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Original article

Clinical-dermatoscopic characterization of macules in the most frequent genodermatoses and congenital skin defects

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ABSTRACT

Introduction:some genodermatoses and congenital skin defects are very similar, necessitating non-invasive techniques such as dermoscopy to guide diagnosis and allow differentiation.

Objective:to clinically and dermoscopically characterize macules in the most frequent genodermatoses and congenital skin defects to enable differentiation.

Methods:A quali-quantitative, descriptive, cross-sectional, prospective study was conducted in Las Tunas from 2025 to 2026. The sample consisted of 155 patients selected by simple random sampling. A polarized light dermatoscope was used. Variables studied included: definitive diagnosis; type of macules; dermoscopic findings; dermoscopy-histopathology concordance. Percentage calculations and positivity index regarding dermoscopic and histopathological diagnosis were performed. To determine the degree of agreement between both techniques, Cohen's kappa index was calculated, and clinical and dermoscopic findings were described.

Results:observation of the distribution of dermoscopic findings in hyperpigmented macules revealed a predominance of the typical pigment network with homogeneity; in

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hypopigmented lesions, the conditions were asymmetric with irregular borders; and in vascular macules, a tendency toward asymmetry was observed with lacunar vascular structures, globular, linear, and arborizing vessels. A high positivity index with high concordance between dermoscopy and histopathology was determined.

Conclusions: The clinical and dermoscopic characterization of macules in patients with genodermatoses and congenital skin defects allowed the establishment of diagnostic patterns useful for dermatological practice, especially in pediatric and genetic contexts.

Keywords: Genodermatoses; Dermoscopy; Congenital skin defects; Nevi.

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Introduction

Genodermatoses constitute a diverse group of diseases of genetic origin whose main manifestation is expressed in the skin, independent of environmental factors. Although some are related to chromosomal or mitochondrial alterations, most are due to mutations in one or more genes, following Mendelian patterns of inheritance. Congenital skin defects, on the other hand, correspond to structural abnormalities originating during prenatal morphogenesis, which may be evident at birth or manifest later through dysfunctions of the affected organ. (1)

The World Health Organization (WHO) has highlighted since 1963 the need to implement strategies for the prevention and control of genetic diseases (2). In Cuba, studies on genodermatoses are scarce and are not included in official records. In the province of Las Tunas, it was identified that 22.22% of genetic diseases present a pattern of cutaneous mosaicism as a clinical phenotype, which hinders their diagnosis. (3) lThe most prevalent conditions presenting with macules are: neurofibromatosis type 1 (NF1) with 13.6:100,000 inhabitants, mastocytosis with 2.4:100,000 inhabitants, oculocutaneous albinism (OCA),

incontinentia pigmenti both with 1.9:100,000 inhabitants, LEOPARD syndrome with 0.9:100,000 inhabitants. (3) Some are very similar, so non-invasive techniques such as dermatoscopy are needed to guide their diagnosis and allow differentiation.

The research of Velázquez et al, (2) validated a methodology that protocolizes the diagnosis, treatment and prevention, with a follow-up algorithm for the most frequent genodermatoses; whose theoretical and practical foundation was validated through the Delphi variant of the expert method, highlighting the usefulness of dermatoscopy, as a non-invasive tool used for the in vivo observation of skin lesions that enables the recognition of structures not visible to the human eye, (4) to differentiate dermatological lesions in genodermatoses and congenital skin defects.

The objective of this research wasTo clinically and dermatoscopically characterize the macules in the most frequent genodermatoses and congenital skin defects, allowing them to be differentiated.

Methods

Type of study, universe and sample

A mixed study was designed, with a qualitative and quantitative approach, of a descriptive, cross-sectional and prospective nature, carried out in the multidisciplinary consultation of genodermatosis of the Provincial Department of Medical Genetics (DPGM) of Las Tunas between 2025 and 2026.

The universe consisted of 256 patients diagnosed with genodermatosis or congenital skin defects, from which a sample of 155 was selected by simple random sampling, with a confidence level of 95% and a margin of error of 5%.

