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Trilateral retinoblastoma

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Imaging description

A two-year-old boy presented with leukocoria (= white pupil). Ophthalmoscopy demonstrated large masses in both globes. A CT scan showed extensive calcifications of both lesions (Fig. 1.1a). An MR scan better delineated the contrast-enhancing masses in the bilateral globes, both of which demonstrated extraocular extension (Fig. 1.1b).
An axial contrast-enhanced MR scan of the brain in a different patient with retinoblastoma shows an additional, inhomogeneously enhancing mass in the pineal gland (Fig. 1.2).

Importance

Retinoblastoma is the most common intraocular tumor of childhood, occurring in one in 15000 to 20000 live births. Approximately 200 new cases a year are diagnosed in the USA. The disease presents in infancy or early childhood, with the majority of cases diagnosed before the age of 4 years.
A second primary malignancy, most commonly a midline intracranial tumor, is found in 5–7% of patients with bilateral retinoblastoma. Often, these other brain tumors occur weeks or months after the diagnosis of the retinoblastoma, with a median interval of 21 months. Trilateral retinoblastoma has traditionally been nearly universally fatal, although a recent study suggests that intensive chemotherapy may improve survival. Early detection is likely an important factor in survival.

Typical clinical scenario

The most frequent presenting sign of retinoblastoma is leukocoria, a white papillary reflex. Other clinical presentations include strabismus, decreased vision, orbital and/or periorbital inflammation, glaucoma, hypopyon (tumor cells anterior to the iris), or ocular pain. The genetic evolution of retinoblastoma follows the Knudson’s two-hit hypothesis: patients who have unilateral unifocal disease have mutations at the retinoblastoma locus in both alleles within a single retinal cell. This is an unlikely event; therefore, these tumors are usually unifocal and unilateral, and are rarely associated with other tumors. By contrast, patients with multifocal and bilateral retinoblastomas harbor an underlying germ-line mutation that results in a mutant *RB* gene in every cell of their bodies. Loss of heterozygosity and loss of the normal allele leads to the development of multiple retinoblastomas in one or both eyes. These patients with germ-line mutations are predisposed to development of additional midline brain tumors and other non-ocular tumors.

A trilateral retinoblastoma is the association of a midline intracranial tumor with familial bilateral retinoblastoma, and has been reported in 6% of children with bilateral retinoblastoma and 10% of those with a family history of retinoblastoma. Classically, the intracranial tumor is located in the pineal region and the most common tumor type is a pinealoblastoma.
On CT scans, a retinoblastoma is recognized as a hyperattenuating intraocular mass, which contains punctate or nodular calcifications in over 90% of cases. The tumor may lead to retinal detachment, subretinal effusion, and/or vitreal hemorrhage.
On MR scans, retinoblastomas are hyperintense to vitreous on T1-weighted and proton density-weighted images, and show marked enhancement after contrast media injection. On T2-weighted MR images, retinoblastomas appear hypointense to adjacent vitreous. Possible extension of the tumor beyond the sclera and along the optic nerve is prognostically important, and needs to be reported.
Pineal gland tumors are delineated as inhomogeneous, contrast-enhancing soft tissue masses in the pineal region. Careful attention has to be paid to possible leptomeningeal metastases and spinal lesions. Of note, the normal pineal gland does not have a blood–brain barrier. Therefore, the presence of contrast enhancement alone should not be confused with a pineal gland mass.
Differential diagnosis
Strongly T2-weighted images (long TE, 120ms) may be useful for differentiating retinoblastoma from Coats’ disease (retinal telangiectasis) or a persistent hyperplastic primary vitreous, which are both hyperintense on these scans (Figs. 1.3, 1.4).
Coats’ disease represents a congenital, non-hereditary, usually unilateral vascular malformation of the retina, which may eventually lead to retinal detachment. The pathophysiology is breakdown of the blood–retina barrier resulting in a subretinal lipoproteinaceous exudate, which typically does not contain calcifications and does not enhance on imaging studies after contrast media injection (Fig. 1.3). Peak prevalence is later than the typical retinoblastoma population, around six to eight years of age, although it can be seen as early as the first year of life. The typical clinical presentation is progressive vision loss. Local therapies include photocoagulation and cryogenic and laser ablation.
Persistent hyperplastic primary vitreous (PHPV): The primary vitreous represents primitive mesenchymal tissue that

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occupies the posterior eye chamber during embryonic stages of life. This tissue is gradually replaced by mature vitreous, persisting only at the small central canal between the retina and the posterior aspect of the lens (Cloquet canal). A proliferation of this primary vitreous leads to hyperplastic fibrovascular tissue posterior to the lens and along the Cloquet canal. PHPV is congenital and usually noted at birth or within a few weeks of life with leukocoria and microphthalmos. It is unilateral in 90–98% of cases. Untreated PHPV frequently progresses to phthisis bulbi, due to recurrent intraocular hemorrhage.

