

# From Pediatrics to Adults: Evaluating Peripheral Globule Characteristics in Melanocytic Nevi and Their Clinical Implications

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## Abstract

**Aim:** Melanocytic nevi in children and adults can differ in growth rate, melanoma risk, and dermoscopic pattern. Peripheral globules (PGs) are common in both groups while being usually benign in pediatric patients and may increase melanoma risk in adults. We aimed to compare baseline and 12-month follow-up, characteristics of melanocytic lesions with PGs (MLPGs) in adult and paediatric age groups.

**Materials and Methods:** A total of 170 MLPGs were evaluated morphologically; histopathological findings were reviewed when lesions were excised. Of these, 148 MLPGs had 12-month follow-up images and were analysed for changes in size, global pattern, and PGs.

**Results:** At baseline, MLPGs in adults most commonly showed a homogeneous pattern, whereas MLPGs in children predominantly displayed a globular pattern. The distribution of PGs did not differ between age groups ( $P > 0.05$ ). Adult nevi PG were more atypical ( $P = 0.001$ ), whereas pediatric nevi PG were more regular ( $P = 0.001$ ). After 12 months, no significant changes were observed in adults, while dynamic changes occurred in the paediatric group. Complete regression of PGs was more frequent in pediatric lesions ( $P = 0.046$ ).

**Conclusion:** MLPGs show distinct age-related behaviour: in adults, lesions remain largely stable while exhibiting more atypical PGs, whereas in children lesions evolve dynamically and PGs regress more frequently.

**Keywords:** Dermoscopy, melanocytic nevi, pediatrics, pathology, skin neoplasm

## INTRODUCTION

Pediatric and adult melanocytic nevi may differ in terms of their pattern, growth rate, and presence of peripheral globules (PGs).<sup>1,2</sup> These differences are clinically significant, particularly in the assessment of melanoma risk, where age-related changes in nevi characteristics are evident.<sup>3</sup> PGs manifest as small brown globules in the periphery of the lesion and have been associated with centrifugally growing junctional and dermal melanocytes, as observed through reflectance

confocal microscopy (RCM).<sup>4</sup> PGs are frequently observed in pediatric patients who present evident nevogenesis and active growth; these lesions are generally considered benign. In adults, however, the incidence of PGs decreases, and PGs are rarely associated with melanoma findings.<sup>5</sup> Therefore, the presence of PGs in pediatric patients can lead to unnecessary anxiety and excisions despite their benign nature. In our study, we aimed to evaluate and compare the pattern, diameter, and

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PG morphology and evolution of melanocytic lesions with PGs (MLPGs) in pediatric and adult age groups.

## MATERIALS AND METHODS

### Study Design and Data Extent

Patients who presented to the dermatology department between January 2010 and April 2022 underwent whole-body nevus examination and received a clinical diagnosis of MLPGs, were included in the study. A total of 53 patients with MLPGs who had indications for videodermoscopic follow-up were included. These patients were monitored for factors such as the number of nevi, atypical appearances of multiple nevi, or a personal and/or family history of melanoma or dysplastic nevus. The included patients had a total of 170 MLPGs on the trunk. Nevi from facial or extremity/acral regions containing PGs were not included because of their variable patterns. The demographic characteristics of the patients, baseline MLPG patterns, PG morphologies, and histopathological examination results were recorded. The changes in nevus diameter during the follow-up were measured in millimeters along the longest axis. MLPGs were classified into the following patterns: globular, globular-homogeneous, homogeneous, homogeneous-reticular, globular-reticular and reticular. Detailed assessments of the PGs, including their evolution and morphology, were recorded. PGs were classified as either focal or circumferential and further categorized as typical or atypical on the basis of shape and color uniformity, arrangement and regularity, (single or multiple rims of globules). MLPGs that met the melanoma criteria or exhibited significant PGs morphological abnormalities were excised. Patients without follow-up data due to excision, and those missing any data, were excluded from follow-up assessments. In the second evaluation, a total of 148 nevi from 47 patients were included in the study. This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, İstanbul Training and Research Hospital (approval number: 120, date: 08.04.2022). Patients provided informed consent. Patient files and photographs were retrospectively reviewed using medical records from hospitals and videodermoscopy databases. A FotoFinder dermoscope (FotoFinder Systems GmbH, Bad Birnbach, Germany) was used to capture the dermoscopic images.

