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Acquired agminated melanocytic naevi as a rare variant of melanocytic nevus: report of two cases

Dear Sir,

Agminated melanocytic nevus is a rare subtype of melanocytic naevi in which congenital or acquired melanocytic lesions are usually clustered on normalbackground skin with a linear,unilateral or segmental distribution resembling the lines of Blaschko.(1-3)Theterm agminated is derived from the Latin word‘agmen’which is referring to aggregation or clusteringof the lesions usually in a segmental pattern.(1)Differentmelanocytic tumors can occasionally appear asagminated lesions.(1-3)In these cases,the agminatedmacules dermoscopicallylacked background pigmentation,unlike speckledlentiginous naevus.This appearance ofagminated naevi was linked to the clonal proliferation ofcells originating from a somaticmutation at an early stage of embryogenesis incongenital variant,however in acquiredcases the pathogenesis isnot clear yet.The riskof malignant transformation from agminatedmelanocytic nevi is uncertain but there are few case reports about melanoma arising from agminated melanocytic nevus.(4,5)

A 32-year-old male presented with a 3-year history of multiple brown macular lesions on his right hand and forearm.He was diagnosed as a primitive neuroendocrine tumorwhen he was 3 years old and he has a radiotherapy andchemotherapy history.There was no history of melanoma in individual or family history.Dermatological examination revealed >100,1-2

mm,brown-black macules, and papules segmentally distributed on extensor and flexor aspects of the right forearm and hand.(Figure1)Dermoscopic examination revealed symmetrical brown reticular lines without any pigmentation on the background.(Figure 2)Histologically,the symmetrical proliferation of melanocytes arranged in nests was detected.(Figure3)No feature concerning malignant disease was detected.His lesions were accepted as acquired agminated melanocytic nevus due to clinical and histopathological findings.BRAFV600E gene mutation analysis was performed due to his neuroendocrine tumor history to define whether there may be an association with his segmentally arranged agminated naevus and neuroendocrine tumor development.Mutation analysis was positive in the lesion.Sun protection and routine dermoscopic follow-up was recommended every 6 months.

A 15-year-male presented with a 2-year-history of multiple melanocytic nevi bilaterally on hips.(Figure 4)Dermoscopic examination revealed symmetrical brown reticular lines.He has no history of immunosuppression or systemic disease.Histologically,the symmetric proliferation of melanocytes arranged in nests was detected.(Figure 5)BRAFV600E,nRAS,kRASmutations were negative in the lesion.The lesions were accepted as agminated melanocytic nevus regarding the clinical distribution and routine dermoscopic follow-up was recommended every 6 months.

There are few case reports andcase series in theliterature about this type of melanocytic lesions.(6)The terminology of“agminated nevus”was first reported in 2001by Marghoob etal in a patient who has atypical mole syndrome.(1)Shimasaki et alreported that acquired agminated melanocytic naevi may be associated with dysplastic naevus syndrome.(7)Afterward,Torchia etal published a review paper about the melanocytic naevi clustered on normal background skin and they described the pattern analysis in different melanocytic naevi.(8)In this review total,181cases were,of these,19cases havecommon

acquired melanocytic naevi and in two cases the occurrence of malignant melanoma within the involved segment was reported.Genetic testing was performed only in one case in the agminated common melanocytic nevus group and they found a mosaic mutation of BRAF.In our cases,BRAFmutation was positive in Case1who has a primitive neuroendocrine tumor.TheBRAF gene mutations were also reported to be rare events in neuroendocrine tumors.The activation of theRAF/mitogen-activated protein kinase pathway was suspected to have a causative role in the development of neuroendocrine tumors.(9)In none of the two cases,we found no mutation in RAS genes.Carreno-Gayosso et al reported two cases of agminated atypical melanocytic nevus associated with Langerhans cell histiocytosis.(10)Interestingly multiple nevi arised in the sites of the skin affected by Langerhans cell histiocytosis.The authors noted that this appearance may be associated with a somatic mutation in BRAFV600E,causing activation and over-expression of the MAPK/ERK proliferation pathway.(10)

Thisuncommon variant of melanocytic naevi still needs to be investigated about genetic mutations in larger populations.We wantto present these two cases with their uncommon clinical manifestations to remind that careful follow-up may be recommended in these patients for thepossible risk of melanomadevelopment.

Disclosure Statement

The authors have no conflicts of interest to disclose and there were no funding sources supporting the work.

Data Availability Statement

Data are openly available in a public repository that issues datasets with DOIs.

Author Contributions

Tugba Kevser Uzuncakmak, Mukaddes Kavala and Ilkin Zindanci involved in conception and design of study; Tugba Kevser Uzuncakmak and Bengu Cobanoglu Simsek involved in acquisition of data; and Tugba Kevser Uzuncakmak and Burce Can kuru involved in analysis and/or interpretation of data.

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Figure legends

Figure 1 More than 100, 1-2 mm in diameter, brown-black macules and papules on extensor end flexor aspects of the right forearm and hand

Figure 2 Dermoscopically, multiple, symmetrical brown reticular lines

Figure 3 Histologically, a symmetrical proliferation of melanocytes arranged in nests in dermo-epidermal junction with mild dysplasia (H&E,x200)

Figure 4 Multiple, 1-2 mm, brown-black macules, and papules on bilateral hips.

Figure 5. Histologically, normal melanocytes arranged in nests in the dermis, melanocyte nests showing mild dysplasia on the dermo-epidermal junction (H&E,x200)