Retinal astrocytic hamartomas represent masses in the globe, which may have calcifications as well but are predominantly seen in patients with tuberous sclerosis. They are also seen rarely in patients with neurofibromatosis or in isolation. The majority of cases are asymptomatic and come to attention due to other clinical manifestations. In patients with tuberous sclerosis, the lesions are frequently congenital, usually multiple, bilateral in 25% of cases, and may calcify. The majority are non-progressive and do not require treatment. Imaging is primarily performed to evaluate and follow other manifestations of tuberous sclerosis.

Teaching point

Staging and follow-up MR exams of patients with retinoblastoma requires imaging not only of the orbit, but also a contrast-enhanced MRI of the whole brain in order to evaluate for possible additional brain tumors. The risk of “trilateral” tumors is particularly high in patients with multifocal and bilateral retinoblastomas.

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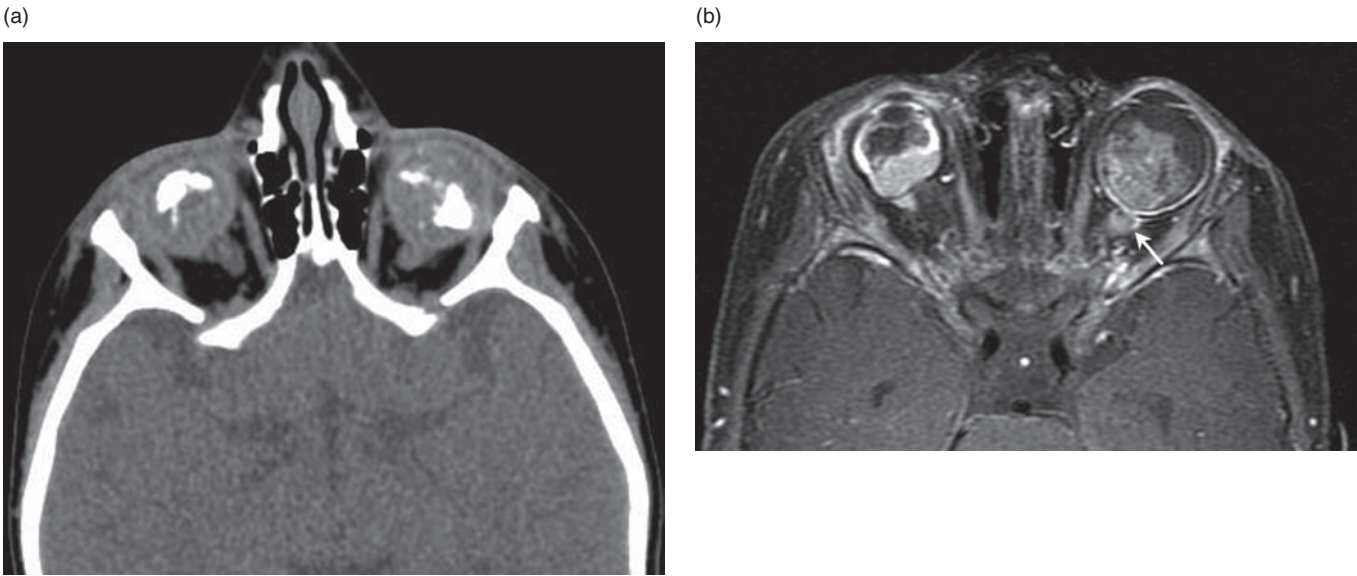


Figure 1.1. (a) An axial CT scan through the orbits shows calcifications in both globes. (b) An axial T1-weighted MR scan after injection of Gd-DTPA demonstrates large, contrast-enhancing tumors in the globes bilaterally, with extraocular extension. The tumor in the right globe shows extrascleral extension and the tumor in the left globe shows extension into the optic nerve with associated contrast enhancement of the proximal optic nerve (arrow).

