

Author's Reply

Sir,

Presence of more than one type of genetically different cells derived from a genetically homogenous zygote in an individual is known as mosaicism. Confirmation of mosaicism necessitates appropriate molecular proof.

However, mosaicism in cutaneous tissues has been successfully identified by the morphologic patterns that can be nonsegmental and segmental.¹ Nonsegmental patterns are more common and consist of single-point mutation (tumors) and disseminated (café au lait macules of neurofibromatosis 1) or patchy patterns without midline separation.² Segmental patterns are represented by Blaschko's lines, checkerboard pattern, flag-like pattern, phylloid (leaf-like) pattern, or lateralization pattern.¹ Sash-type presentation is a new inclusion in the list. Although science is known to evolve continuously, zosteriform segment, dermatome or vague terms like anatomical segments are not well-accepted to represent mosaicism.

The lines of Blaschko, the most common archetype of mosaicism, have defined patterns on every part of the body.³ Although there have been some modifications to the lines on the head and neck, the original description of the lines on other parts of the body has remained the same.^{4,5} A complete diagram of the lines on the entire body can be found in most of the textbooks of the dermatology. Blaschko's lines are just not any horizontal, curved or other lines described in medical science.

In my paper, I analyzed the patterns of isolated nonsegmental vitiligo, specifically on the head and neck region, and compared the observed patterns with the distribution patterns of Blaschko's lines.⁶ On the basis of the morphological similarity, I suggested possible role of mosaicism in nonsegmental vitiligo.

In contrast, Attili *et al.* have worked on both segmental and nonsegmental vitiligo (retrospective, based on photographs) and identified various 'anatomical segmentation' patterns on the entire body.^{7,8} However, they did not compare the patterns with the Blaschko's lines or any other known patterns of mosaicism.

Thus, there were significant differences between the methodology and results in our works. However, based on various anatomical segmentation patterns like mirror-image symmetry, sharp anatomical cutoff, bathing trunk distribution, periappendageal distribution and others, they also concluded affirming the role of mosaicism in all forms of vitiligo.

Considering the apparent similarity, in conclusion, they believe that I just redemonstrated their observations.

In the 'methods' section of their first publication, which appeared to have focused primarily on histopathological evaluation of inflammatory infiltrates, Attili *et al.* did not even mention whether they did any clinical pattern analysis. However, in the 'results,' they mentioned having found interesting patterns. They wrote: "In 9/154 GV cases... the lesions on both halves of the body were exact mirror images. Some had horizontal and some curved anatomical cut off lines giving an impression of unusual bilateral segmentation/ mosaicism [Figure 7a-f]."⁷

I must highlight that 'mirror-image symmetry,' a rather common and well-known feature in nonsegmental vitiligo, lacks evidence as a valid representation of mosaicism.

Second, 'some' is not an acceptable quantitative value in a scientific article, especially to generate a hypothesis.

Third, 'horizontal and some curved anatomical cut off lines', without any further specifications, does not equate with blaschoid distribution. There was a lack of clarity if those lines were compared to Blaschko's lines at all and how they defined mosaicism.

It was more confusing when they equated 'unusual bilateral segmentation' with mosaicism. Morphological relation with Blaschko's lines was not at all assessed or mentioned. However, they asserted the role of mosaicism in all forms of vitiligo.

In a review article, they claimed to have found intimate relation of 'melanocytorrhagy' and mosaicism.⁸ To the best of my knowledge, the relation between melanocytorrhagy and mosaicism has never been proven nor has anyone done any study on it. None of the references that Attili *et al.* have quoted were relevant to this field. I did not find any relevance of this comment: "...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."

I believe no evidence supports this statement. "Repetitive and complementary segments" are not known to represent mosaicism.

Attili *et al.* stated that: "...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." They did not provide any evidence to support their statement.

They stated: “We fail to understand how an observational study across 615 patients and elaborate discussion regarding the role of mosaicism, is considered ‘weak’ evidence!”

I believe that only the number does not create evidence. In this publication, they forgot to mention even a single quantitative datum in the ‘results’ section. A study aiming at analyzing a pattern failed to mention how many of those 651 cases had a representative pattern; thus it lacked the necessary data to inform its conclusion.⁹

The said publication followed a complicated classification system. All the nonsegmental vitiligo cases (n = 464) were divided into the following subtypes:

1. Generalized vitiligo with dominant trunk involvement or generalized nonacromioclavicular vitiligo (n = 131)
2. Acral vitiligo (n = 193)
3. Focal lesions limited to one anatomical area (n = 83)
4. Multifocal lesions involving more than one area, but with no bilateral symmetry (n = 57)

I found it difficult to understand in which group the patients with typical bilaterally distributed (often symmetrical) nonsegmental vitiligo of isolated head–neck regions (my area of focus) were incorporated.

This study had serious methodological flaws. Much essential information was conspicuously absent, such as:

1. The ‘results’ section lacked any quantitative data.
2. There was no mention of the inclusion and exclusion criteria. They included highly atypical cases such as giant congenital melanocytic nevus with superimposed depigmentation [Figure 10e]⁹ for pattern analysis of vitiligo. It clearly indicated an absolute lack of inclusion criteria.
3. The article mentioned: “Similar unilateral/bilateral segmented lesions were identified among all forms of vitiligo during relatively stable phases of the disease.” However, it was not mentioned how a ‘relatively stable case’ was defined.
4. Authors worked on anatomical segmentation, but they never explained how they defined ‘anatomical segments’.
5. They did not mention whether they included the same cases in both the studies and the number of such common subjects. Figure 7e in the earlier study and Figure 6d in the second paper appeared to be the same person. It is logical to assume that results will be biased if the same subjects are included in two different studies. This seemed to be a significant flaw.

Instead of comparing the patterns of vitiligo patches to Blaschko’s lines, they followed a very innovative method. They said: “Lesions were mapped and screened for repetitive

unilateral or bilateral segmentations. When a segmented pattern was seen to be repeated in two or more patients, it was marked as a template to compare with others.” Thus, a pattern of distribution found in two or more patients formed a template pattern for subsequent cases. Expectedly, many templates were found. However, no quantitative values were provided. One of their figures shows their observed patterns.⁹ I could not find any morphological similarity with Blaschko’s lines from this figure. It was hard to understand how they arrived at a conclusion on mosaicism based on these patterns. The article started with the title of “anatomical segmentations in all forms of vitiligo” and it ended with an unrelated conclusion of ‘mosaicism.’

Although the methodology or the observations did not provide any scientific basis for their conclusion, and despite many serious methodological flaws, I acknowledged that they hypothesized ‘mosaicism in all forms of vitiligo.’ However, I had to mention that the hypothesis was not backed with sufficient evidence.

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Conflicts of interest

There are no conflicts of interest.

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