EDORIUM Journals

Int J Case Rep Images 2023;14(2):57–62.
www.ijcasereportsandimages.com

CASE REPORT PEER REVIEWED | OPEN ACCESS

A supraclavicular mass with skin macules «café-au-lait»: Neurofibromatosis 1

Romeo Thierry Yehouenou Tessi, Chaimae Lahlou, Soufiane Rostoum, Siham El Haddad, Nazik Allali, Latifa Chat

ABSTRACT

Neurofibromatosis type 1 is a genetic disorder representing one of the most common forms of Von Recklinghausen's disease. The neurofibromatoses are a group of heterogeneous, yet distinct, autosomal-dominant inherited neurogenetic disorders that include neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis. It is characterized by a large clinical polymorphism with the development of «café-au-lait» skin spots, benign tumors affecting the skin, peripheral nerves, optic pathway, and can involve the brain, bones, and vessels. We report the case of an 8-year-old child with neurofibromatosis type 1 diagnosis confirmed with clinical presentation and histological examination. He was referred for multidisciplinary management. There are clear diagnostic criteria according to a consensus (two or more criteria for diagnosis). The diagnosis is foremost clinical; the role of imaging is threefold: firstly, to confirm the diagnosis, secondly, to delineate extent of disease, and thirdly, suggests the type of the tumors in the affected patient. It helps to manage complications and follow-up. Histological examination confirms the diagnosis.

Romeo Thierry Yehouenou Tessi[1], Chaimae Lahlou[1], Soufiane Rostoum[1], Siham El Haddad[2], Nazik Allali[3], Latifa Chat[4]

Affiliations: [1]MD, Radiology Department, Ibn Sina Paediatric Teaching Hospital, Mohammed V University, Rabat, Morocco; [2]MD, Professor, Radiology Department, Ibn Sina Paediatric Teaching Hospital, Mohammed V University, Rabat, Morocco.

Corresponding Author: Romeo Thierry Yehouenou Tessi, MD, Radiology Department, Ibn Sina Paediatric Teaching Hospital, Mohammed V University, BP 6527, Rabat, Morocco; Email: nactessi@yahoo.fr

Received: 08 August 2023
Accepted: 07 September 2023
Published: 21 September 2023

Keywords: Café-au-lait macules, CT scan, MRI, Neurofibroma, Neurofibromatosis 1

How to cite this article

Yehouenou Tessi RT, Lahlou C, Rostoum S, El Haddad S, Allali N, Chat L. A supraclavicular mass with skin macules «café-au-lait»: Neurofibromatosis 1. Int J Case Rep Images 2023;14(2):57–62.

Article ID: 101411Z01RT2023

****

doi: 10.5348/101411Z01RT2023CR

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a relatively common inherited disorder. It is a genetic disorder representing one of the most common forms of Von Recklinghausen's disease. The neurofibromatoses comprise a trio of diverse disorders known as neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis. It is an autosomal dominant disease with the development of «café-au-lait» skin macules, benign tumors affecting the skin, peripheral nerves, optic pathway, and can involve the brain, bones, and vessels. It is characterized by a large clinical polymorphism. Previous studies reported that almost all patients with multiple «café-au-lait» macules will eventually develop NF1 based on clinical criteria, recent studies and clinical observations suggest that a significant percentage of them do not have NF1. The severity of the disease is related either to the malignant transformation or to the internal locations, in particular intracerebral, optic, and medullary pathways with the risk of neurological disorders, blindness, or spinal cord compression. A multidisciplinary approach is

necessary to its management, with a team of specialists throughout the lifetime of the patient.

CASE REPORT

We report the case of an 8-year-old child. He presented with a left supraclavicular mass of progressive evolution for more than two years. The medical history does not find any family history of the condition. The skin assessment found multiple «café-au-lait» spots and skin nodules (Figure 1) which appeared on ultrasound examination as heterogeneous mass with echogenic formations (Figure 2).

A cervicothoracic computed tomography (CT) scan was ordered to investigate the mass. The scan revealed multiple dense nodular formations above the clavicle, extending into the subscapular and left axillary regions. There was an anterior mediastinal and right paravertebral extension without intramedullary extension (Figures 3 and 4).