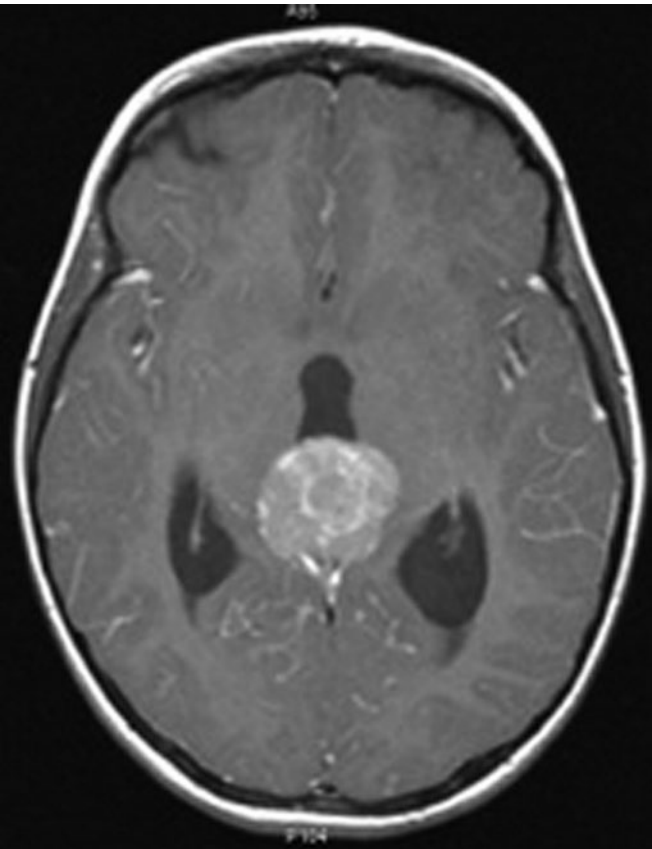


Figure 1.2. Axial T1-weighted MR scan after injection of Gd-DTPA demonstrates a large, inhomogeneously enhancing mass in the pineal gland in a different patient.

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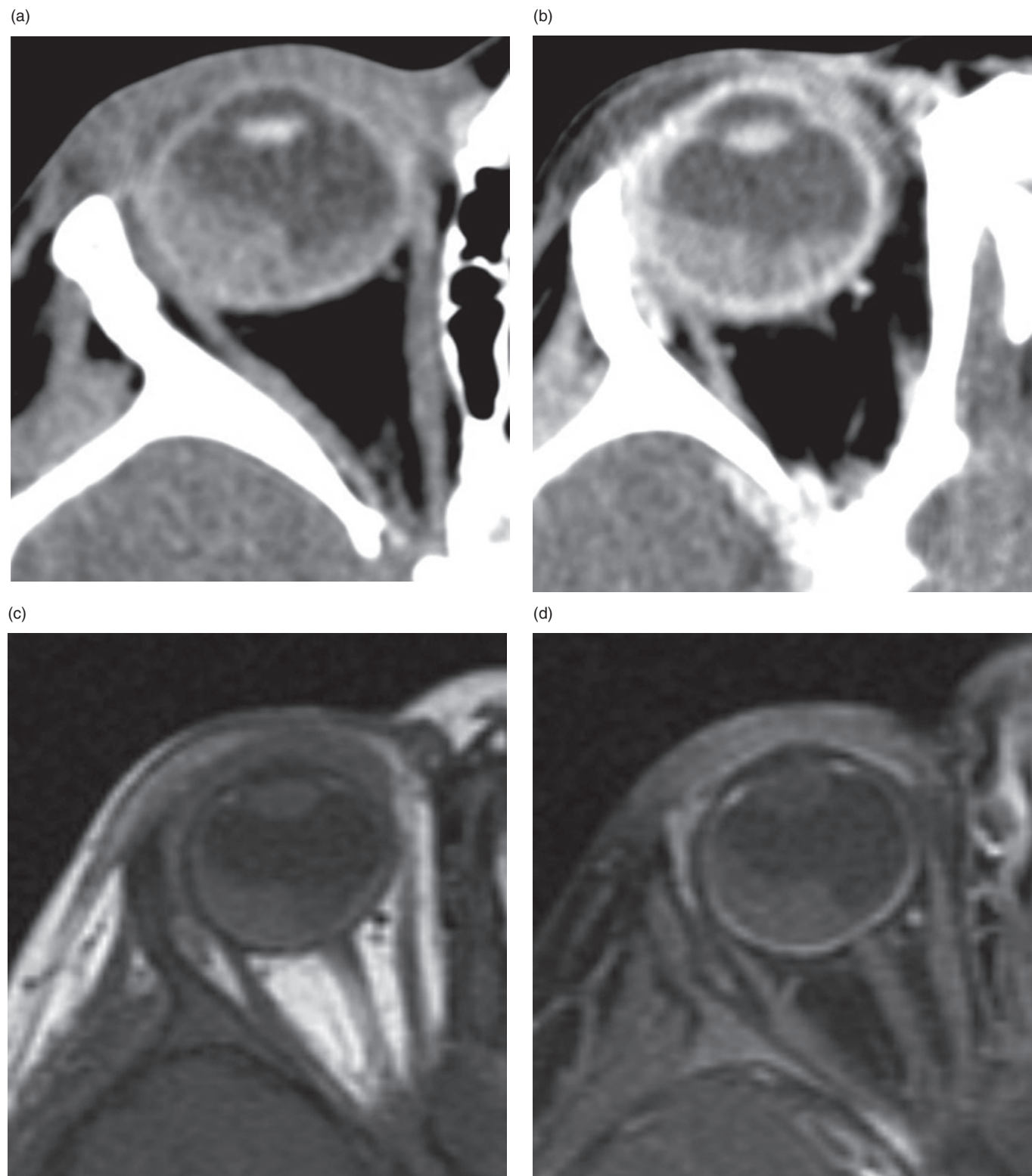


