

# Large Solitary Café au Lait Spots: A Report of 5 Cases and Review of the Literature

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*The presence of multiple café au lait spots (CALs) has been well described and associated with several neurocutaneous and genetic syndromes including, most commonly, neurofibromatosis. However, scant literature exists regarding the clinical significance of the large solitary CAL. We describe 5 patients with congenital large solitary CALs without associated abnormalities. Our cases and review of the literature suggest that large solitary CALs are uncommon benign lesions that most likely are not associated with any neurocutaneous syndromes or developmental anomalies.*

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Café au lait spots (CALs) generally are discussed in the context of multiplicity and size as they relate to the diagnosis of underlying systemic diseases such as neurofibromatosis, McCune-Albright syndrome, and tuberous sclerosis, among others. By contrast, the solitary large congenital CAL is an entity that rarely is reported. We have observed several patients in which this condition led to diagnostic or therapeutic concerns. Our experience, combined with the little information in the literature, indicates the solitary large CAL is a benign isolated birthmark with no known internal associations.

## Case Reports

**Patient 1**—A 21-year-old black woman was referred for excision of a large congenital nevus on the left arm. The lesion had been present since birth and had been diagnosed previously on clinical grounds as a giant congenital melanocytic nevus. As a result, her

primary care physician had been monitoring the lesion annually for changes indicative of melanoma. However, she decided to seek excision rather than undergo continued yearly observation and endure the fear of future malignant degeneration.

The patient's history revealed that the lesion had not changed in appearance or size over the years, aside from expansion proportional to her growth. She had no personal or family history of hereditary diseases, including melanoma or neurofibromatosis. She had no developmental abnormalities, and the results of an extensive history and physical, screening blood work, and chest x-ray performed 3 years previously on her entry into the military were normal.

Physical examination was notable for a 5×23-cm, evenly pigmented, sharply demarcated brown patch extending from her shoulder to her elbow, localized mostly to the flexural surface of her left arm (Figure 1). The lesion contained neither terminal hairs nor papules. The clinical appearance of the lesion was diagnostic of a CAL. In an effort to convince the patient that there was no need for extensive surgery, a 2-mm punch biopsy was performed. Results of the biopsy showed hyperpigmentation of the basal epithelium consistent with the diagnosis of a CAL.

**Patient 2**—A 6-month-old white girl presented with a congenital, large, solitary, light-tan melanocytic patch covering her buttocks, groin, and posteromedial thighs and legs bilaterally. The lesion measured approximately 11×20 cm (Figure 2). The patient's pediatrician had been concerned about the possibility of neurofibromatosis and had undertaken an extensive workup that included a magnetic resonance imaging scan of the head and an ophthalmologic examination, both of which yielded negative results. Her personal and family history did not reveal any evidence suggestive of a neurocutaneous or endocrinologic syndrome. Results of a complete cutaneous examination of the patient and parents by a dermatologist and a full ophthalmologic examination of the parents were normal.

**Patient 3**—A 37-year-old white woman presented with a 4.5×8.2-cm, uniformly pigmented,

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**Figure 1.** A 21-year-old woman with a large solitary café au lait spot on the left arm.

well-circumscribed tan patch on the left flank since birth. Having recently developed headaches, she was evaluated by her primary care physician, who noticed the lesion on her flank and promptly referred her for a magnetic resonance imaging scan of her head as well as a consultation with a dermatologist. The family history was negative for hereditary neurocutaneous or endocrinologic disease, and a review of systems was negative for developmental or internal findings. The patient's examination by a dermatologist was otherwise unremarkable. Results of the magnetic resonance imaging scan were negative, and her headaches resolved with analgesics.

*Patient 4*—A 14-year-old white girl presented with a lifelong history of a 14×25-cm well-defined tan patch overlying her right flank. She was followed until the age of 19 years, during which an extensive review of systems, family history, and physical examination failed to reveal additional cutaneous abnormalities or internal disease.

*Patient 5*—A 5-year-old white boy presented with a 3×7-cm sharply circumscribed brown patch on his left cheek and preauricular area that had been present since birth (Figure 3). No abnormalities were noted on a review of his systems, his personal and family history, or his physical examination.

### Comment

The clinical lesions described in this report consist of large solitary, sharply circumscribed, uniformly pigmented tan to brown melanocytic patches. The biopsy results of Patient 1 revealed the characteristic histologic features of a CALS, namely, increased activity of melanocytes at the epidermal base without epidermal hyperplasia. The clinical characteristics of the patients are summarized in

the Table. The 5 lesions were notable for their isolated nature and their large size. None of the lesions had any terminal hairs, increased skin markings, surface irregularity, or papular components. No specific anatomic preference was observed. All of the lesions had a congenital onset, but the patients presented at various ages and for a variety of reasons, not uncommonly because of concern that the lesions were premalignant or represented a skin sign of systemic diseases. Four of the 5 patients were female. Moreover, 4 of the 5 patients were white, and one was black. None of the patients exhibited any developmental or other associated abnormalities.