Inclusion criteria: that the patients studied resided in the province of Las Tunas, that they presented macules as part of the dermatological manifestations of genodermatosis or some congenital defect, that they underwent dermatoscopy and the prior informed consent of the guardian.

Exclusion criterion: abandonment of follow-up in consultation.

All patients underwent a medical history review, dermatological examination, and dermatoscopy. The first step was to examine the healthy skin adjacent to the lesion using dermatoscopy to identify normal skin characteristics based on age, skin phototype, and anatomical location. If findings consistent with premalignant or malignant lesions were present, a histopathological study was performed to correlate the dermatoscopy findings.

The dermatoscope used was a polarized light type, model Dermlite DL100, designed for the examination of skin lesions by magnification and cross-polarized illumination, which includes: 8 white LEDs, 10x lens, cross polarization, with removable separator.

The variables to be studied were: Definitive diagnosis as genodermatosis: AOC, ataxia telangiectasias, tuberous sclerosis, whorled linear hypermelanosis (HLA), hypomelanosis of Ito, incontinentia pigmenti, mastocytosis, NF1, piebaldism, Legius syndrome, LEOPARD syndrome, Noonan syndrome, Waardenburg syndrome (SW); or congenital skin defects: cavernous and flat hemangiomas, Mongolian spot, anemic nevus, Becker's nevus, Ota's nevus, speckled nevus (NLM), simple nevus (NLS), congenital melanocytic nevus (NMC), giant nevus (NG), segmental vitiligo; type of macules; dermatoscopic findings; dermatoscopy-histopathology concordance.

Among the quantitative biostatistical methods used were the calculation of percentages as a measure of frequency; the positivity index (PI) with respect to the dermatoscopic and histopathological diagnosis, considered effective when the PI ≥ 85%; and to determine the degree of agreement between both techniques, Cohen's kappa index (KC) was determined, which was interpreted as follows: weak agreement <0.20; acceptable agreement: 0.20-0.40; moderate agreement: 0.40-0.60; considerable agreement: 0.60-0.80; very good agreement: >0.80. The hypotheses H0: there is no agreement and HA: there is agreement were considered.

Qualitatively, the dermatoscopic clinical findings that allowed differentiation between genodermatoses and the most frequent congenital skin defects were described.

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The differential diagnosis of pigmented and vascular macules was summarized in a table that exceeded the standardized lengths specified in the Multimed journal guidelines. Therefore, it was decided to use AI (Artificial Intelligence) to convert it into descriptive plain text. Specifically, chat.deepseek.com was used. The data in the table were collected by the authors, so the AI tool was only used for the conversion from one format to another.

Ethical considerations: The protocol was approved by the Ethics Committee and the Scientific Council of the Mártires de Las Tunas Provincial Teaching Pediatric Hospital, following the Declaration of Helsinki. (5)

Results

Observation of the distribution of dermatoscopic findings in hyperpigmented macules (Figure 1) revealed that the typical pigment network predominated, with homogeneity and irregular borders, although it was not homogeneous in Becker's nevus, the medial longitudinal nerve (MLN), or the nasopharyngeal nerve (NPN). In genodermatoses, the presence of hypopigmented areas without a pigment network was particularly notable in 16.67% of patients with incontinentia pigmenti, while 83.33% showed café-au-lait hyperpigmented macules. In congenital defects, the parallel pattern was observed in congenital malformations (CMN) (20%), which were located on the palms and soles. Black globules were detected in Becker's nevus, MLN, and lateral sulcus nerve (LSN) (14.29%), CMN, and NP (22%).