### Statistical Analysis

Statistical analyses were conducted using SPSS version 25.0. The normality of the variable distributions was assessed via the Shapiro-Wilk test. Descriptive analyses included the mean, standard deviation, median, minimum, and maximum values. For variables that followed a normal distribution, an

independent samples t-test was used to evaluate differences between two groups. Categorical variables are presented as frequencies and percentages. Relationships between categorical variables were examined via the Fisher-Freeman-Halton exact test. When an expected frequency is less than 5, the Fisher-Freeman-Halton test is used to ensure accurate statistical analysis. *P* values less than 0.05 were considered statistically significant.

## RESULTS

### Patient Characteristics

A total of 170 nevi from 53 patients with MLPGs were included in the study. According to the baseline data for these 170 MLPGs, adult nevi accounted for 59.4% of the total nevi, whereas pediatric nevi accounted for 40.6%. There was no significant difference in nevus distribution by sex ( $P > 0.05$ ). The mean age of the adult patients was  $31.1 \pm 10.8$  years, whereas the mean age of the pediatric MLPG patients was  $12.8 \pm 3.8$  years. Only nevi on the trunk were included in the study, and MLPGs on the face and extremities were excluded. The average total nevus count was 76.41 for adults and 48.66 for pediatric patients. Patients were categorized according to the number of nevi, as shown in the Table 1.

### Baseline Dermoscopy Features

With respect to morphology, 80.2% of PGs were circumferential, 62.4% were regular, and 73.3% had a typical appearance in the adult population. In the pediatric population, 87% of the PGs were circumferential, 89.9% were regular, and 95.7% had a typical appearance. The PGs in the adult group had significantly more atypical appearances ( $P = 0.001$ ), and the pediatric PGs were more regular in appearance ( $P = 0.001$ ). Figure 1 presents examples of nevi with various morphological characteristics.

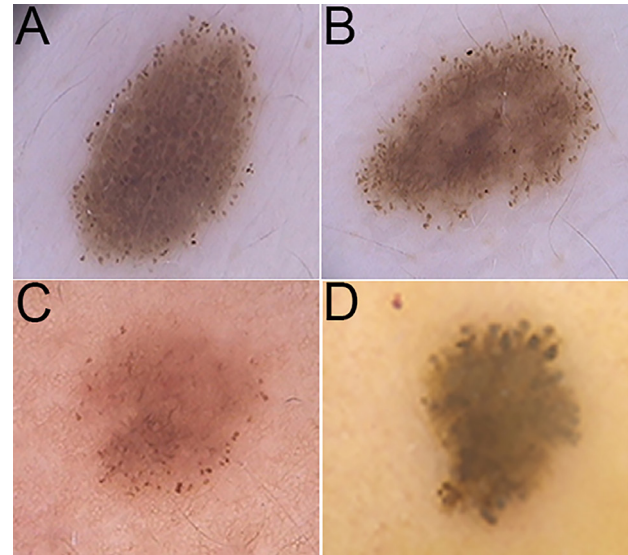
### Histopathological Findings

In adults with excised nevi, the most common diagnosis was dysplastic nevus (11.9%), followed by compound nevus (7.9%), junctional nevus (6.9%), and malignant melanoma (3%). The melanoma patients were aged 30, 37, and 71 years. No malignant melanoma was detected in the pediatric age group. The most common diagnosis in pediatric patients with excised nevi was dysplastic nevus (4.3%), followed by compound and junctional nevus (2.9% each) and Spitz nevus (1.4%). No significant difference was found between the adult and pediatric age groups in terms of diagnosis ( $P > 0.05$ ). Table 1 presents the clinical features of 170 MLPGs in adult and pediatric patients.