Figure 1.3. Coats' disease. Congenital, non-hereditary, vascular malformation of the retina, which produces a lipoproteinaceous exudate in the subretinal space. Non-contrast and contrast-enhanced CT images of the right orbit **(a, b)** show an intraocular high-density lesion, which represents the lipoproteinaceous exudate. No calcification and no enhancement after contrast media administration are noted. Axial T1-weighted non-contrast **(c)** and T1 postcontrast **(d)** fat-saturated images showing homogeneous intermediate signal of the intraocular lesion without contrast enhancement.

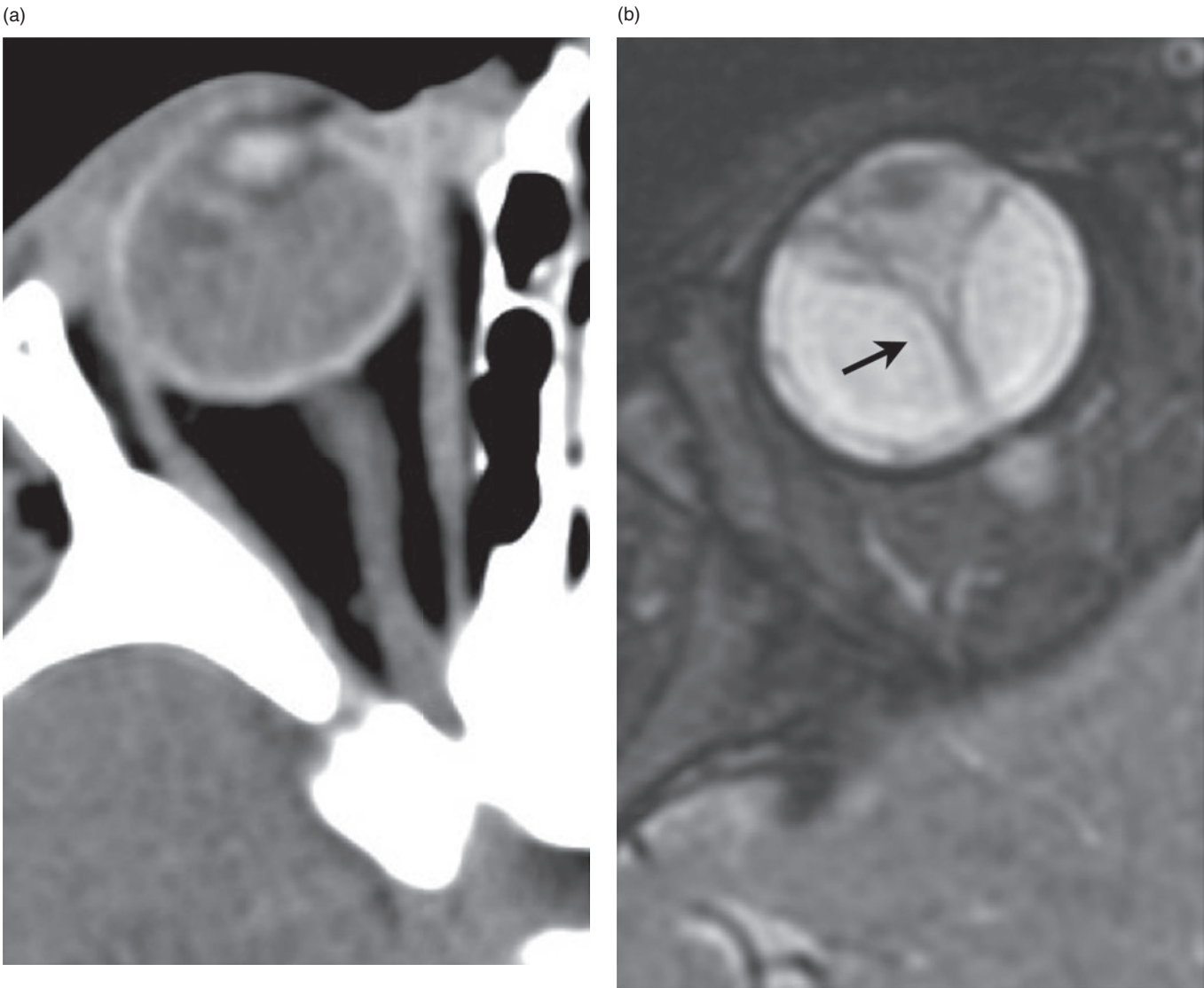


Figure 1.4. Persistent primary hypertrophied vitreous. Axial CT image through the right orbit **(a)** showing uniform high attenuation of the vitreous. T2-weighted image **(b)** shows the Cloquet canal (arrow), very characteristic of this condition.

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(c)



Figure 1.4. (cont.) A postcontrast T1-weighted image (c) shows enhancement of the retrolental primary vitreous (arrow)

CASE 2

Fibromatosis colli

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Imaging description

A one-month-old male presented with a palpable right neck mass, which had been noticed 10 days previously. The mass was not perceived to be painful or bothersome to the patient. There was no reported fever or weight loss. He was feeding normally and there was ipsilateral mild torticollis. He was born at 37 weeks by cesarean section due to cardiac decelerations during labor. Imaging evaluation with ultrasound (US) (Fig. 2.1a) demonstrated heterogeneous, mass-like enlargement involving the right inferior sternocleidomastoid muscle (SCM). The mass tapered gently toward the SCM and was surrounded by normal appearing SCM. The fascial planes surrounding the muscle were preserved. There were morphologically normal appearing prominent ipsilateral cervical chain lymph nodes. The lesion did demonstrate moderate internal vascularity on Doppler ultrasound (Fig. 2.1b).

An MRI was also performed in spite of the fact that the US appearance was strongly suggestive of fibromatosis colli. This demonstrated enlargement of the inferior right SCM, with intact surrounding fascial planes. The process was confined to the inferior SCM. There was increased T2 signal and heterogeneous enhancement of the involved muscle (Fig. 2.1c, d, e). There were no calcifications present in the lesion. The MRI findings also supported the diagnosis of fibromatosis colli.

Clinically, the lesion decreased in size over time confirmed by follow-up ultrasound.

Importance