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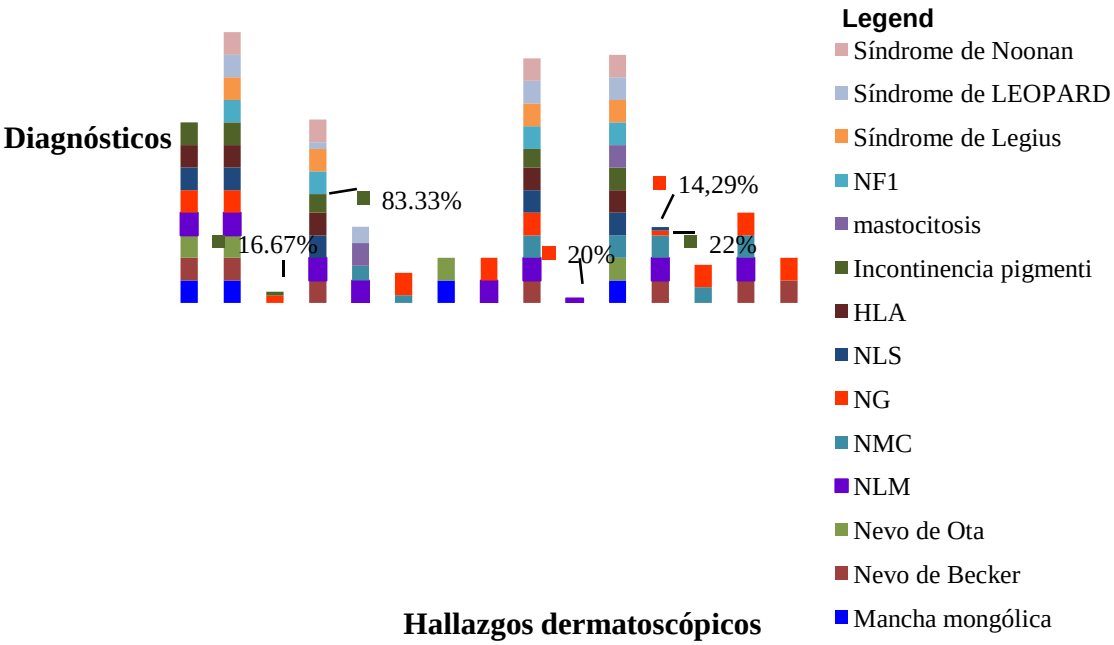

Chart 1. Distribution of dermatoscopic findings in hyperpigmented macules.

Regarding the distribution of dermatoscopic findings in hypopigmented macules (graph 2) the conditions were asymmetric with irregular borders and achromia was identified in the AOC, piebaldism, poliosis in the SW and segmental vitiligo and only the didymosis macules in the SW presented polychromia with pigment network (45.45%).

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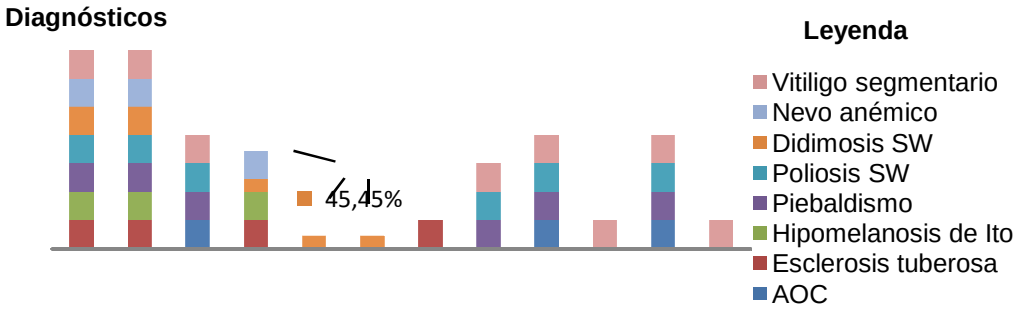

Chart 2. Distribution of dermatoscopic findings in hypopigmented macules.

In the vascular macules (graph 3) it was foundtendency towards asymmetry with lacuna-like vascular structuresin cavernous hemangiomas and 14.3% of flat hemangiomasglobular, linear, and arboriform vessels were identified.