The presence of multiple CALSs has well-documented associations with various neurocutaneous syndromes, with the best known being neurofibromatosis.<sup>1-4</sup> By contrast, the relationship of large solitary CALSs to neurocutaneous or other syndromes has not been established. A MEDLINE search reveals limited information on this entity, with only a few references specifically addressing solitary or large CALSs.

In 1966, Whitehouse<sup>5</sup> examined a total of 365 white and black children between the ages of 1 month and 5 years to establish the incidence of CALSs in normal children. The prevalence of solitary CALSs in this population was 18.9% (69/365). The exact sizes of these lesions were not reported, though the minimum size for inclusion was 0.5 cm. Furthermore, a substantially greater proportion of black children possessed solitary CALSs (22%) compared with white children (11%). None of the children with these lesions had any evidence of neurocutaneous syndromes or developmental anomalies. Also of note, a 1-year-old black boy in the study was reported to have



**Figure 2.** A 6-month-old girl with a large solitary café au lait spot in the diaper area.



**Figure 3.** A 5-year-old boy with a large solitary café au lait spot in the left preauricular area.

2 CALSs, including one that was rather large, extending from his left chest to his axilla and inner aspect of his left arm. No disease was evident in the child, and the family history was negative for disease. Whitehouse concluded that though multiple CALSs are rare in normal children and should arouse suspicion for a neurocutaneous syndrome, a solitary CALS in a child is common and harmless.<sup>5</sup>

Other studies<sup>6,7</sup> that included older school-aged children revealed roughly similar prevalence rates for solitary CALSs. Burwell et al<sup>6</sup> examined 732 white children between the ages of 4 and 11 years and reported a 20% (146/732) prevalence of solitary CALSs. Rivers et al<sup>7</sup> studied 1123 white Australian children ranging from 6 to 15 years of age and found a 26.1% prevalence rate for solitary CALSs. Neither study mentioned the specific sizes of the lesions nor any abnormalities associated with them.

In 1983, a larger study by Alper and Holmes<sup>8</sup> examined 4641 newborns for congenital cutaneous lesions and, among other lesions, recorded the prevalence of solitary CALSs, regardless of size, as 1.9% (88/4641). This is considerably less than the prevalence rates of the previously mentioned studies that included older children, thereby supporting that CALSs appear to increase in frequency during the first 2 decades of life. The sizes of all the CALSs

detected in this study varied between 0.2 to 4.0 cm in length and 0.2 to 3.5 cm in width, which is a significantly smaller size range than that observed in our series of patients. Although our small series does not allow us to generalize about anatomic distribution, Alper and Holmes<sup>8</sup> noted that the lesions in their study were seen more commonly on the buttocks and less commonly on the scalp. Regarding the racial distribution, 12% of black infants, 3.2% of Hispanic infants, 1.0% of mixed black and white infants, and 0.3% of white infants had solitary CALSs, supporting the conclusion that patients with darker skin were more likely to have CALSs. None of these patients showed any other evidence of neurocutaneous syndromes.<sup>8</sup>

Alper and Holmes<sup>8</sup> identified 7 infants in their study with giant CALSs. The exact sizes of these lesions and whether they were solitary in nature were not specified. Six of the affected infants were black and one was of mixed black and white descent. Thus, while the overall incidence of giant CALSs was relatively low at 0.2%, the incidence in the black population was significantly higher at 1.2%. The vast majority of these lesions involved the buttocks and posterior leg, though one each was located on the chest and back. Five of these infants were seen on follow-up examinations

## Summary of Case Studies\*

Patient No.	Age of Onset	Age of Presentation (sex)	Ethnic Background	Size of Lesion, cm	Location	Associated Conditions	Age Last Evaluated
1	Birth	21 y (F)	Black	5×23	Left arm	None	21 y
2	Birth	6 mo (F)	White	11×20	Buttocks, groin, thighs, legs	None	6 mo
3	Birth	37 y (F)	White	4.5×8.2	Left flank	None	37 y
4	Birth	14 y (F)	White	14×25	Right flank	None	19 y
5	Birth	5 y (M)	White	3×7	Left cheek	None	5 y

\*F indicates female; M, male.

between 7 to 21 months later, and none of them showed evidence of neurocutaneous syndromes. They concluded that solitary CALSs, including giant CALSs, were a benign, normal racial variant seen more frequently in the black population. Johnson et al<sup>9</sup> also conclude from these reports that CALSs are more common in the black population and that giant CALSs appear to be benign lesions not associated with any pathologic conditions.