Fibromatosis colli is a form of infantile fibromatosis which is rare and occurs solely in the SCM. Most cases present at two to four weeks of age as a palpable neck mass. They typically occur in the inferior third of the SCM and can occur in either the sternal or clavicular head. Cases are usually unilateral, occur more often on the right, and males are affected slightly more often than females. Torticollis toward the affected side is seen in about 20% of cases and is thought to be due to shortening or contraction of the affected SCM. The precise mechanism is unclear. Suggested etiologies have included birth trauma or an in utero compartment syndrome related to fetal crowding and abnormal head position causing venous obstruction and muscle injury followed by necrosis and fibrosis. Initially, the mass may grow rapidly. Growth, however, slows and eventually ceases. In two-thirds of cases, lesions completely regress by the age of one year.

US is the preferred imaging modality for diagnosis since it is low cost, lacks ionizing radiation, and can well assess superficial lesions. The US appearance, although variable, is

usually diagnostic. US can demonstrate heterogeneous enlargement of the SCM, with at times the appearance of a focal mass with variable echogenicity. Extended field of view imaging to show the entire length of the SCM can be useful. Color Doppler imaging may show hyperemia during the acute phase and decreased vascularity during the fibrotic phase. Key findings include confinement within the SCM in the inferior one-third of the muscle and a characteristic spindle-shaped transition to normal muscle. It can be useful to image the contralateral SCM for the purpose of comparison.

MR is not required to make the diagnosis of fibromatosis colli, but is at times obtained during the initial workup of the condition. MRI demonstrates fusiform enlargement of the affected SCM, with variable T2 signal hyperintensity. Signal intensity decreases as the fibrotic stage ensues. There can be hemorrhage in the affected muscle and the lesion can appear very heterogeneous. However, it is not the appearance of the primary lesion that should raise concern for an aggressive neoplastic process such as neuroblastoma or rhabdomyosarcoma, but rather location or extension outside of the SCM and infiltration into surrounding soft tissues. The presence of calcifications in fibromatosis colli is very rare, and should raise concern for neuroblastoma.

Radiographs may be requested by the clinician in cases of torticollis, which will help exclude spinal fusion abnormalities. Rarely, there can be lytic change in the clavicle at the site of attachment of the affected SCM in fibromatosis colli.