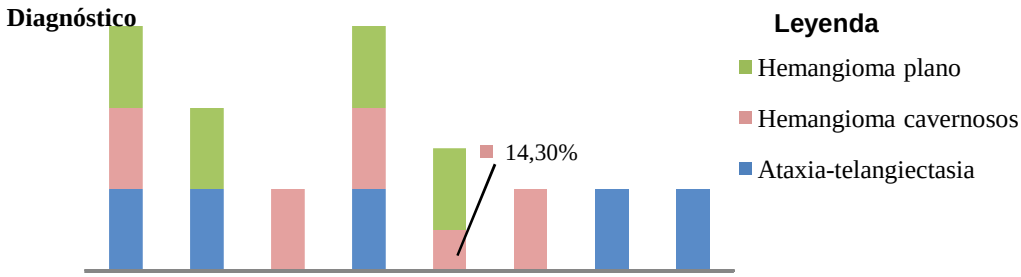

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Chart 3. Distribution of dermatoscopic findings in vascular macules.

34.84% of patients required histopathological study (Table 1) which corresponded mainly to mastocytosis (8.39%) and NMC (6.46%), and IP=90.74 was found with high concordance between dermatoscopy and histopathology (KC=0.89) which supports the reliability of this non-invasive technique, especially in pediatric and genetic contexts where biopsy may be limited or risky.

Table 1. Dermatoscopy-histopathology concordance for diagnosis.

Diagnostics	Dermatoscopy		histopathology		IP
	No.	%	No.	%	
Ataxia-telangiectasia	1	0.65	1	0.65	100
Tuberous sclerosis	3	1.94	3	1.94	100
HLA	3	1.94	3	1.94	100
Hypomelanosis of Ito	4	2.58	5	3.23	80
Incontinentia pigmenti	3	1.94	5	3.23	60
Mastocytosis	13	8.39	15	9.69	86.67
Piebaldism	4	2.58	3	1.94	75
Anemic nevus	2	1.29	2	1.29	100
Becker's Nevus	3	1.94	3	1.94	100
NLM	2	1.29	2	1.29	100
NMC	10	6.46	10	6.46	100
Segmental vitiligo	1	0.65	2	1.29	50
Total	49	31.61	54	34.84	90.74
KC= 0.89					

Clinical-dermatoscopic characteristics of pigmented macules

NF1 (Neurofibromatosis type 1): Café-au-lait macules with smooth or irregular borders, without hair loss, present from birth. More than six are present, accompanied by axillary or inguinal freckling, two or more neurofibromas, plexiform neurofibromas, Lisch nodules, optic nerve glioma, and typical bone lesions. Dermatoscopically, a symmetrical pattern with irregular borders, a homogeneous café-au-lait color, and a typical pigmented network is observed.

Legius syndrome: Café-au-lait macules with irregular borders, present from birth, in numbers greater than 6, accompanied by axillary or inguinal freckling. Dermatoscopically, a symmetrical pattern of irregular borders, homogeneous café-au-lait color, with a typical pigment network is observed.

Noonan syndrome: Café-au-lait macules and lentigines, symmetrical, with irregular borders, accompanying a characteristic triangular facial appearance, cardiac defects, and thoracic deformity. Dermatoscopically, a symmetrical pattern with irregular borders, a homogeneous café-au-lait color, and a typical pigment network is observed.

Leopard syndrome: Lentiginosis presents as a symmetrical, café-au-lait or dark brown lesion with irregular borders, present from birth and affecting the skin and mucous membranes. It is accompanied by an abnormal electrocardiogram, ocular hypertelorism, pulmonary stenosis, genitourinary abnormalities, growth retardation, and sensorineural hearing loss. Dermoscopy reveals a symmetrical pattern with irregular borders, a homogeneous café-au-lait or dark brown color, and a characteristic pigment network.

Mastocytosis: Macules that may be papular, dark brown in color, with a positive Darier sign. Dermatoscopically, a symmetrical macule with regular borders, dark brown in color, and a homogeneous pattern is observed.

Nevo de Ota:A brown or dark blue melanic macule affecting the skin, sclera, and conjunctiva unilaterally and sometimes bilaterally, present from birth. Dermoscopy reveals a bluish, asymmetrical macule with irregular borders and a homogeneous pattern.

Mongolian spot:A bluish or grayish macule present from birth, located in the sacrococcygeal region and buttocks. (No dermatoscopic findings in the table).

Becker's Nevus: Dermatoscopically: asymmetrical macule, café au lait color, irregular borders, with hypertrichosis on its surface.

