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Case Report

PHACE syndrome and congenitally absent thyroid gland at MR imaging

Mark D. Mamlouk [a,b,*], John-Paul J. Yu [a,c], Sarah Asch [d,e], Erin F. Mathes [d]

[a] Department of Radiology and Biomedical Imaging, University of California, San Francisco, 505 Parnassus Avenue, L352, San Francisco, CA 94143
[b] The Permanente Medical Group, Kaiser Permanente Medical Center, Santa Clara, 700 Lawrence Expy, Santa Clara, CA 95051
[c] Department of Radiology, University of Wisconsin School of Medicine and Public Health, E3/366 Clinical Science Center, 600 Highland Avenue, M/C 3252, Madison, WI 53792
[d] Department of Dermatology, University of California, San Francisco, 1701 Divisadero Street, Third Floor, San Francisco, CA 94115
[e] Department of Dermatology, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905

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ABSTRACT

PHACE syndrome is a rare neurocutaneous disorder characterized by posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, and abnormalities of the eye. Thyroid disorders associated with PHACE syndrome have been described, although there are limited reports of this rare occurrence. We report a case of PHACE syndrome with congenital hypothyroidism in an infant, for which absent thyroid gland was diagnosed at magnetic resonance imaging.

1. Introduction

PHACE is an acronym referring to a rare neurocutaneous syndrome made up of *P*osterior fossa malformations, *H*emangiomas, *A*rterial anomalies, *C*ardiac defects, and abnormalities of the *E*ye. There are established major and minor criteria for diagnosis, which comprise numerous abnormalities, including thyroid dysfunction [1]. However, there are few reports about patients with PHACE syndrome and hypothyroidism and even fewer where the hypothyroidism is congenital. We describe a case of PHACE syndrome and congenital absence of the thyroid gland diagnosed at magnetic resonance (MR) imaging in an infant.

2. Case report

A 4-month-old girl was referred to our institution for suspicion of PHACE syndrome after recognition of an S1 (frontotemporal) segmental infantile hemangioma that extended from the left periorbital face to the nape of the neck (Fig. 1). The patient's birth history was uneventful; however, congenital hypothyroidism was diagnosed on newborn screening, for which the patient was administered levothyroxine. At the time of birth, the thyroid-stimulating hormone was 458 mIU/l (normal range 0.45–4.12 mIU/l), and the free T4 was 10 pmol/l (normal range 11–24 pmol/l). All other laboratory markers and physical examination findings were normal.

Formal workup for PHACE syndrome at our hospital includes a cardiac echocardiogram and formal ophthalmologic examination, which were both normal. MR imaging was performed and showed multiple enhancing cutaneous lesions around the left orbit and left frontal, parietal, and suboccipital scalp (Fig. 2), corresponding to the physical examination findings. Magnetic resonance angiography (MRA) imaging showed a hypoplastic left cervical internal carotid artery with significant tortuosity, an aberrant left ophthalmic artery arising from the basilar artery (Fig. 3), and a left-sided aortic arch with aberrant right subclavian artery (Fig. 4). Based on these findings, a diagnosis of PHACE syndrome was made. In the context of congenital hypothyroidism, scrutiny of the lower neck on the MR images revealed no perceivable thyroid tissue on the available contrast-enhanced T1-weighted images or MRA images (Fig. 4). Given these findings, absence of the thyroid gland was diagnosed and confirmed with subsequent ultrasound imaging (Fig. 4). Of note, MR imaging of the hypothalamic-pituitary axis showed full development of all structures and actually mild enlargement of the adenohypophysis (Fig. 5). Subsequent to the diagnosis of PHACE syndrome and absent thyroid tissue, the patient underwent propranolol treatment for her infantile hemangiomas and continuation of levothyroxine administration for thyroid hormone replacement, both with good responses.

3. Discussion

PHACE syndrome is a poorly understood complex association of various genetic and phenotypic anomalies. While certain anomalies

* Corresponding author. Department of Radiology, The Permanente Medical Group, Kaiser Permanente, Medical Center, Santa Clara, 700 Lawrence Expy, Santa Clara, CA 95051. Tel.: +1-408-851-5028.
E-mail addresses: mark.d.mamlouk@kp.org, mark.mamlouk@ucsf.edu (M.D. Mamlouk).

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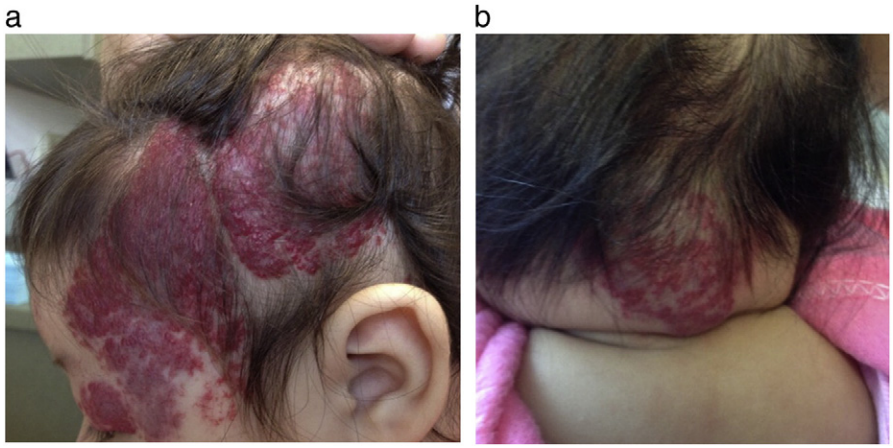