### Longitudinal Dermoscopic Changes

After the MLPGs that were initially excised or had missing follow-up data were excluded, 148 MLPGs from 47 patients were included. The average age of the adults was 29.07 years, whereas the average age of the pediatric patients was 12.8 years. The initial MLPG size was 4.66 mm in the adult age group and 4.3 mm in the pediatric age group. At 12 months, the average MLPG size was 5.31 mm for adults and 5.07 mm for the pediatric group. No significant difference was found between baseline and 12-month MLPG sizes in either age group. In adults, the most common patterns were homogeneous (53%), homogeneous-reticular (22.9%), and reticular (16.9%), whereas, in the pediatric age group, the most common patterns were globular (58.5%), reticular (16.9%), and homogeneous (12.3%). Homogeneous and homogeneous-reticular nevi were significantly more common in adults ( $P = 0.001$ ), whereas globular and globular-homogeneous nevi were significantly more common in pediatric patients ( $P = 0.0001$ ,  $P = 0.0050$ ). At the 12-month evaluation, the number of nevi with homogeneous-reticular and reticular patterns increased in both age groups. Additionally, in the pediatric age group, the number of nevi with a globular pattern decreased, whereas the number of nevi with a globular-homogeneous pattern increased.

With respect to morphology, in the adult age group, 84.3% of PGs were circumferential, 68.7% were regular, and 80.7% had a typical appearance. In the pediatric age group, 86.2% of the PGs were circumferential, 89.2% were regular, and



**Figure 1.** (A) Circumferential, regular (single rim), typical peripheral globules. (B) Circumferential, irregular (double rim), typical peripheral globules. (C) Focal, irregular, typical peripheral globules (dysplastic nevus). (D) Focal, irregular, atypical peripheral globules (melanoma *in situ*)

**Table 1. Clinical characteristics and comparisons of nevi with peripheral globules in pediatric and adult age groups**

|                                          |                                | Adult nevi (n = 101) |       | Pediatric nevi (n = 69) |       | P                   |
|------------------------------------------|--------------------------------|----------------------|-------|-------------------------|-------|---------------------|
|                                          |                                | n                    | %     | n                       | %     |                     |
| Female                                   |                                | 15                   | 48.4  | 9                       | 40.9  | <sup>b</sup> 0.59   |
| Male                                     |                                | 16                   | 51.6  | 13                      | 59.1  |                     |
| Age, avg ± SD/min.-max.                  |                                | 31.16±10.80          | 18-71 | 12.79±3.75              | 5-17  | <sup>a</sup> 0.0001 |
| Number of total nevi, avg ± SD/min.-max. |                                | 76.41±64.54          | 8-323 | 48.66±29.14             | 5-96  |                     |
| Number of total nevi                     | 1-10 nevi                      | 2                    |       | 3                       |       |                     |
|                                          | 10-50 nevi                     | 10                   |       | 8                       |       |                     |
|                                          | 50-100 nevi                    | 10                   |       | 11                      |       |                     |
|                                          | > 100 nevi                     | 9                    |       | 0                       |       |                     |
| Peripheral globule distribution          | Focal                          | 20                   | 19.8% | 9                       | 13.0% | <sup>b</sup> 0.250  |
|                                          | Circumferential                | 81                   | 80.2% | 60                      | 87.0% | <sup>b</sup> 0.250  |
| Peripheral globule regularity            | Regular                        | 63                   | 62.4% | 62                      | 89.9% | <sup>b</sup> 0.001* |
|                                          | Irregular                      | 38                   | 37.6% | 7                       | 10.1% |                     |
| Peripheral globule morphology            | Atypical                       | 27                   | 26.7% | 3                       | 4.3%  | <sup>b</sup> 0.001* |
|                                          | Typical                        | 74                   | 73.3% | 66                      | 95.7% |                     |
| Histopathological results                | Atypical pigmented Spitz nevus | 1                    | 1.0%  | 0                       | 0.0%  | <sup>c</sup> 0.795  |
|                                          | Compound nevus                 | 8                    | 7.9%  | 2                       | 2.9%  | <sup>c</sup> 0.671  |
|                                          | Dysplastic nevus               | 12                   | 11.9% | 3                       | 4.3%  | <sup>c</sup> 0.640  |
|                                          | Junctional nevus               | 7                    | 6.9%  | 2                       | 2.9%  | <sup>c</sup> 0.607  |
|                                          | Malignant melanoma             | 3                    | 3.0%  | 0                       | 0.0%  | <sup>b</sup> 0.492  |
|                                          | Spitz nevus                    | 0                    | 0.0%  | 1                       | 1.4%  | <sup>b</sup> 0.205  |

<sup>a</sup>: Independent samples t-test, <sup>b</sup>: Exact chi-square test, <sup>c</sup>: Fisher-Freeman-Halton exact test, \*: Statistically significant  
Min.: Minimum, Max.: Maximum, SD: Standard deviation, Avg: Average

