SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	COSTA RICA		PRIVACY		64 Years	Female	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [LOWER LEVEL TERM] (Related symptoms if any separated by commas)

Extending agminated blue nevus [Blue nevus]
Extending agminated blue nevus [Disease progression]

Case Description: The initial report was received on 21-APR-2025.
Aspen central receipt date was 22-APR-2025.
Additonal information received on 23-APR-2025 via MS Pharm.

GLO2025CR003196 is a literature case report received from a physician via global literature monitoring and EMA download (CR-MLMSERVICE-20250414-PI478956-00059-1) concerning a 64-years-old female patient who had

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ OTHER

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Azathioprine (Azathioprine) Unknown
#2) Prednisolone (Prednisolone)
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 100 milligram, qd	#1) Unknown
#2) 5 milligram, qd	#2) Unknown

17. INDICATION(S) FOR USE
#1) Systemic lupus erythematosus (Systemic lupus erythematosus)
#2) Systemic lupus erythematosus (Systemic lupus erythematosus)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown	#1) Unknown
#2) Unknown	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Current Condition since birth, agminated	Blue nevus (Melanocytic naevus)
Unknown to Ongoing	Current Condition since her early twenties	Systemic lupus erythematosus (Systemic lupus erythematosus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Aspen
Dublin, IRELAND

26. REMARKS

24b. MFR CONTROL NO.
GLO2025CR003196

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2025

24d. REPORT SOURCE
☐ STUDY ☒ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
06-MAY-2025

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

experienced Melanocytic naevus and Disease progression with administration of Azathioprine for systemic lupus erythematosus.

Literature:
Journal - Portuguese Journal of Dermatology and Venereology
Author - Martin-Zamora A.C, Arguedas-Gourzong E, Campos-Hidalgo M
Title - Extending agminated blue nevus in an immunosuppressed patient: a case report.
Vol - 83(1)
Year - 2025
Pages - 44-47

The patient has a medical history of Melanocytic naevus (unknown date - ongoing) and Systemic lupus erythematosus (unknown date - ongoing).

No concomitant medications were reported.

The patient-initiated administration of Azathioprine for systemic lupus erythematosus on unknown date. The last drug administration date is not reported.

Co-suspects included:
Prednisolone was administered for systemic lupus erythematosus from unknown date to unknown date.
Methotrexate was administered for systemic lupus erythematosus from unknown date to unknown date.

The patient experienced Non-serious Extending agminated blue nevus (Melanocytic naevus) on unknown date and Non-serious Extending agminated blue nevus (Disease progression) on unknown date.

