Case Report

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An approach to café au lait macules in primary care setting

Seereen R. Almuhaidib, Fajar A. Aldulijan, Najlaa A. Alkanaan, Abdulmohsin K. Almulhim[1], Khalid S. Alyami[1]

Abstract

Café au lait macules (CALMs), if solitary, are benign lesion with no clinical meaning, and are common in the general population. Multiple CALMs may be the hallmark of some disorders and need to be assessed by an interprofessional team. The diagnosis and evaluation of a patient with a suspected condition may include a team of pediatric neurologists, dermatologists, ophthalmologists, geneticists, and orthopedic surgeons. To evaluate the progression of the disease, an annual follow-up is required.

Keywords:

Café au lait macules, neurofibromatosis, primary care approach

Introduction

Café au lait macules (CALMs) are well-defined, flat, localized hyperpigmentation, uniformly light brown in color with a diameter ranging from 2 mm up to more than 20 cm. Histopathological findings indicate increased melanin pigmentation with a higher number of basal keratinocytes and melanocytes. The presence of one or two lesions in a healthy child is not of any concern.[1] Furthermore, 10%–20% of the normal general population have this lesion at birth or during childhood. However, the presence of more than five lesions measuring >5 mm in young children and >15 mm in older children should raise the suspicion of an underlying pathology.[2] CALMs may present as a manifestation of different syndromes such as neurofibromatosis Type 1 (NF1), McCune Albright syndrome, Fanconi's anemia, and tuberous sclerosis complex (TSC).[3] CALMs are usually present after birth or in early age and can increase in number over time in some disorders such in NF1.[3] Primary care physicians should know how to approach pathological CALMs and be aware of the typical clinical presentations and differential diagnoses.

This is a case report of an 8-month-old baby who presented with CALMs at the primary healthcare clinic of a University Hospital, in the Eastern Province of Saudi Arabia.

Case Report

An 8-month-old female baby was delivered through cesarean section after full-term pregnancy (37 weeks) one of monozygotic twins; her mother had a bleeding during second trimester of pregnancy; her hemoglobin dropped to 7 g/dL and was managed by blood transfusion of two units. The baby's weight at the time of delivery was 2.5 kg, with APGAR score of 7 and 9 in 1 and 5 min, respectively. The baby was accompanied by her mother to the primary care clinic with multiple hyperpigmented lesions that had been present since birth and were increasing in number (>9). The baby was the result of *in vitro* fertilization. Regarding her developmental history, gross motor function: she could crawl and sit without support. Fine motor: she could

College of Medicine, Imam Abdulrahman bin Faisal University, Dammam, [1]Department of Family and Community Medicine, King Fahad University Hospital, Al Khobar, Saudi Arabia

Address for correspondence:
Miss Seereen R. Almuhaidib, 34432, Al Khobar, Saudi Arabia.
E-mail: 2170000177@iau.edu.sa

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transfer things from one hand to another. Language: she could say some words like "mama," and understood such words as "No" said to her. There were no developmental delays compared to other patients of that age group. The patient was breastfed only for the first 75 days after delivery as the mother's breast milk secretion was interrupted thereafter. There was no history of fever, itching, redness, conjunctivitis, dry eye, bowel changes, fatigue, weight loss, or neurological deficits. The patient is a twin, and vaccinations were up to date.

Dermatological examination revealed several hyperpigmented macules on the skin with a diameter of >1.5 cm and a number of 10–20 on the chest, abdomen [Figure 1], and back [Figure 2]. There was no axillary or inguinal freckling, and mucous membranes were unaffected. Ophthalmological examination found that the lacrimal system, conjunctiva, cornea, and anterior chamber were within normal limits. Bilateral Lisch nodules were not seen in the iris of either eye. Fundus examination revealed no abnormality in the right and left eye. No retinal breaks or retinal detachment was seen bilaterally. An annual follow-up was suggested for that.

Discussion

One of the most important pathologies of CLAMs is NF1, which is one of the most common autosomal dominant neurocutaneous disorders, with an incidence rate of 1 per 3000.[4,5] However, 50% of cases are sporadic. The National Institutes of Health consensus development conference established a set of criteria for the diagnosis of NF1. This required the presence of ≥2 of the following: (1) ≥6 CLAMs (≥0.5 cm in children and ≥ 1.5 in adult); (2) freckles in axilla or groin; (3) ≥2 cutaneous or subcutaneous neurofibromas or one plexiform neurofibromas; (4) ≥2 Lisch's nodules (iris hamartomas); (5) optic glioma; (6) cortical thinning of a long bone or sphenoid wing dysplasia; (7) A diagnosis of NF1 in a first-degree relative.[6] The sole presence of ≥ 6 CLAMs in children must be followed up as NF1 patient, as 95% of them will develop the disease.[7] After considering the diagnosis, a referral should be made to an NF1-skilled clinician who may be a neurologist, a pediatrician, a dermatologist, or a geneticist.[5] Moreover, a visual assessment should be made to detect optic gliomas and Lisch's nodules (iris hamartomas).[5] Mentoring for behavioral and cognitive deficits is essential, as it could be a complication of NF1 as most of the cases have shown.[5]