We then completed the examination with cervicothoracic magnetic resonance imaging (MRI) that showed: the same mass in low signal intensity at T1, hyperintense on T2, T2 Spair and non-enhancing after gadolinium administration, with no further foraminal extension or spinal cord compression. A target sign pathognomonic for plexiform neurofibroma is visible as central low intensity surrounded by a rim of high intensity (yellow arrows in Figure 5). The child had no eye disorders or other associated abnormalities. No abnormality of brain MRI identified. A biopsy of the supraclavicular mass was performed. Histological analysis showed neurofibromatosis with no evidence of degeneration. The rest of the examinations (ophthalmological and neurological) did not reveal any significant abnormalities.

Given the association of «café-au-lait» skin spots, the presence of nodular lesions of the neurofibroma type, and histological confirmation, the diagnosis of neurofibromatosis type 1 was retained. The child was referred for multidisciplinary management.

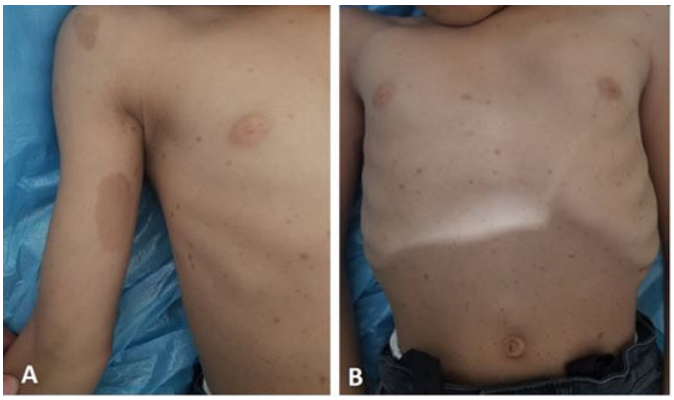

Figure 1: Clinical appearance of patient. (A) and (B) show "café-au-lait" skin macules of the thorax extending to the upper limbs characteristic of NF1 in an 8-year-old child.

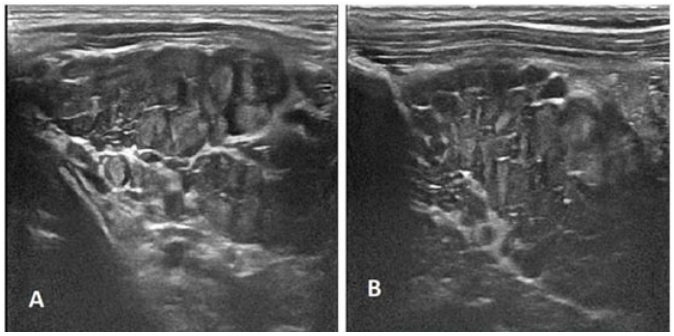

Figure 2: Ultrasound reveals neurofibromas in the form of heterogeneous nodular formations limited to the left supraclavicular region.

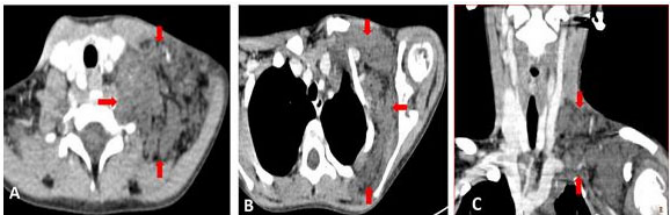

Figure 3: Cervicothoracic CT scan in parenchymal window in axial (A, B) and coronal (C) sections shows neurofibromas in the form of heterogeneous nodular formations under the clavicular, axillary, and left subscapular areas (red arrows).