NLM (Café au lait macule nevus): Café-au-lait colored macule with small dark brown macules inside, irregular borders. Dermatoscopy: asymmetric macule, heterochromia with

café-au-lait pigmentation and dark brown internal macules, irregular borders with typical pigment network, perifollicular hyperpigmentation and presence of brown globules.

NLS (Small Lesion Nevus): Café-au-lait macules, regular borders, no hair disturbance, present from birth, small in size, few in number (less than six). Dermatoscopically: symmetrical pattern with irregular borders, homogeneous café-au-lait color, with typical pigment network, sometimes with brown globules.

NMC (Congenital melanocytic nevus): Rounded, brown macules ranging from light to dark shades, generally appearing at birth or in early childhood, with regular borders, sometimes with hypertrichosis. Dermatoscopy: symmetrical macule, dark brown or black in color, with regular borders and a typical pigment network, perifollicular hyperpigmentation, presence of brown globules, parallel pattern on the finger ridges, and follicular hypertrophy.

NG (Giant Nevo):A large, dark, brownish, or even blackish macule covering an area of skin, resembling a swimsuit, with a thick appearance, giving the impression of animal skin. The surface may be smooth or rough with wart-like or nodular elevations, and hypopigmented patches that appear with growth. Dermatoscopy: asymmetrical macule, dark brown or black in color, irregular borders with a typical pigment network, presence of brown globules, cobblestone pattern, perifollicular hyperpigmentation, possible heterochromia with hypopigmented areas of regression, and follicular hypertrophy.

HLA (Linear Blaschkoid Hyperpigmentation): Hyperpigmented café-au-lait macules with irregular borders and a linear Blaschkoid distribution, present since birth. Dermatoscopy: asymmetric pattern with irregular borders, homogeneous café-au-lait color, with a typical pigment network.

Incontinentia pigmenti: It progresses through the vesicobullous and verrucous phases. Around one year of age, the hyperpigmented phase appears, characterized by a café-au-lait color, irregular borders, and a linear Blaschkoid distribution. Around adolescence, the hypopigmented phase appears, also with irregular borders and a linear Blaschkoid

distribution. Dermatoscopy: asymmetric pattern with irregular borders, homogeneous white color, without a pigment network.

Hypomelanosis of Ito: Hypopigmented macules with irregular borders, linear Blaschkoid distribution, present from birth. Dermatoscopy: asymmetric pattern with irregular borders, homogeneous white color, without pigment network.

SW (Waardenburg Syndrome): Didymosis is characterized by the coexistence of hyper- and hypopigmented lesions within the same macule, which do not affect the hair follicles. These lesions have irregular, sometimes diffuse, borders and are present from birth. Other findings include poliosis, hypopigmented or achromic macules on the trunk or extremities, heterochromia of the iris, dystopia canthorum, and sensorineural hearing loss. Dermatoscopy reveals heterochromia with hypopigmentation and a typical, asymmetrical pigment network with diffuse borders and no hair follicles affected; or asymmetrical achromia with irregular borders, a diffuse white sheen, follicular depigmentation, and some visible normal skin vessels.

Piebaldism: Poliosis is generally localized to the frontal area; in addition, there are areas of depigmentation on the skin. Dermatoscopy: heterochromia with hypopigmentation and a typical, asymmetrical pigment network with diffuse borders and no hair involvement; or asymmetrical achromia with irregular borders, a diffuse white sheen, follicular depigmentation, and some normal skin vessels visible.

Segmental vitiligo: Acquired achromic macule, with a segmental mosaic distribution, asymmetrical, irregular borders, depigmented hair within the lesion, and a leukomelanodermic border. Dermatoscopy: asymmetrical achromia, irregular borders, with diffuse white shine, peripheral hyperpigmentation, follicular depigmentation, some normal vessels visible, and a micro-Koebnerization sign.

AOC (Oculocutaneous Albinism):A nearly generalized lack of pigmentation affecting the skin, hair, and eyes. Pink, thin skin, very sensitive to the sun, with erythema or burns. Fine, pale yellow hair. Ocular manifestations: red iris, nystagmus, and photophobia.

