Published Articles

Comments on: ‘‘Nonsegmental vitiligo follows Blaschko’s lines and embryonic pigmentary segments”

Sir,

We read with interest Dr. Nilendu Sarma’s paper,[1] redemonstrating what we have already shown in our previous publications,[2-4] i.e., anatomical segmentation in nonsegmental vitiligo. Though we are happy that our findings have been independently seconded by another author, we would like to correct the following misinterpretations of our findings referenced in the manuscript.

At the outset, Blaschko's lines and anatomical segmentations in vitiligo are not contradictory as the former represent the finer anatomical segmentations of the skin while the latter represents the segmental development of big and small appendages of the body along with that of skin. We would like to correct the basic premise of the manuscript that mosaicism in nonsegmental vitiligo is a new finding and has “never been demonstrated” before, as Dr. Sarma states in the introduction. We have already demonstrated mosaicism in our previous publications![2-4] Indeed, our concept that mosaicism is involved in the pathogenesis of vitiligo has been acknowledged, and our figures reproduced in Dr. Alain Taieb’s book “Vitiligo.”[5]

Dr. Sarma, while referring to our study, states: “A role of mosaicism in non-segmental vitiligo was hypothetically suggested.[2] However, the authors did not compare the patterns in those cases with Blaschko’s lines or any of the known patterns of mosaicism.” We find this statement quite baffling. As far back as 2013 in our paper titled “Segmental and Generalized Vitiligo: Both Forms Demonstrate Inflammatory Histopathological Features and Clinical Mosaicism,” we had stated that bilateral segmental lesions and pleuri segmental lesions considered earlier as segmental forms, cases reported as mixed vitiligo and bilateral and sharply segmented lesions in generalized vitiligo among our case series, support mosaicism as a common factor in the pathogenesis of all forms of vitiligo.[3] This was further elaborated upon in a larger series of patients in our paper titled: “Anatomical segmentations in all forms of vitiligo: A new dimension to the etiopathogenesis.”[2] In Figure 10 of this manuscript, we presented four patients who had evolving vitiligo lesions over the back along Blaschko’s lines and demonstrated that rapidly evolving disease on the trunk demonstrated Blaschko’s line/band patterns, highlighted in a patient with evolving vitiligo patches interspersed within a preexisting giant melanocytic nevus, both assuming Blaschkoid lines. We did not attribute facial segmented lesions in our series to Blaschko’s lines (in narrow bands, i.e., Type 1a) because the lesions converged into broader bands (Type 1b) prominently around eyes, mouth and ears which appeared as anatomical segmentations. Nevertheless, Blaschko’s lines or bands which are considered as ectodermal developmental segments of skin (or embryonal pigmentary segments as Dr. Sarma refers to) cannot be missed in such lesions.[6] We had clearly stated that linear, curvilinear and circular bands around appendages and orifices on the face were consistent with Blaschko’s patterns. We also demonstrated segmental involvement of vitiligo in different combinations and permutations within the anatomic segments of the body as well. All such segmentations on the face and the body were shown in a composite diagram.

Dr. Sarma excluded nonfacial and mixed vitiligo cases from his study. Dr. Sarma states that nonfacial lesions were excluded because facial segmentation patterns are easier to map, and Happle’s paper was referenced to support this viewpoint.[7] However, contrary to what Dr. Sarma states, Happle stated that the results obtained in their study clearly show that on the head and neck, the system of Blaschko’s lines is more complex with the direction of embryonic movements being strikingly variable in these areas, in some cases, the lesions crossing perpendicularly across boundaries. They in fact cautioned that in some areas, the proliferation of cutaneous structures during embryogenesis may go in the opposite direction! Similarly, the reason for excluding mixed vitiligo cases is unclear. Mixed vitiligo cases provide valuable evidence for mosaicism in vitiligo.

Dr. Sarma confirms our previous findings showing that the various anatomical segments in vitiligo are complementary to one another but fails to elaborate further. In fact, we stated previously that the observation of repetitive and complementary segments in different patients akin to a jigsaw puzzle is one of the most compelling evidence for mosaicism in vitiligo. We had clearly stated that “such a phenomenon we believe cannot be explained by any other hypothesis.

Further, Dr. Sarma states: "Recently, the role of mosaicism in non-segmental vitiligo has been hypothesized on the basis of some form of distributional patterns. However, evidence provided by the authors appeared to be weak as the patterns of distribution of the vitiligo patches were not compared to any of the established patterns of mosaicism." We fail to understand how an observational study across 615 patients and elaborate discussion regarding the role of mosaicism are considered "weak" evidence! A summary of our observations was further discussed recently in a paper titled "Vitiligo pathogenesis is interlinked with pigment homeostasis: A new concept," where we clearly stated that: "Anatomical segmentation when considered along with melanocytorrhagy (intrinsic anchoring and survival problems of melanocytes) suggests that the clinical expression of vitiligo is a mosaic developmental malady."[4]

Another misinterpretation we would like to point out in the statement: "Rather, to support the role of mosaicism, authors highlighted some common distribution patterns like 'bilateral symmetry' which are already well-known to be a typical phenotypic expression in non-segmental vitiligo and do not indicate mosaicism." We would like to clarify that nowhere in our publication, bilateral symmetry alone was suggested as evidence for mosaicism. However, bilateral symmetrical anatomical segments do indeed support the role of mosaicism at an earlier stage in the embryonic development pathway. Dr. Sarma might have misconstrued our conclusions because, instead of Blaschko's lines, broader anatomical segmentations are highlighted in support of mosaicism.

Dr. Sarma introduced a new term "embryonic pigmentary segments" without elaboration and evidence. We believe that these are the same anatomical segments as presented in our total body mapping of vitiligo lesions [Table 1 and Figures 3-8].[3]

Despite the above misinterpretations of our publication, we are indeed happy that Dr. Sarma's publication supports what we have already published in a larger study, vindicating our concept of mosaicism in the pathogenesis of all forms of vitiligo. We believe that the clinical expression of vitiligo depends upon the number of anatomically defective mosaics (melanocytorrhagy) and the nature/severity of immune reaction – localized or disseminated.

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Conflicts of interest
There are no conflicts of interest.

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