Typical clinical scenario

Fibromatosis colli typically presents within the first 8 weeks of life, most often in the first two to four weeks. The affected SCM can continue to enlarge for two to three months. Eventually, the fibrotic phase ensues, after which the size typically decreases over time.

Once confirmed by a combination of clinical assessment and imaging, treatment of fibromatosis colli is conservative, and involves clinical observation and muscle stretching exercises. Most cases resolve by the age of one year. Surgical intervention is necessary in 10–15% of cases, where there is severe refractory disease after 1 year of age. The purpose of surgery is to prevent permanent contracture and plagiocephaly. Surgical treatment consists of proximal or distal release of the SCM. Excision of the fibrous lesion is rarely indicated. More recently, use of *Botulinum* toxin type A has been used for treatment of refractory cases and may further prevent the need for surgical intervention.

Fibromatosis colli has been associated with hip dysplasia, perhaps also related to intrauterine crowding. More recent

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series have suggested that the association is less important than previously thought. US screening of the hips for dislocation or instability may be useful in the presence of fibromatosis colli and vice versa.

Differential diagnosis

The differential diagnosis for a neck mass in an infant of this age includes cervical lymphadenopathy, congenital neuroblastoma (consider if calcifications are present and involves the paraspinal soft tissues medial to the SCM), and cervical extension of mediastinal thymus (common on the left side, medial and posterior relative to the SCM). Rhabdomyosarcoma and cervical teratoma (consider if fat and calcifications are present) are very uncommon neoplasms in this age group and location.

The presence of torticollis in an infant without a soft tissue mass raises additional diagnostic possibilities. Spinal fusion anomalies are osseous causes that can usually be excluded with cervical spine radiographs. Neurologic causes of torticollis include posterior fossa and cervical spine tumors as well as the Arnold Chiari malformation and syringomyelia. Other miscellaneous causes include ocular deficiency, hearing deficits, and Grisel (C1/C2 subluxation associated with inflammatory conditions such as retropharyngeal cellulitis) and Sandifer (torticollis or unusual neck movement associated with gastroesophageal reflux) syndromes.

Teaching point

Fibromatosis colli is the most common cause of a cervical “mass” during infancy. It presents typically within the first 8 weeks of life. The process is usually confined to the inferior SCM and surrounding fascial planes should be intact. The best imaging modality for diagnosis is US, and that is usually all that is necessary. The appearance can be heterogeneous and variable. If the mass is centered outside of the SCM or there is extension beyond the affected SCM or if there are internal calcifications, consider a neoplastic process such as neuroblastoma.

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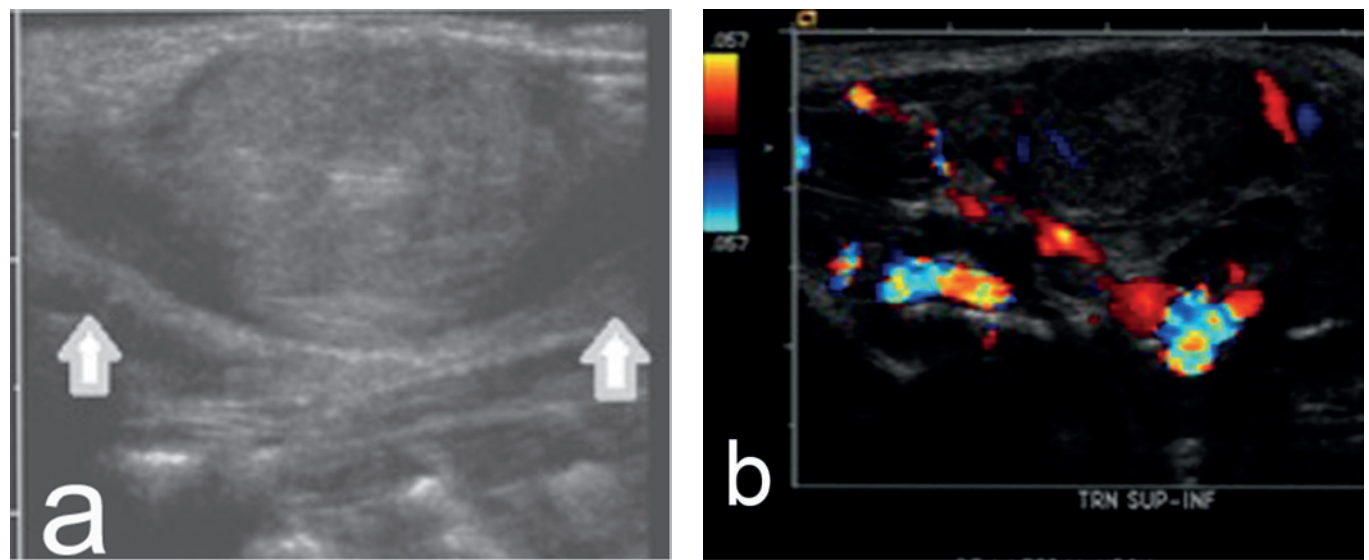