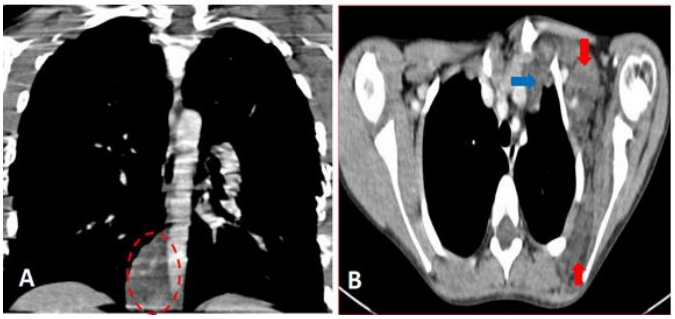

Figure 4: Chest CT scan in parenchymal window in coronal (A) and axial (B) sections shows a neurofibroma in the form of a right paravertebral mass (red circle), anterior mediastinal mass (blue arrow), and left subscapular extension (red arrows).

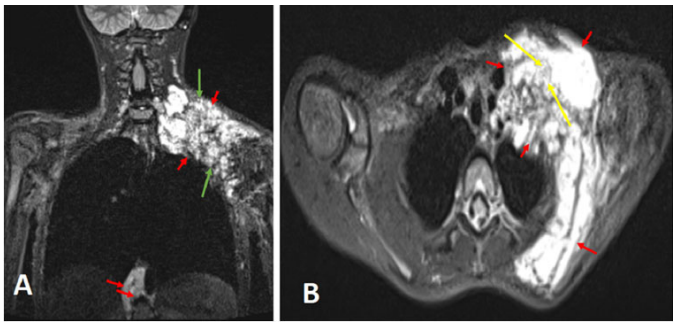

Figure 5: MRI cervicothoracic T2 Spair on coronal slices (A), axial slice (B) shows neurofibromas in the form of heterogeneous nodular formations under the clavicular, axillary with left subscapular extension, chest wall (green arrows) and a right paravertebral mass in hyposignal T1, hypersignal T2, T2 Spair (red arrows) with the target sign (yellow arrows).

DISCUSSION

Neurofibromatosis type 1 (NF1) is the most common phakomatosis. It is an autosomal dominant genetic disease caused by a mutation in the gene coding for neurofibromin synthesis which is a tumor suppressor gene on chromosome 17. Its incidence is approximately 1 in 2500 births and its prevalence 1 in 2000–4000 births [1]. It was recognized as a multisystem clinical entity in 1882 by Friedrich von Recklinghausen who gave his eponymous name to the disease (von Recklinghausen disease or NF1) [2]. There is no difference in the involvement of races or gender.

There are clear diagnostic criteria according to a consensus (two or more criteria for diagnosis) [3, 4]:

An individual who lacks a parent with an NF1 diagnosis can meet the diagnostic criteria for NF1 if two or more of the following conditions are fulfilled:

1. Prepubertal individuals with six or more café-au-lait macules, each measuring over 5 mm in greatest diameter, and postpubertal individuals with those measuring over 15 mm in greatest diameter.
2. Freckling observed in the axillary or inguinal regions.
3. Presence of two or more neurofibromas of any type, or a single plexiform neurofibroma.
4. Identification of an optic pathway glioma.
5. Identification of either two or more iris Lisch nodules through slit lamp examination, or the presence of two or more choroidal abnormalities (CAs), characterized as bright, patchy nodules visualized by optical coherence tomography (OCT)/near-infrared reflectance (NIR) imaging.
6. Occurrence of a distinct osseous lesion, such as sphenoid dysplasia, anterolateral bowing of the tibia, or pseudarthrosis of a long bone.
7. Identification of a heterozygous pathogenic NF1 variant, with a variant allele fraction of 50% in apparently normal tissue, such as white blood cells.

If one or more of the criteria listed in paragraph below are present, a child of a parent who satisfies the specified diagnostic criteria qualifies for an NF1 diagnosis.

Neurofibromatosis type 1 is characterized by polymorphic and multisystem involvement. These abnormalities are varied [3, 5]:

- Benign abnormalities are pigmentation abnormalities including «café-au-lait» spots that develop during the first two years of life. It is associated with axillary and inguinal freckles and Lisch nodules (benign melanocytic hamartoma of the iris).
  Also mentioned are neurofibromas, a benign Schwann cell tumor of variable composition, and plexiform neurofibromas (which may begin at birth and develop into adulthood).
- Bone anomalies (congenital bone dysplasia, pseudoarthrosis, scoliosis).
- Cardiovascular anomalies (congenital heart disease, valvulopathy and hypertension).
- Nervous system tumors (gliomas of the optic tract and brain stem, neurocognitive deficits, glioblastomas, malignant tumors of the peripheral nerve sheath).
- Other tumors (gastrointestinal stromal tumors, breast cancer, leukemia and lymphoma, pheochromocytoma, duodenal carcinoids, rhabdomyosarcoma).