A 64-year-old female patient was referred to the dermatology clinic for evaluation of an extensive pigmented lesion on her posterior left arm. Her medical history was notable for systemic lupus erythematosus (SLE) since her early twenties, currently using azathioprine 100 mg daily, prednisolone 5 mg daily, and methotrexate 10 mg weekly PO. The patient indicated the lesion was present since birth; however, she noticed progressive growth in size since puberty and new pigmented papules inside the main lesion. Family history of skin cancer was negative. On physical examination, the patient had an 8X7 cm bluish plaque on her posterior left arm filled by multiple isolated maculopapular lesions of blue and dark brown colors, with different sizes and forms. Dermatoscopy revealed light brown patches with round dark brown and blue structures with a homogeneous pattern. An elliptical incisional biopsy was performed. Histopathologic examination revealed intradermal islands of spindle cells with little pigment and a focal nodular downgrowth into the hypodermis mixed with melanophages. No atypia, mitoses, or necrosis was found. Clinical and histopathologic findings were consistent with the diagnosis of an agminated blue nevus with common and cellular blue nevus components. The patient is currently being followed up in the dermatology clinic for the last three years, with periodic checkups and evaluation of the lesion. Besides a 1 cm growth, the lesion has not undergone other significant changes. Conclusion: There are three types of solitary blue nevi: common, cellular, and combined. Unusual variants of grouped blue nevi have also been described. Agminated blue nevi represent a rare entity with an unclear incidence and pathogenesis. Cutaneous trauma was originally proposed as a predisposing factor after a case report of a cluster of blue nevi appearing after a severe sunburn; however, since then, most reported cases have had no associated cutaneous injury. In contrast to isolated blue nevi, agminated forms appear to be more commonly congenital or manifesting at earlier ages in life. They have no predilection for specific body sites and have been documented on the face, trunk, extremities, and genitalia. Somatic mutations in GNAQ and GNA11 are frequent in blue nevi, appearing in more than more than 80% of cases. These mutations produce a constitutive activity of heterotrimeric G proteins, which permanently activate the Ras signaling pathway, implicated in the regulation of cell proliferation. A case report in a patient with an agminated blue nevus and genetic profiling revealed a mutation in GNAQ4, indicating these mutations may also be prevalent in this variant. Dermoscopic findings appear to be similar to those of common blue nevi. A review of the reported cases demonstrated a structureless homogeneous pattern to be the prevailing finding. One case report also described linear pigmented structures appearing as "darker sulci". Our patients dermoscopy revealed consistent findings, with dark brown and bluish structures with a homogeneous pattern. Differential diagnosis of this entity includes agminated intradermal Spitz nevus combined with speckled lentiginous nevus, malignant blue nevi, and even melanoma, reason why histopathologic examination is usually recommended6. Microscopic findings in agminated blue nevi consist of proliferation of melanocytic cells in the upper and deeper dermis. Most reported cases showed elements consistent with common blue nevi, with dermal pigmented spindle-shaped dendritic melanocytes and a branching network of dendritic processes. A few cases have also documented a cellular blue nevi-type component, exhibiting a biphasic appearance with classic blue nevi features and cellular areas composed of spindled to oval melanocytes with clear or finely pigmented cytoplasm, such as in our case. Recent data suggest that blue nevi tend to remain stable throughout the years. There are some cases however that tend to have an expanding nature, documented mostly on the cellular blue nevi subtype. Progression to melanoma is also more common in cellular blue nevi Even though the exact nature and prognosis of agminated blue nevi have not been defined, malignant melanoma arising in these lesions has been documented9. A case report of a changing agminated blue nevi in a patient with dermatomyositis has been documented, suggesting a potential role for immunosuppression in this progression. This is comparable to our patients immunosuppressive treatment and the behavior of her lesion. Agminated blue nevi represent a rare subtype of blue nevi. Most of the few reported cases have exhibited a benign course; however, there is no validated evidence of the benign course. We report this case of an agminated blue nevus in a patient with systemic lupus erythematosus and immunosuppressive treatment. Because of ongoing changes within the lesion and uncertainty of behavior in this pathology, our patient remains in follow-up with periodic examinations.

Action taken with Prednisolone is Unknown.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Action taken with Methotrexate is Unknown.
Action taken with Azathioprine is Unknown.

Melanocytic naevus was reported as event outcome Not Recovered/Not Resolved/Ongoing.
Disease progression was reported as event outcome Not Recovered/Not Resolved/Ongoing.

Causality
Azathioprine
Event: Melanocytic naevus
Reporter's causality: Related
Company's causality: Related
Seriousness: Non-serious
Outcome: Not Recovered/Not Resolved/Ongoing

Causality
Azathioprine
Event: Disease progression
Reporter's causality: Related
Company's causality: Related
Seriousness: Non-serious
Outcome: Not Recovered/Not Resolved/Ongoing

13. Relevant Tests

On an unknown date, physical examination revealed the patient had an 8 * 7 cm bluish plaque on her posterior left arm filled by multiple isolated maculopapular lesions of blue and dark brown colors, with different sizes and forms.
On an unknown date, dermatoscopy examination revealed light brown patches with round dark brown and blue structures with a homogeneous pattern.
On an unknown date, histopathologic examination revealed intradermal islands of spindle cells with little pigment and a focal nodular downgrowth into the hypodermis mixed with melanophages. No atypia, mitoses, or necrosis was found.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#3) Methotrexate (Methotrexate) ; Regimen #1	10 milligram, 1 dose Weekly; Oral use	Systemic lupus erythematosus (Systemic lupus erythematosus)	Unknown; Unknown

24d. Report Source Literature
Journal: Portuguese Journal of Dermatology and Venereology
Author: Martin-Zamora A.C, Arguedas-Gourzong E, Campos-Hidalgo M
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