Although the literature suggests that CALSs are more prevalent in the black population and in patients with darker skin in general,<sup>5,8,9</sup> most patients in our series were white. This is striking considering that in our clinical setting, the ethnic composition of our patients consist of 60% white; 30% black; and 10%, a combination of Asian, Native American, and Hispanic.

As in the aforementioned studies, none of the patients in our series had any personal or family history to suggest a neurocutaneous or endocrinologic syndrome. No associated medical abnormalities were noted on physical examination or on laboratory testing, nor did any manifest during the follow-up period. However, some references in the literature have reported abnormalities associated with large solitary CALSs. One case report<sup>10</sup> has noted an association of large solitary CALSs in conjunction with contralateral facial neurofibromas, and other sources indirectly have suggested an association with McCune-Albright syndrome.<sup>11-13</sup>

Wasserteil et al<sup>10</sup> described 2 women who each presented with a large solitary CALS on the thigh associated with neurofibromas on the contralateral

side of the face. Both patients were white women in their early 30s who underwent extensive workups that revealed no other signs or family history of neurofibromatosis. The first patient had a 10×10-cm CALS on her medial right thigh and inguinal area. The age at which her CALS was first noticed was not stated, but the histologically confirmed plexiform neurofibroma, which covered her left hemiface, had been present since birth. She was otherwise healthy until she developed multiple meningiomas after her second pregnancy. The second patient was first noted at the age of 6 weeks to have a large CALS that eventually involved almost her entire left thigh, extending from 6 cm below the inguinal crease to below the patella. At age 19 years, she began to develop multiple neurofibromas on the right side of her face. The authors classified these patients as the rare variant form of neurofibromatosis.

McCune-Albright syndrome, or polyostotic fibrous dysplasia, is a noninheritable syndrome characterized by CALSs, fibrous dysplasia of bones, and endocrine dysfunction, namely precocious puberty.<sup>11,14</sup> The reported frequency of CALSs has varied between 35% to 90% of patients,<sup>3,12,15</sup> and the sizes can vary from a few centimeters to large areas.<sup>12</sup> They can occur on any part of the body, but are more prevalent on the forehead, nuchal area, sacrum, and buttocks,<sup>11,12,15</sup> which are a somewhat different localization than most typical CALSs. The hyperpigmented lesions may be located ipsilaterally to or overlying the bony lesions.<sup>11,12,15</sup> The CALSs seen in this syndrome are histologically and

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clinically identical to those in neurofibromatosis, except they tend to respect the midline, be fewer in number (less than 6), be larger in size, and have more jagged borders.<sup>11,12,14,15</sup>

In the original report, Albright et al<sup>11</sup> described a patient who had the remains of what was seemingly a solitary CALS at the base of her neck that had been almost completely removed by carbon dioxide snow. Furthermore, they cited a previous description<sup>13</sup> of a possible case of McCune-Albright syndrome in which a 9-year-old girl had a hand-sized area of hyperpigmentation on her left buttock associated with osteitis fibrosa cystica. Thus, these reports, and possibly others,<sup>12</sup> suggest that large solitary CALSs may represent a manifestation of McCune-Albright syndrome.

A prudent approach to the patient with a large solitary CALSs would include a thorough history and physical examination, with special attention to any family history of neurocutaneous syndromes, as well as signs and symptoms of precocious puberty or bony abnormalities. In cases where McCune-Albright syndrome is suspected, screening with x-ray and measurement of serum alkaline phosphatase levels, which may be elevated in affected patients, may be performed.

Possibly due to the relative obscurity of the lesion, the large solitary CALS in Patient 1 was initially misdiagnosed as a giant congenital melanocytic nevus, thereby causing unnecessary emotional stress and observation. Knowledge of the characteristic clinical features of pigmented lesions generally will lead to an accurate diagnosis; thus, performance of a biopsy is rarely needed.

### Conclusion

The current literature regarding large solitary CALSs is sparse, and the consequences of making such a diagnosis in a particular patient have not been well established. Contrary to previous studies that state CALSs are more common in the black population, 4 of our 5 patients were white. In addition, the lesions were all congenital in onset, and no other abnormalities were found.

We conclude that a large solitary CALS is a benign entity not associated with any neurocutaneous syndromes or developmental anomalies. This is in agreement with the conclusion drawn by Landau and Krafchik<sup>16</sup> that "no investigation is needed for a child presenting with solitary lesions, even with an unusual morphology or an exceptional size." Nevertheless, isolated reports do exist that link large solitary CALSs with a variant form of neurofibromatosis and McCune-Albright syndrome.

Because our data is limited by a small sample size and a lack of long-term follow-up, we encourage others to report their findings on large solitary CALSs in an effort to better document this entity and more accurately determine the frequency, epidemiology, and clinical significance of this uncommon finding.

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