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Dermatoscopy: generalized achromia with follicular depigmentation and visualization of the normal vascular structure of the skin.

Anemic nevus: Hypopigmented macules with irregular borders present from birth. No erythema occurs when rubbed. Dermatoscopy: asymmetric hypopigmentation, irregular borders, no hair involvement.

Tuberous sclerosis: Hypopigmented macules, present from birth or childhood, single or multiple, on the trunk or extremities. These are accompanied by facial angiofibromas, shagreen patches, facial fibrous plaques, and nail fibromas. Dermatoscopy: hypopigmented, asymmetric macule with irregular borders and the presence of pseudopods or striae.

Ataxia telangiectasia: Progressive ocular and cutaneous telangiectasias accompanying ataxia established in childhood, primarily affecting the humoral immune response. Dermatoscopy: asymmetry with irregular borders, reddish color, with linear and arborizing vascular structures.

Cavernous hemangioma: Mature cavernous hemangiomas are congenital, less common on the face, deeper, subcutaneous, and bluish-purple in color. They can be flat or raised, affect large blood vessels, and do not tend to grow or disappear. Dermatoscopy reveals asymmetry with irregular borders, a wine-red or blue color, with lacunae and no vascular structures.

Flat hemangioma: The flat hemangioma, also known as a port-wine stain or nevus flammeus, is congenital and unilateral, restricted to the facial territory of the trigeminal nerve (forehead, cheek, palate, or conjunctiva). It is dark red, sometimes with hemorrhagic lesions or pyogenic granuloma. Dermoscopy reveals asymmetry with irregular borders, a wine-red color, and the presence of lacunae and globular vessels. Flat hemangiomas of the newborn, also called salmon-colored spots (stork bites or angel's kiss), are congenital, predominantly affecting the forehead, eyelids, and nape of the neck.

They are flat and pink. Dermoscopy reveals asymmetry with irregular borders, a reddish color, and the presence of globular vessels.

The analysis of the clinical-dermatoscopic characteristics of pigmented macules allowed us to identify that although NF 1, Legius syndrome, Noonan syndrome and LEOPARD syndrome shared common features, with dermatoscopy they can be distinguished from similar lesions such as Becker's nevus or NLM, thanks to specific findings such as follicular hypertrophy or polychromia with brown globules.

In hypopigmented dermatoses, achromia was a common finding, but the presence of diffuse white sheen, peripheral hyperpigmentation, and the micro-Koebner phenomenon in segmental vitiligo offered differentiating criteria from atopic dermatitis and piebaldism. Vascular macules, although clinically similar, showed distinctive dermatoscopic patterns: lacunae in cavernous hemangiomas, globular vessels in flat hemangiomas, and linear or arborescent structures in ataxia-telangiectasia.

Discussion

Several studies have demonstrated that dermatoscopy is a non-invasive and effective tool for diagnosing nevi and other dermatoses. However, regarding its application in the study of genodermatoses, the authors found no reports in the scientific literature specifically addressing this approach.

Some authors highlight the importance of knowing the dermatoscopic characteristics of healthy skin, considering variables such as phototype, age, and anatomical location. (6,7) From a histological point of view, the pigment network corresponds to pigmented keratinocytes and melanocytes located in the walls of the epidermal ridges, while the spaces of the mesh coincide with the dermal papillae. (8)

In incontinentia pigmenti, the pigment network manifests during the hyperpigmented phase as hyperchromic macules with a Blaschkoid distribution. In contrast, during the

hypopigmented phase, this network is absent, reflecting the natural evolution of the disease. (9)

Gauray et al., (10) documented two cases of Becker's nevus in which they described the presence of a typical pigment network, perifollicular hyperpigmentation and follicular hypertrophy, findings that coincide with those observed in this study.

Fontaine et al. (11), in analyzing the clinical and histological correlation of pigmented nevi, reported a predominance of the homogeneous reticular pattern, consistent with the results described here. Torres et al. (12) identified a predominance of the cobblestone pattern (27.7%), brown globules (24.5%), and described the parallel pattern (2.7%) in lesions with a palmoplantar location of the MCN. When comparing these findings, the present study observed a higher frequency of brown globules, followed by the cobblestone pattern, and this coincided with the location of lesions with a parallel pattern, which corresponds to the ridges of the fingers.

