# Neonatal Neurofibromatosis: Diagnosis at Birth

Ana Cristóvão Ferreira[1], Marta P. Soares[2], Rita Espírito Santo[3], Joana Saldanha[3]

Port J Pediatr 2023;54(2):126-8
DOI: https://doi.org/10.25754/pjp.2023.26447

## Keypoints

**What is known:**

- Neurofibromatosis type 1 is an autosomal dominant disorder, with half of the cases being familial.
- Manifestations can vary in the same family: café-au-lait macules are present in almost all patients, but not frequent at birth.

**What is added:**

- In the 2021 revised criteria, the affected first-degree relative has to be a parent.
- Multidisciplinary surveillance is now even more important as new treatments are approved for some neurofibromatosis type 1 complications.

## Introduction

The patient was a male newborn who was the first child of an African non-consanguineous couple with a positive family history of neurofibromatosis type 1 (mother). Prenatal ultrasounds identified intrauterine growth restriction at the 27th week. Results of the pregnancy analysis were normal, and the mother decided not to perform genetic screening.

The birth was through vaginal delivery at 36 weeks of gestation with an Apgar index of 8/9/10. The newborn was small for his gestational age, length was between the third and 10th percentiles and the head circumference was in percentile 10.

On the first examination, he presented six or more café-au-lait macules with > 5 mm on the thorax, back, and left limbs (Figs. 1, 2 and 3), without other relevant features. A clinical diagnosis of neurofibromatosis type 1 was established, based on these findings and the family history.[1] He was discharged and referred to genetics, pediatric cardiology, ophthalmology, and neuropediatric. At 15 months old, he had normal neurodevelopment and growth, presenting only a right cryptorchidism. Moreover, he had a normal ophthalmological and cardiac evaluation.

The neurofibromatosis type 1, also known as von Recklinghausen disease, is an autosomal dominant disorder caused by pathogenic variants in the NF1 gene (chromosome 17), encoding neurofibromin synthesis, a tumor suppressor. It affects 1:2000-3000 people and is characterized by typical skin and pigmentary defects of the eye and multiple neurofibromas. Additional features include an increased risk of tumors, neurodevelopmental disabilities, and growth and musculoskeletal anomalies, among others.

Its phenotype is highly variable and age-dependent, making genetic counseling challenging.[2,3] Its clinical diagnosis requires two or more of the revised diagnostic

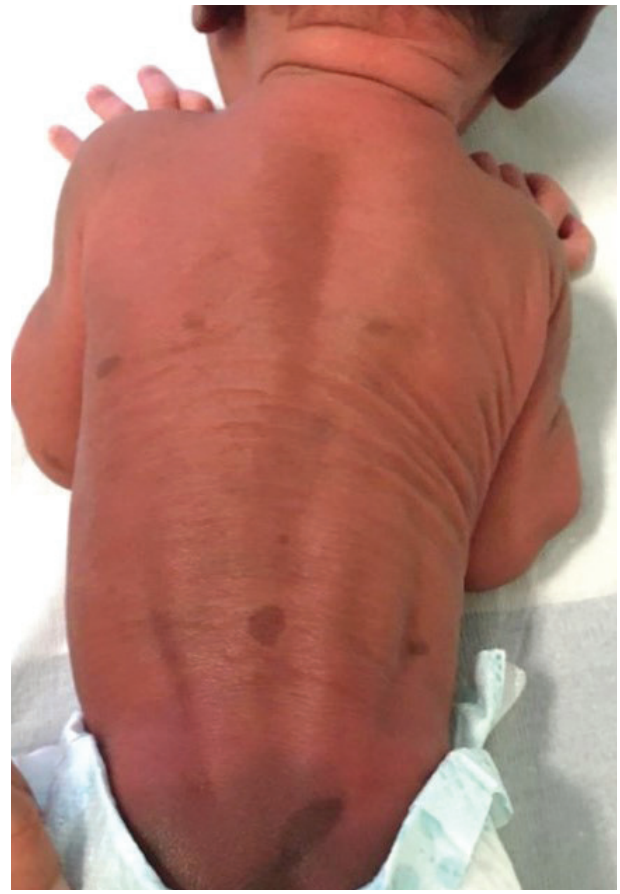

**Figure 1.** Multiple café-au-lait macules on the newborns back.

1. Medical Pediatrics Service, Department of Pediatrics, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal
2. Medical Genetics Service, Department of Pediatrics, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal
3. Neonatology Service, Department of Pediatrics, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal
**Corresponding Author**
Ana Cristóvão Ferreira | E-mail: ana.rcferreira@sapo.pt
Address: Centro Hospitalar Universitário de Lisboa Norte, Avenida Professor Egas Moniz MB, 1649-028, Lisboa, Portugal
Received: 22/04/2022 | Accepted: 04/05/2022 | Published online: 15/03/2023 | Published: 01/04/2023