Different radiological means are used for diagnosis, in particular the CT scan for the detection of neurofibromas and cerebral lesions, the MRI which has a better accuracy in the detection of intramedullary extensions, cerebral lesions and optic tracts, the standard radiography for the detection of bone lesions, the NIR spectroscopy (near-infrared reflectance spectroscopy) for the visualization of intraocular lesions.

Genetic testing for NF1 diagnosis, searching for inactivating mutations in the NF1 gene is essential for the diagnosis. It allows making the differential diagnosis with the Legius syndrome by the detection of the gene SPRED1.

The role of imaging is important and threefold: firstly, to confirm the diagnosis, secondly, to delineate extent of disease (extent of involvement and effect on adjacent structures), and thirdly, suggests the type of the tumors in the affected patient. Three modalities can be used: ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).

The significant contribution of sonography to the assessment of soft tissue tumors, particularly plexiform neurofibromas, tends to be inadequately emphasized in radiology literature [6].

The characteristic CT characteristics of plexiform neurofibroma are often associated with low attenuation, attributed to the presence of myelin lipids, trapped fat, and the high water content within the endoneurial myxoid tissue. Evaluating potential bony involvement (osseous remodeling) is crucial in these cases [6, 7].

Magnetic resonance imaging (MRI) stands as the gold standard imaging technique for both assessing neural tissues and outlining the parent nerve in instances of tumors with neural origins. The tumor has been described as being characteristically lobulated with a hyperintense signal on T2W imaging. The presence of a “target sign” has been identified as a distinctive marker for plexiform neurofibromas, where each individual “target” area is thought to represent an involved nerve fascicle. Within the lesion, there exists a central region of reduced intensity, encircled by a zone of heightened intensity, particularly when aligned along the nerve’s longitudinal axis. The central low intensity is attributed to the fibrous constituents, while the encompassing

myxoid components contribute to the intensified signal [6, 7].

The differential diagnosis is mainly with other types of neurofibromatosis type 2 and other pathologies such as schwannomatosis, Legius syndrome, Noonan syndrome, constitutional mismatch repair deficiency syndrome [1]. Legius syndrome or NF1-like is characterized by the presence of «café-au-lait» spots and lentigines, which may be associated with macrocephaly, facial dysmorphia, and cognitive disorders. It is autosomal dominant and therefore shares a number of diagnostic criteria with neurofibromatosis type 1. On the other hand, neurofibromas, Lisch nodules, and gliomas are absent, thus significantly reducing the risk of tumors. The gene involved (SPRED1) is located at 15q13.2 and consists of 7 exons [4].

Treatment requires a multidisciplinary team based primarily on the severity of the symptoms and the different organ involvement. Surgical treatment of neurofibromas is difficult due to infiltration, with therapeutic trials with Imatinib chemotherapy, interferons. Surgical treatment is recommended for optic tract gliomas with severe visual loss, disfiguring proptosis. Other combinations of carboplatin-based chemotherapy with vincristine remain the gold standard in the treatment of low-grade gliomas [5]. As per Gross et al., in April 2020, selumetinib was approved for the treatment of children with NF1-related symptomatic plexiform neurofibroma in the United States [8].

The evolution of NF1 associated with the optic tract glioma after chemotherapy is approximately one-third and the patient will regain vision after treatment. These visual impairments in NF1 reduce life experience by 10–15 years [5].

The most common cause of death in NF1 is cancer. Patients with NF1 have a 5-fold increased risk of cancer and a 2000-fold increased risk of neurogenic malignancy compared to the general population [9].

Neurofibromatosis type 1 remains a disease with multiple and variable visceral involvement. Ocular involvement results in uni- or bilateral visual loss. Early diagnosis is essential for good management and to avoid irreversible complications in order to improve patients' quality of life.