Brown or black globules are rounded structures that, in the cobblestone pattern, take on large, angular shapes similar to cobblestones. These structures correspond to clusters of melanocytes in nests or thecae. (13,14) In the study by Mejía et al., (15) a relationship was demonstrated between asymmetric globules with the presence of inverted reticulum and progression to melanoma. Dermatoscopic monitoring of all pigmented lesions, especially those of nevus origin, is of particular importance.

In the present investigation, similar findings were found to those described by Sharma and collaborators, (16) in a cross-sectional study carried out in India on dermatoscopy in vitiligo and other hypopigmented lesions, documenting the total absence of pigment network in 66.7% of cases, presence of a faint network in the anemic nevus, pseudopods in ash leaf macules (64.3%) and diffuse white brightness in all patients with vitiligo.

Similarly, Wang et al., (17) who evaluated the use of dermatoscopy in vitiligo, described characteristics such as absence of pigment network within the lesions, poorly defined

borders, perilesional hyperpigmentation, satellite lesions, micro-Koebner phenomenon, telangiectasias and leukotrichia or perifollicular depigmentation.

It is difficult to differentiate thin malignant melanomas from atypical nevi, as they can present similar clinical, dermatoscopic, and even histopathological characteristics. According to the two-step method and Stolz's ABCD rule, the appearance of polychromia is a sign suggestive of melanoma (6,15), although this can be observed in other pigmented lesions such as those described in this study.

Vascular lesions encompass a wide range of entities, including hemangiomas, which are very common in childhood. These are characterized by well-defined lacunae, without internal vascular structures, and are round or oval in shape with variable coloration (red, bluish, purplish, or blackish). Histologically, these lacunae correspond to the proliferation of dilated capillaries in the dermis. (18) This description matches the hemangiomas evaluated in this study, given the presence of globular vascular structures and lacunae.

In the case of ataxia-telangiectasia studied in a young patient, the dermatoscopic findings were consistent with those described by Knöpfel and colleagues, (19) when they reported that recent telangiectasias show linear and branched vessels of red color, while older lesions may present tortuous vessels of violet color with a serpiginous arrangement in dermatoscopy.

When comparing the findings with those reported by Torres and collaborators, (12) who carried out a clinical-dermatoscopic characterization of NMC in the pediatric population of Villa Clara, a notable coincidence was evident between the studies in terms of the diagnostic correspondence between dermatoscopy and histopathology, as well as in the absence of malignant lesions.

While no prior studies were found on the use of dermatoscopy in genodermatous macules, this research demonstrates the clinical and dermatoscopic similarities between some genodermatoses, such as RASOpathies, and the dermatoscopic findings that allow them to be differentiated from other hyperpigmented genodermatoses and congenital

skin defects. Among hypopigmented genodermatoses, dermatoscopy is particularly useful for differentiating them from congenital defects such as nevus anemicus and mosaicisms such as segmental vitiligo. Regarding genodermatoses that present with vascular macules, the findings described in this research coincide with reports from other authors and contribute to guiding the differential diagnosis from other dermatoses.

A significant limitation of this research lies in the heterogeneity of the group of entities analyzed, which necessitates a larger sample size to establish robust correlations between dermatoscopic findings and clinical manifestations. Even so, the results obtained offer a useful framework for the diagnostic guidance of genodermatoses and congenital skin defects.

Conclusions

The clinical and dermatoscopic characterization of macules in patients with genodermatoses and congenital skin defects has allowed for the establishment of diagnostic patterns useful for dermatological practice, especially in pediatric and genetic contexts. Dermatoscopy has proven to be an effective tool for distinguishing entities with similar clinical manifestations, as it provides objective criteria that complement clinical evaluation and reduce the need for invasive procedures.

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Conflict of interest

The author declares no conflict of interest in conducting this study. All photos were obtained with informed consent.

Authorship contribution

Yordania Velázquez Avila: Conceptualization, form analysis, research, methodologies, original draft writing, revision writing and editing.