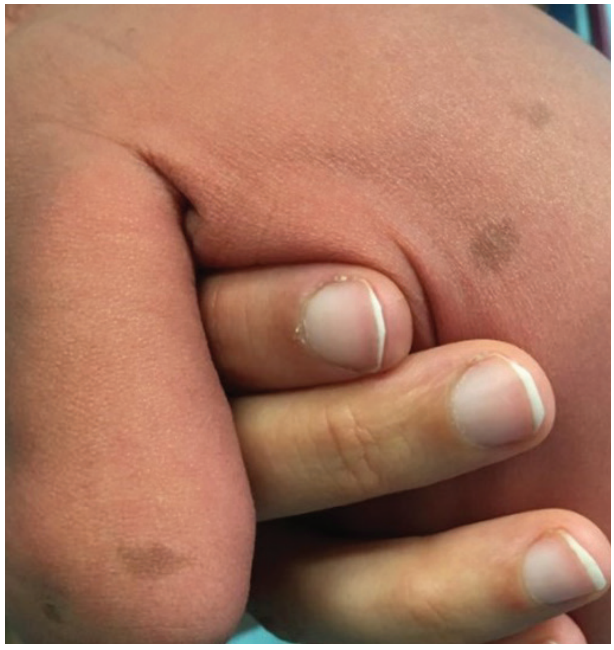

**Figure 2.** Café-au-lait macule on the left arm.

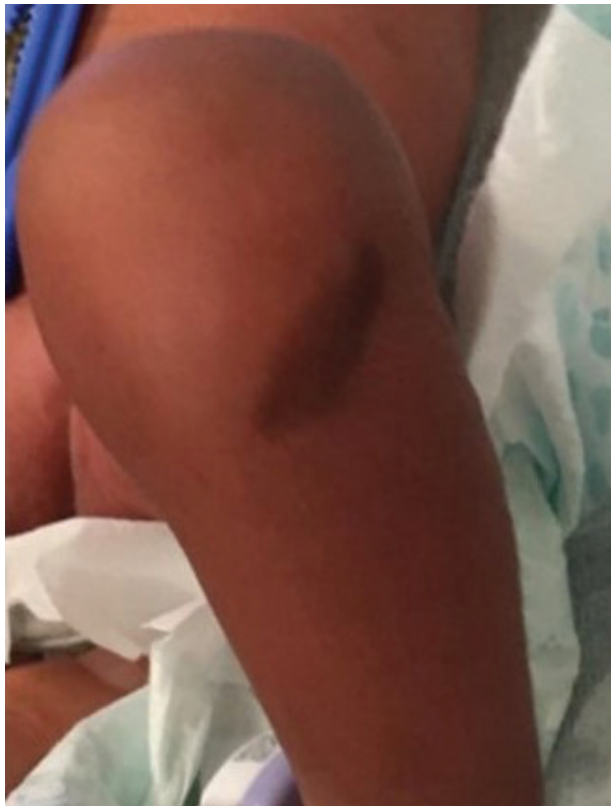

**Figure 3.** Oval-shaped café-au-lait macule on the left leg.

criteria if no parent has neurofibromatosis type 1. However, if one parent has neurofibromatosis type 1, its clinical diagnosis requires only one more criteria[4]:
- Six or more café-au-lait macules (> 5 mm in prepubertal or > 15 mm in post-pubertal individuals):
- Axillary or inguinal lentiginous macules;
- Two or more neurofibromas or one plexiform neurofibroma;
- Optic pathway glioma;
- Two or more Lisch nodules / choroidal abnormalities;
- Distinctive osseous lesion;
- Heterozygous pathogenic neurofibromatosis type 1 variant.

The café-au-lait macules are hyperpigmentary lesions with well-demarcated regular borders that are typically oval-shaped and usually develop in the first year. Nevertheless, they are infrequently presented at birth in a number which allows the diagnosis.[3-5] Early diagnosis is crucial for the prompt detection of complications, morbidity, and life quality. It should be noted that these children require multidisciplinary follow-up.[3]

**Keywords:** Cafe-au-Lait Spots/etiology; Infant, Newborn; Neurofibromatosis 1/diagnosis; Neurofibromatosis 1/genetics

## Author Contribuitions

ACF and MPS participated in acquisition of data. participated in the analysis or interpretation of data. ACF and MPS participated in the drafting of the manuscript. RES and JS participated in the critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

## Funding Sources

There were no external funding sources for the realization of this paper.

## Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013).

## Provenance and peer review

Not commissioned; externally peer reviewed

## Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data

## Awards and Presentations

Clinical case presented at the webinar 1ª Jornadas Digitais de Pediatria, 29-30 October 2020.

## References

1. Legius E, Messiaen L, Wolkenstein P, Pancza P, Avery RA, Berman Y, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: An international consensus recommendation. Genet Med 2021;23:1506-13. doi: 10.1038/s41436-021-01170-5.

2. Leppävirta J, Kallionpää RA, Uusitalo E, Vahlberg T, Pöyhönen M, Peltonen J, et al. Congenital anomalies in neurofibromatosis 1: A retrospective register-based total population study. Orphanet J Rare Dis 2018;13:5. doi: 10.1186/s13023-017-0756-4.

3. Drouin V, Marret S, Petitcolas J, Eurin D, Vannier JP, Fessard C, et al. Prenatal ultrasound abnormalities in a patient with generalized neurofibromatosis type 1. Neuropediatrics 1997;28:120-1. doi: 10.1055/s-2007-973684.

4. Radtke HB, Sebold CD, Allison C, Haidle JL, Schneider G. Neurofibromatosis type 1 in genetic counseling practice: Recommendations of the National Society of Genetic Counselors. J Genet Couns 2007;16:387-407. doi: 10.1007/s10897-007-9101-8.

5. Ozarslan B, Russo T, Argenziano G, Santoro C, Piccolo V. Cutaneous findings in neurofibromatosis type 1. Cancers 2021;13:463. doi: 10.3390/cancers13030463.