95.4% had a typical appearance. While adult PGs were significantly more atypical ( $P = 0.008$ ), pediatric PGs were significantly more regular ( $P = 0.003$ ). Most PGs completely regressed in both age groups (48.2% vs. 64.6%, respectively). Complete regression was significantly more common in the pediatric age group, whereas a decrease in PG number was more common in the adult age group (30.1% vs. 13.8%). An increase in PG number was relatively rare in both age groups (6% vs. 4.6%). Table 2 summarizes the changes in patterns and morphological features of the 148 MLPGs that were monitored in this study.

## DISCUSSION

This comparative study reveals a marked age-related contrast in MLPGs: in adults PGs are more often atypical and lesions remain homogeneous and stable over 12 months, whereas in children the globules are usually regular, regress more frequently, and lesions change dynamically.

The presence of PGs is associated with horizontal growth in nevi, with MLPGs growing at a rate of 0.25 mm<sup>2</sup>/month before stabilizing. According to Bajaj et al.<sup>6</sup>, MLPGs take an average of 58.6 months to stabilize, and PGs are lost during this phase. The MLPGs also have an average size of

**Table 2. Comparison of adult and pediatric nevi with peripheral globules after 12 months of follow-up**

|                                 |                         | Adult nevi (n = 83) |              | Pediatric nevi (n = 65) |              | P                    |
|---------------------------------|-------------------------|---------------------|--------------|-------------------------|--------------|----------------------|
|                                 |                         | Avg ± SD            | Median (IQR) | Avg ± SD                | Median (IQR) |                      |
| Age                             |                         | 29.07±7.95          | 28 (11)      | 12.79±3.75              | 13.5 (4.5)   | <sup>a</sup> 0.0001* |
| Baseline average size           |                         | 4.66±1.76           | 4.35 (2.13)  | 4.3±1.93                | 3.7 (2.75)   | <sup>a</sup> 0.247   |
| 12-month average                |                         | 5.31±1.73           | 5 (1.95)     | 5.07±2.02               | 5 (2)        | <sup>a</sup> 0.452   |
|                                 |                         | n                   | %            | n                       | %            |                      |
| Sex                             | Male                    | 13                  | 52.0%        | 13                      | 59.1%        | <sup>b</sup> 0.626   |
|                                 | Female                  | 12                  | 48.0%        | 9                       | 40.9%        |                      |
| Baseline pattern                | Globular                | 6                   | 7.2%         | 38                      | 58.5%        | <sup>b</sup> 0.0001* |
|                                 | Globular + homogeneous  | 0                   | 0.0%         | 6                       | 9.2%         | <sup>c</sup> 0.005*  |
|                                 | homogeneous             | 44                  | 53.0%        | 8                       | 12.3%        | <sup>b</sup> 0.001*  |
|                                 | homogeneous + reticular | 19                  | 22.9%        | 2                       | 3.1%         | <sup>c</sup> 0.001*  |
|                                 | Reticular               | 14                  | 16.9%        | 11                      | 16.9%        | <sup>b</sup> 0.993   |
| 12-month follow-up pattern      | Globular                | 4                   | 4.8%         | 22                      | 33.8%        | <sup>b</sup> 0.001*  |
|                                 | Globular + homogeneous  | 0                   | 0.0%         | 11                      | 16.9%        | <sup>c</sup> 0.001*  |
|                                 | Globular + reticular    | 0                   | 0.0%         | 1                       | 1.5%         | <sup>c</sup> 0.439   |
|                                 | homogeneous             | 43                  | 51.8%        | 11                      | 16.9%        | <sup>b</sup> 0.001*  |
|                                 | homogeneous + reticular | 20                  | 24.1%        | 4                       | 6.2%         | <sup>b</sup> 0.003*  |
|                                 | Reticular               | 16                  | 19.3%        | 16                      | 24.6%        | <sup>b</sup> 0.434   |
| Peripheral globule distribution | Focal                   | 13                  | 15.7%        | 9                       | 13.8%        | <sup>b</sup> 0.819   |
|                                 | Circumferential         | 70                  | 84.3%        | 56                      | 86.2%        | <sup>b</sup> 0.758   |
| Peripheral globule regularity   | Regular                 | 57                  | 68.7%        | 58                      | 89.2%        | <sup>b</sup> 0.003*  |
|                                 | Irregular               | 26                  | 31.3%        | 7                       | 10.8%        |                      |
| Peripheral globule morphology   | Atypical                | 16                  | 19.3%        | 3                       | 4.6%         | <sup>b</sup> 0.008*  |
|                                 | Typical                 | 67                  | 80.7%        | 62                      | 95.4%        |                      |
| Change in peripheral globules   | Increased               | 5                   | 6.0%         | 3                       | 4.6%         | <sup>b</sup> 0.707   |
|                                 | Same                    | 13                  | 15.7%        | 11                      | 16.9%        | <sup>b</sup> 0.836   |
|                                 | Decreased               | 25                  | 30.1%        | 9                       | 13.8%        | <sup>b</sup> 0.020*  |
|                                 | Disappeared             | 40                  | 48.2%        | 42                      | 64.6%        | <sup>b</sup> 0.046*  |