It requires multidisciplinary management and close collaboration between radiologists and clinicians in order to reduce the morbidity and mortality associated with NF1.

CONCLUSION

Neurofibromatosis type 1 is the most common autosomal dominant genetic disease. It is a pathology with multiple and variable visceral damage. The presence of characteristic cutaneous features and certain types of tumors should raise suspicion for the possibility of NF1 and prompt clinicians to refer patients to the appropriate specialists. A notable proportion of patients who initially present with solitary «café-au-lait» macules may not necessarily have NF1. Genetic testing could offer valuable insights to steer the subsequent care for these patients, but additional evidence is necessary to formulate concrete recommendations. Genetic counseling to families could also be greatly improved by the knowledge of the true presence or absence of NF1 in a child. Early detection is crucial for quality care and reduction of disability, enhancing the importance of diagnostic criteria. Strong collaboration between radiologists and clinicians of different subspecialties from making an early diagnosis and multidisciplinary management up to the follow-up is valuable to offer a quality of care and therefore improve morbidity and mortality.

REFERENCES

1. Ly KI, Blakeley JO. The diagnosis and management of neurofibromatosis type 1. Med Clin North Am 2019;103(6):1035–54.
2. Cimino PJ, Gutmann DH. Neurofibromatosis type 1. Handb Clin Neurol 2018;148:799–811.
3. Hirbe AC, Gutmann DH. Neurofibromatosis type 1: A multidisciplinary approach to care. Lancet Neurol 2014;13(8):834–43.
4. Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: An international consensus recommendation. Genet Med 2021;23(8):1506–13.
5. Karaconji T, Whist E, Jamieson RV, Flaherty MP, Grigg JRB. Neurofibromatosis type 1: Review and update on emerging therapies. Asia Pac J Ophthalmol (Phila) 2019;8(1):62–72.
6. Grover DSB, Kundra DR, Grover DH, Gupta DV, Gupta DR. Imaging diagnosis of plexiform neurofibroma-unravelling the confounding features: A report of two cases. Radiol Case Rep 2021;16(9):2824–33.
7. Hamdani O, Al-Yahyai B, Stephen E, et al. Don't miss the target: A case of neurofibromatosis type 1. Sultan Qaboos Univ Med J 2022;22(4):589–90.
8. Gross AM, Wolters PL, Dombi E, et al. Selumetinib in children with inoperable plexiform neurofibromas. N Engl J Med 2020;382(15):1430–42.
9. Peltonen S, Kallionpää RA, Peltonen J. Neurofibromatosis type 1 (NF1) gene: Beyond café au lait spots and dermal neurofibromas. Exp Dermatol 2017;26(7):645–8.

****

Acknowledgments
We thank the following individuals for their review of earlier drafts of the manuscript: Prof. Latifa Chat and Prof. Nazik Allali, chief service and deputy chief service of Radiology Department, Ibn Sina Paediatric Teaching Hospital, Mohammed V University, Rabat, Morocco.

Author Contributions

Romeo Thierry Yehouenou Tessi – Conception of the work, Acquisition of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Chaimae Lahlou – Conception of the work, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Soufiane Rostoum – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Siham El Haddad – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Nazik Allali – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Latifa Chat – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be 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

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

ABOUT THE AUTHORS

Article citation: Yehouenou Tessi RT, Lahlou C, Rostoum S, El Haddad S, Allali N, Chat L. A supraclavicular mass with skin macules «café-au-lait»: Neurofibromatosis 1. Int J Case Rep Images 2023;14(2):57–62.

Romeo Thierry Yehouenou Tessi is a medical officer from Benin. He earned the undergraduate Doctorat in Medicine from Faculty of Medicine and Pharmacy of University Abomey-Calavi (Benin). He is currently undergoing postgraduate training in Radiology at University Mohamed V of Rabat (Morocco). He is a peer reviewer for outstanding international journals and an Associate Editor at the Pan African Medical Journal. He has published scientific papers and co-authored different reviews in his field. His research interests include medical imaging and association of imaging to others medical disciplines. He is member of French, Tunisian, and Moroccan society of radiology.