The cornerstone of managing NF1 is patient education and age-specific mentoring of the disease manifestations and complications on an annual basis.[5] Malignant peripheral nerve sheath tumors belong to the few life-threatening complications of NF1.[5] The average life expectancy can be reduced by 10–15 years in patients with NF1 with malignancy being the most common cause of mortality.[4] However, a routine imaging of different parts of the body to detect for asymptomatic tumors is not recommended and will not alter the management.[5]

Another possible differential of CALMs is TSC.[8] The diagnosis of TSC requires two major features or one major and two or more minor features.[8] Major clinical features are angiofibromas (≥3) or fibrous cephalic plaque, ungual fibromas (≥2), Shagreen patch, cortical dysplasias, multiple retinal hamartomas, subependymal nodules, subependymal giant cell astrocytoma, lymphangioleiomyomatosis and angiomyolipomas, and cardiac rhabdomyoma.[8] Minor clinical features include confetti skin lesions, retinal achromic patch, dental enamel pits, intraoral fibromas, multiple renal cysts, and non-renal hamartomas.[8] A positive genetic test for a pathogenic TSC1 or TSC2 mutation in nonlesional tissue is sufficient to make a definite diagnosis of TSC. Physical examination should focus on the dermal,

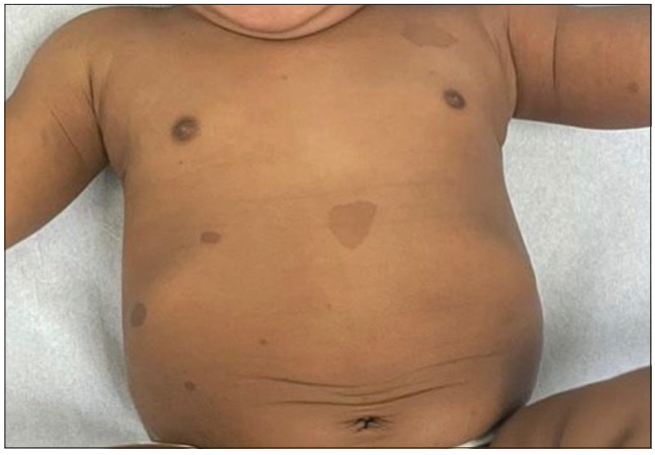

Figure 1: Café au lait macules

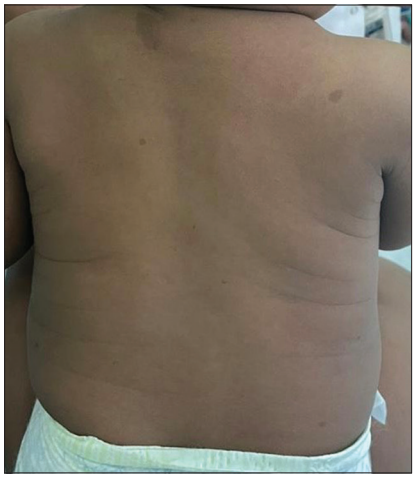

Figure 2: Café au lait macules

ophthalmical, and neurological systems.[8] The skin should be thoroughly examined for the characteristic dermatologic features of TSC including CALMs, fibroadenomas, distinctive brown fibrous plaque often present on the forehead, and Shagreen patches. Cranial and abdomen MRI should be performed, and renal ultrasound is indicated to evaluate for the presence of renal cysts or renal angiomyolipomas.[8]

The management of TSC is directed at its neurologic and systemic manifestations, which include seizures. Vigabatrin should be considered first line.[8] Corticotropin should be considered as an adjunctive or alternative to vigabatrin. Skin lesions in TSC may improve with laser therapy, dermabrasion, and possibly with topical mTOR inhibitors.[8] Children with TSC, particularly those younger than 3 years of age, should have baseline echocardiography and electrocardiography to evaluate for rhabdomyoma and arrhythmia.[8]

Fanconi's anemia is another differential of CALMs, and the widespread area of CALMs will assist early diagnosis. Primary care physicians should closely inspect the skin at least once a year for CALMs. When any are discovered, the primary care practitioner should check for the involvement of others and count and report the result.[4] A request for genetic testing for a definitive diagnosis of Fanconi's anemia based on the child's age should be made. The number of café au lait spots, the child's family history, and the existence of any other clinical findings indicative of Fanconi's anemia such as hematological and oncological manifestations should be mentioned.[9] Furthermore, primary care physicians may be the first to identify the symptoms and characteristics of Fanconi's anemia and make the necessary referrals for confirmation of the diagnosis.[9]

Conclusion

Every primary healthcare physician should be familiar with CALMs and its possible differential diagnoses. Being acquainted with the latter will help in making proper and early diagnosis of the associated disease, with a subsequent significant impact on the prognosis.

Declaration of parents' consent

The author certifies that all appropriate consent forms were obtained from the parents to publish the case report. In the form, the parents gave their consent for their images and other clinical information to be reported in the journal. The parents understood that their name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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