<sup>a</sup>: Independent sample t-test, <sup>b</sup>: Exact chi-square test, <sup>c</sup>: Fisher-Freeman-Halton exact test, \*: Statistically significant  
Avg: Average; SD: Standard deviation, IQR: Interquartile range

4.10 mm, with nevi that are still growing are smaller. In our study, the average nevus size was  $4.66 \pm 1.7$  mm in adults and  $4.3 \pm 1.9$  mm in pediatric patients, indicating that MLPGs are generally small. Another study reported that PG nevi grow at an average rate of  $0.16 \text{ mm}^2/\text{month}$ , independent of age, sex, or location.<sup>7</sup> Similarly, in our study, no difference in growth rate was found between the pediatric and adult groups, even though there was a significant increase in nevus size from baseline to follow-up.

When age and PG morphology were evaluated in our study, most MLPGs exhibited circumferential, typical, and regular globules. There were clear age-related differences in PG morphology, with pediatric patients showing significantly more regular, typical PGs than adult patients. However, no significant difference was found between the two age groups in terms of the presence of circumferential or focal globules, which is an important criterion in melanoma detection according to previous studies.<sup>8</sup> All melanomas in our study occurred after age 30 and exhibited suspicious PGs. The observed PGs in the patients with melanoma were all atypical and irregular; in one patient, the PGs were circumferential, whereas in the other two patients, they were focal. In a study of melanomas with PGs, 63.4% occurred in individuals aged 30-50 years, whereas 31.7% occurred in those over 50 years. The presence of atypical globules was identified as a risk factor for melanoma.<sup>9</sup> In a study monitoring 154 high-risk melanoma patients, the following criteria were considered for excision: asymmetry in two axes, the presence of PGs in less than 25% of the circumference with a history of less than 1 year, reappearance of PGs, and irregular size, shape, or color of PGs.<sup>10</sup> PG morphology may vary, and completely circumferential typical globules (single rim or tiered) are less likely to be found in melanoma. Conversely, atypical or asymmetrically distributed PGs increase the risk of melanoma. Even when PGs are present in melanoma patients, at least two melanoma-specific structures accompany the PGs.<sup>8</sup>

The prepubertal age group typically exhibits a dominant globular pattern, whereas the reticular pattern becomes prevalent in adulthood. Globular nevi are most common in pediatric patients, but the prevalence decreases to 0.9% in older age groups, whereas reticular nevi are the predominant pattern after age 30.<sup>3</sup> In our study, pattern modifications during follow-up were more frequently observed in the pediatric age group than in the adult age group. In addition, the transition from globular nevi to reticular nevi was not observed in the pediatric age group. According to cohort studies conducted in adolescents, the rate of transformation from reticular to globular nevus patterns was only 1%, whereas the opposite change occurred in 4% of cases. Although these transformations are rare, an increase in reticular nevi and a decrease in globular nevi were observed over the monitoring

period. This finding supports the previously reported concept of dual nevogenesis. In childhood, globular nevi develop from dermal melanoblasts, whereas in adulthood, mature melanocytes in the epidermis create a reticular pattern, primarily due to ultraviolet exposure.<sup>4,11-13</sup> Similar trends were observed in our study, suggesting that MLPGs exhibit age-dependent distribution patterns comparable to those of nevi without PGs.