Figure 2.1. Fibromatosis colli, 1-month-old male. **(a)** Longitudinal gray-scale ultrasound image demonstrates a heterogeneous superficial lesion that is contained in the sternocleidomastoid muscle (SCM), with smooth tapering to normal appearing SCM (arrows). Surrounding fascial planes are intact. **(b)** Sagittal color Doppler imaging demonstrates moderate internal vascularity to the lesion.

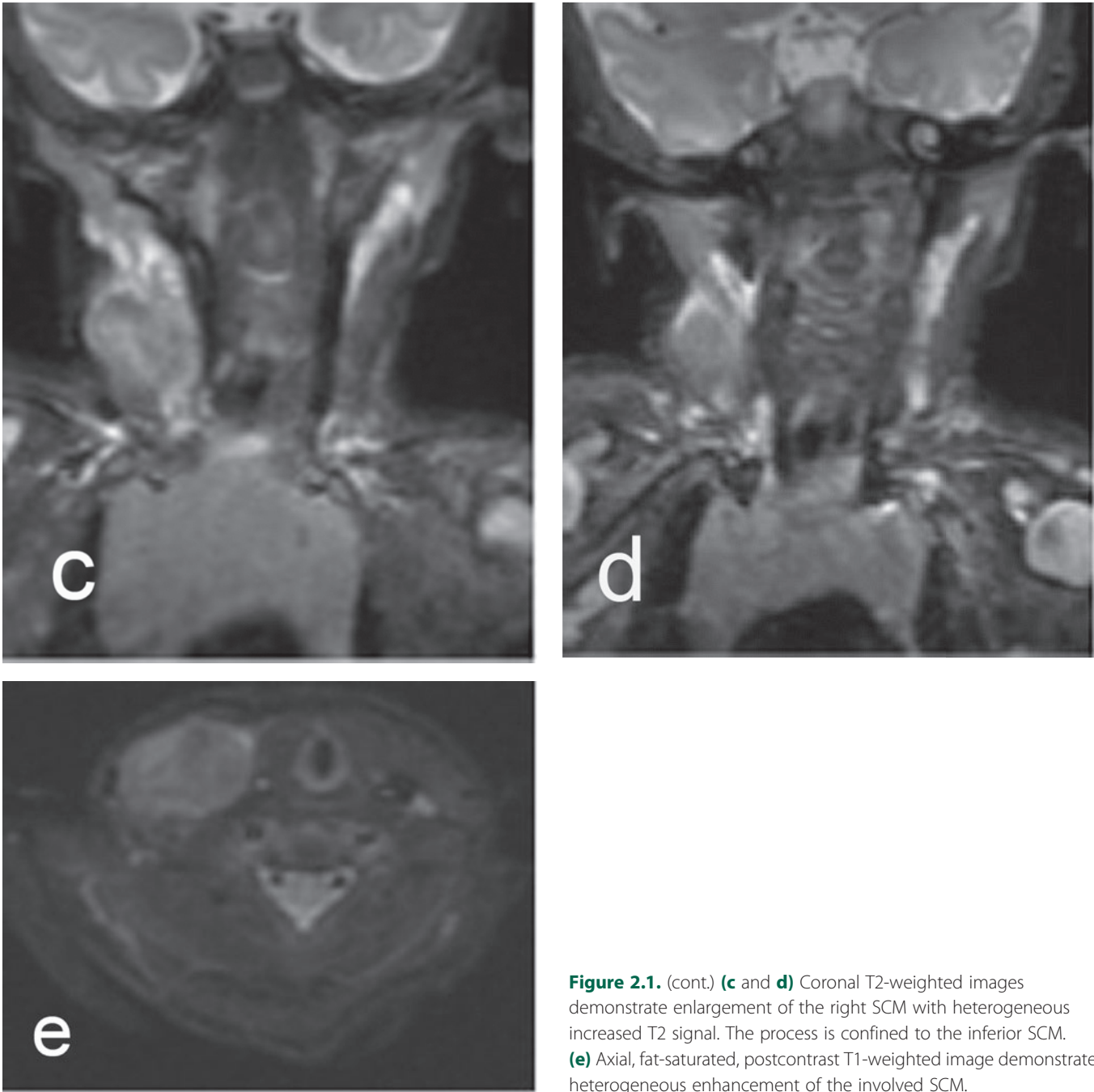


Figure 2.1. (cont.) **(c and d)** Coronal T2-weighted images demonstrate enlargement of the right SCM with heterogeneous increased T2 signal. The process is confined to the inferior SCM. **(e)** Axial, fat-saturated, postcontrast T1-weighted image demonstrates heterogeneous enhancement of the involved SCM.