Fig. 1. Photographs of the patient's left scalp and nape of the neck show bright red vascular plaques overlying a soft subcutaneous mass in an S1 (frontotemporal) segmental distribution, compatible with an infantile hemangioma. (Informed consent was obtained from all individual participants included in the study.)

within the PHACE spectrum are more common, namely the acronymic entities, there are numerous and less common anomalies that have been reported with the syndrome [1]. Our patient with PHACE syndrome and congenitally absent thyroid tissue suggests another possible association.

To our knowledge, there have been 13 total reported cases of PHACE syndrome and hypothyroidism. Six of those cases had congenital hypothyroidism [2–7], four had central hypothyroidism from hypopituitarism [8–11], one had a mixed pattern of hypothyroidism from an absent right thyroid gland and hypopituitarism [11], one had lingual thyroid tissue with hypothyroidism [12], and one patient had unspecified hypothyroidism [13]. Of the six congenital hypothyroidism cases, only one patient had imaging that revealed an absent thyroid gland (on ultrasound) [3]. Our case is the second radiologic case of PHACE syndrome with absent thyroid tissue and the first reported case demonstrating the absence of the thyroid gland at MR imaging.

The association of PHACE syndrome and hypothyroidism is poorly understood. Perhaps the most straightforward of scenarios is central hypothyroidism from hypopituitarism. In these cases, the pituitary gland is absent or poorly developed, manifesting as a partially empty sella. In these cases, thyroid-stimulating hormone and other pituitary hormones may not be secreted normally, leading to hypothyroidism. With regard to congenital absence of the thyroid gland, there are no definitive explanations published. There have been reported associations between endocrinopathies with midline cerebral and cranial abnormalities, but these examples were largely in the context of endocrinopathies from the hypothalamic-pituitary axis [14]. Thus, it is unclear if this association would translate to the thyroid gland itself, also, as our patient did not have any midline cerebral or cranial anomalies. There is a correlation of athyreosis (absence of thyroid gland) with increased risk for cardiac malformations, including anomalies of septation and great vessel formation [15,16]. Interestingly, both PHACE and thyroid athyreosis are female predominant [1,17]. It has been proposed that coincident thyroid and cardiac malformations may represent impaired function of a common signaling pathway or may represent a reciprocal dependence between these embryonic structures for proper morphogenesis [16]. It is also thought that segmental hemangiomas develop around 6–8 weeks gestation with the facial prominences, around the same time that the thyroid gland is developing and descending [18]. In cases of acquired hypothyroidism, hemangiomas, namely hepatic hemangiomas, can result in low thyroid hormone due to the production of type 3 iodothyronine deiodinase, which catalyzes the conversion from active to inactive thyroid hormone [19].

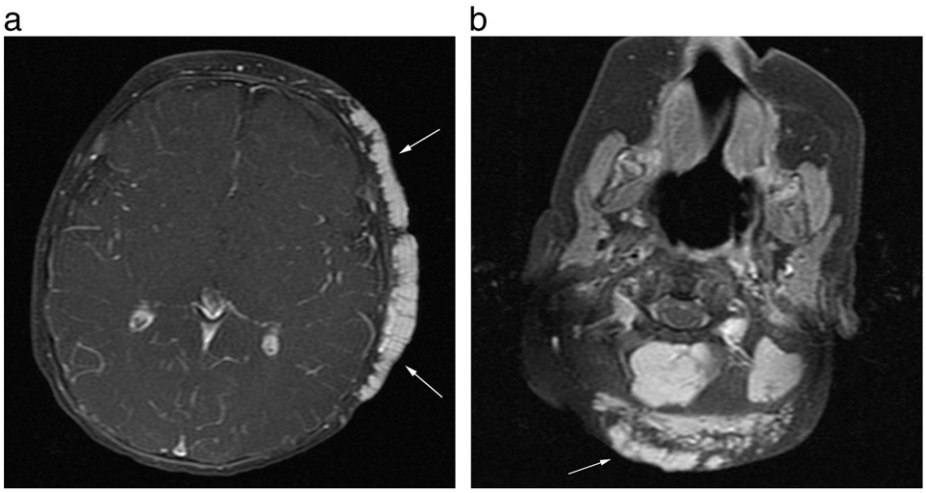

Fig. 2. Axial fat-suppressed contrast-enhanced T1-weighted images show enhancing lesions along the left frontal, parietal, and suboccipital scalp (arrows), which represent infantile hemangiomas and correspond to the physical examination findings in Fig. 1.