When examining the rates of PG regression, we observed decrease in or the complete disappearance of PGs in both age groups. Considering that MLPGs stabilize over time and lose the associated PGs, a longer follow-up period could have increased the disappearance rates. When analyzed individually, the disappearance of PGs was more prevalent in the pediatric age group, whereas a reduction in PGs was more frequently observed in the adult age group. Interestingly, the overall rates of PG reduction and disappearance were similar, 78.3% in the adult group and 78.4% in the pediatric group, respectively. These rates are similar to findings reported in a study with an average follow-up of 25 months, which showed a 75% reduction in PGs.

Atypical and irregular features, which are associated with melanoma, were more frequently observed in adult MLPGs. This finding is consistent with the increased melanoma risk observed with age in MLPGs. In our study, PG morphology in both age groups generally showed benign characteristics and regressed or disappeared in the majority of cases within one year. The relationship between MLPGs and the frequency of melanoma in our study indicated that melanoma is rare and is detected in approximately 3% of adults. In a study evaluating MLPGs in high-risk patients, the melanoma rate was 1.9%.<sup>10</sup> Additionally, in an MLPG cohort of 121 lesion which received histopathological evaluation, no melanomas were observed.<sup>6</sup> In a different study evaluating MLPGs, a melanoma rate of 10% was observed, which is higher than previous findings.<sup>9</sup> In summary, although melanoma rates varied based on the age group included in the study and the presence of risk factors, the rates generally remained low. In one study, the number of patients who needed biopsy to detect one melanoma in the pediatric age group was 1,035.<sup>14</sup> These findings indicate that risk factors should be well characterized, especially in the pediatric age group, to decrease unnecessary skin excisions. According to the currently recommended management algorithm, which incorporates age and PG morphology, regular dermoscopic monitoring is recommended for individuals under 35 years of age. This is particularly important for lesions showing an organized rim of globules with a reticular, globular, or mixed central pattern, including PGs. In cases where nevi with PGs present two or more new atypical dermoscopic structures, advanced evaluation and follow-up with RCM are recommended. For

individuals between 35 and 55 years of age, surgical excision of any atypical dermoscopic structures is recommended. Even in the absence of melanoma-specific dermoscopic criteria, evaluation with RCM is advised. For individuals aged 55 and above, surgical excision is recommended for all patients.<sup>5</sup>

### Study Limitations

The exclusion of high-risk nevi from follow-up because they were excised could introduce bias in parameters such as growth rate, pattern changes, and PG morphology. This potential bias represents a key limitation of our follow-up data.

Another significant limitation is that, since PGs are more common in younger populations, the average age of our adult patients was relatively young. As a result, we are limited in our ability to comment on older populations, where the risk of melanoma associated with PGs is significantly greater. Other limitations of this study are the small sample size and the retrospective design.

In conclusion, PG morphology changes with age, and higher-risk morphologies may be observed in adults. Larger studies that include older patients are needed.

### CONCLUSION

Our study demonstrates that MLPG exhibit distinct age-related behaviors. In adults, MLPG are more likely to remain stable but can present with atypical and irregular features that may indicate a higher melanoma risk. In contrast, pediatric MLPG display dynamic changes with frequent regression of peripheral globules and generally benign characteristics. These findings highlight the importance of age-specific evaluation in the management of MLPG. Tailored follow-up strategies can help minimize unnecessary excisions in children while ensuring timely detection of suspicious changes in adults. Larger studies that include older patients are needed.

### Ethics

**Ethics Committee Approval:** This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, İstanbul Training and Research Hospital (approval number: 120, date: 08.04.2022).

**Informed Consent:** Patients provided informed consent.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: D.İ.E., D.Y., C.L., Concept: D.İ.E., A.E.K.A., V.A.T.E., A.K.P., Design: D.İ.E.,

A.E.K.A., V.A.T.E., A.K.P., Data Collection or Processing: D.İ.E., A.E.K.A., V.A.T.E., D.Y., C.L., A.K.P., Analysis or Interpretation: D.İ.E., A.E.K.A., V.A.T.E., D.Y., C.L., A.K.P., Literature Search: D.İ.E., A.K.P., Writing: D.İ.E., A.E.K.A., V.A.T.E., A.K.P.

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