CASE
3

Craniopharyngioma

Camilla Mosci and Andrei Iagaru

Imaging description

A five-year-old girl presented to the emergency room with new onset of nausea, vomiting, and headaches. MRI showed a 36 × 26 × 30 mm multicystic suprasellar mass extending superior to the third ventricle (Fig. 3.1a, b) with areas of calcification and ventriculomegaly. An Ommaya device was placed in the right frontal lobe for cyst drainage. Pathology was consistent with craniopharyngioma. She was followed with serial MRI and CT scans. The imaging studies were stable for one and a half years when an MRI scan demonstrated further increase in the cystic and solid components of the suprasellar mass with increased ventriculomegaly. The patient underwent a right frontal endoscopic fenestration and partial resection of the suprasellar mass, with removal of the blocked Ommaya reservoir and placement of an external ventricular drainage system. Follow-up MRI showed increased size of the cystic mass and ventricles stable in size. However, there was evidence of mass compression of the optic chiasm. The patient underwent MRI-guided placement of a new right frontal Ommaya reservoir into the cystic portion of her tumor. Therapy with ³²P (β emitter) colloid chromic phosphate was recommended by the treating physician. A diagnostic ^{99m}Tc sulphur colloid scan of the cystic tumor was performed to evaluate the distribution of the injected material on the inner surface of the tumor and to exclude the presence of a leak from the craniopharyngioma to the cerebrospinal fluid (CSF) space. The ^{99m}Tc sulphur colloid scan showed radiotracer migration from the Ommaya reservoir and coating of the suprasellar mass. However, uptake was also seen into the ventricular system, due to a leak (Fig. 3.1c, d). Due to this leak to the CSF space, the ³²P chromic phosphate treatment was aborted in order to avoid excess radiation of normal central nervous system (CNS) structures.

Importance

Craniopharyngioma is a benign tumor that arises along the path of the craniopharyngeal duct. It accounts for 2–5% of all intracranial tumors and 5.6–13% of pediatric intracranial tumors and is classified into cystic, solid, and mixed. Despite its benign histologic appearance, prognosis may often be unfavorable due to mass effect on adjacent structures and the optimal therapeutic approach remains controversial. Total resection is the treatment of choice, but when the tumor localization is unfavorable (proximity

and adherence to hypothalamus, pituitary stalk, visual apparatus, circle of Willis, floor of the third ventricle) limited resection followed by local irradiation is recommended. The rate of tumor recurrence is about 10–30% even after total resection. The utilization of radiotherapy can decrease the rate of tumor recurrence in patients who undergo limited resection. However, it also may cause endocrine dysfunction, visual deterioration, radiation-related tumors, and cognitive impairment. In cystic tumors, radionuclide therapy with ³²P chromic phosphate colloid is indicated. ³²P is a β emitter that has been shown to ablate the epithelial lining of the cyst, effectively reducing the rate of cystic fluid reaccumulation and reducing the cyst size. Compared to conventional external beam radiotherapy, radionuclide therapy delivers a higher dose of radiation directly into the inner surface of the cyst, while reducing the radiation dose to tissues adjacent to the tumor. It is important not only to obtain long-term tumor control but also to preserve the patient’s quality of life and stereotactic instillation of ³²P chromic phosphate colloid causes minimal risk and is effective as either primary or adjuvant treatment of craniopharyngiomas (Fig. 3.2).

Typical clinical scenario

Clinical presentation is dependent on the size and site of the lesion and can vary from non-specific manifestations of increased intracranial pressure to more specific symptoms as a result of pituitary hormone deficiencies or excess. Symptoms include headache, nausea, vomiting, visual disturbance, seizures, and endocrine dysfunction (diabetes insipidus, amenorrhea, sexual inadequacy, growth retardation).

Differential diagnosis

Craniopharyngioma can be misdiagnosed as a pituitary tumor, metastasis, meningioma, epidermoid or dermoid tumors, hypothalamic-optic pathway glioma, hypothalamic hamartoma, and teratoma. Other differential diagnoses that should be considered include congenital anomalies (arachnoid cyst and Rathke’s cleft cyst), infectious/inflammatory processes (eosinophilic granuloma, lymphocytic hypophysitis, sarcoidosis, syphilis, and tuberculosis), and vascular malformations (aneurysm of the internal carotid or anterior communicating artery, arteriovenous malformation).