Iris Ectopic Thyroid Tissue: Report of a Case

Ectopic benign thyroid tissue outside the normal migration path of the thyroid is an extremely rare condition that, to our knowledge, has never been described in the eye. A 15-year-old boy was seen with a pink, multinodular tumor arising from the peripheral iris and the anterior chamber angle. An iridocyclectomy was performed. Histopathological examination of the resected tumor showed well-differentiated thyroid follicular tissue in the iris. Immunohistochemistry demonstrated immunoreactivity for nuclear thyroid transcription factor 1 and thyroglobulin. Well-differentiated follicular thyroid carcinoma was considered but was excluded by systemic examination and the absence of any evidence of other primary or secondary tumors after more than a year of surveillance. We concluded that the thyroid tissue in the iris of our patient was ectopic.

Ectopic thyroid tissue is a rare entity that usually occurs at the base of the tongue, as a lingual thyroid, and in the region of the thyroglossal duct in the neck, where its location can be explained by the embryogenesis of the thyroid gland. Ectopic benign thyroid tissue has rarely been described outside the normal migration path of the thyroid.

Report of a Case. A 15-year-old boy was referred to the Ocular Oncology Unit, Royal Liverpool University Hospital, Liverpool, England, with an intraocular tumor in his right eye. This lesion was detected on routine eye examination when he reported a 6-week history of floaters and headaches. The patient was not previously aware of this tumor, and no prior ocular disease was reported. Systemic assessment was unremarkable apart from mild asthma. At his first visit to us, his visual acuity was 20/20 OD and 20/20 OS. Slit-lamp examination of the right eye showed a temporal, pink, multinodular lesion that involved the iris root and anterior chamber angle (Figure 1). At gonioscopic examination, the mass obstructed the view into the anterior chamber angle from the 8- to 9-o’clock positions. The intraocular pressure was 19 mm Hg OD and 15 mm Hg OS. The fundus and the left eye were healthy. On ultrasonography, the tumor measured approximately 3.8 mm longitudinally and 2.5 mm transversely with a thickness of 1.2 mm. The internal acoustic reflectivity suggested small cystic spaces within the lesion (Figure 2). The differential diagnosis included lacrimal gland choristoma and medulloepithelioma. An excision biopsy consisting of iridocyclectomy was performed under general anesthesia without complications. The postoperative recovery was uneventful. At follow-up examination 9 months after surgery, the unaided visual acuity was 20/20 OD. The intraocular pressure was 15 mm Hg OD and 14 mm Hg OS. Biomicroscopy showed a small surgical coloboma corresponding to the excised lesion. There were no complications.

Histopathological Examination. Histopathological examination confirmed that the specimen comprised inner corneoscleral tissue including the peripheral Descemet membrane, trabecular meshwork, Schlemm canal, ciliary muscle, ciliary processes, and peripheral iris.
The Descemet membrane was reflected back onto the surface of the peripheral iris, and the iris component was expanded by follicular tissue in which each follicle contained colloidal material (Figure 3). The follicles were lined by cuboidal cells. These cells were immunoreactive for cytokeratins 7 and 8/18 (Figure 4) but not cytokeratin 20. The cells also stained for nuclear thyroid transcription factor 1 (Figure 5). Both the cells and the colloidal material stained for thyroglobulin (Figure 6). No calcitonin or Ki-67 labeling was seen.

No continuity was observed between the follicular lesion and the ciliary epithelium. Indeed, the ciliary epithelium showed a different cytokeratin expression pattern and, unlike the lesional epithelium, was positive for S100 protein. Moreover, S100 protein labeled adjacent uveal nerves.

**Systemic Management.** Ultrasoundographic examination of the thyroid gland and a total body computed tomographic scan were performed to exclude the diagnosis of iris metastasis from a highly differentiated follicular thyroid carcinoma and ectopic thyroid tissue. Ocular metastases from the thyroid are rare and usually develop in the choroid and ciliary body.1-3 Iris metastases have been reported in only 4 patients. Two patients had concurrent ciliary body and choroidal involvement with metastases from medullary thyroid carcinoma.3 One patient had a solitary iris metastasis from mixed papillary and follicular thyroid carcinoma.3 Only 1 patient had a highly differentiated follicular thyroid carcinoma metastatic to the iris.4 These cancers were excluded in our patient, as neither a primary tumor nor secondary tumors were detected at subsequent follow-up. Malignancy was also unlikely because of a negative family history for thyroid cancer, the young age of the patient, the lack of mitotic activity, and negative Ki-67 labeling within the lesion. Because primary thyroid carcinoma may be very small (microcarcinoma) and difficult to detect, we monitored the patient to promptly identify any sign of tumor within the thyroid gland scans with iodine 123 were performed after 6 months and 1 year, and the results were negative.

**Comment.** We report a case of iris ectopic thyroid tissue in a young patient with no history of any relevant systemic disorder and a normally located and well-functioning thyroid gland.

To our knowledge, this is the first case of ectopic thyroid tissue reported in the eye. At initial examination, the differential diagnosis included lacrimal gland choristoma and medulloepithelioma. Ectopic lacrimal gland in the iris usually appears as a yellow-red vascular tumor with an irregular surface and a characteristic cystic structure on ultrasonography. This condition is rare and is usually detected in infancy. Medulloepithelioma is often cystic and can be pink. It tends to appear in the first decade of life and can be benign or malignant. It is usually located in the ciliary body but rarely arises in the iris.

The biopsy results showed thyroid follicles containing colloidal material (Figure 3), and the differential diagnosis showed a metastasis from follicular thyroid carcinoma and ectopic thyroid tissue. Ocular metastases from the thyroid are rare and usually develop in the choroid and ciliary body.1-3 Iris metastases have been reported in only 4 patients. Two patients had concurrent ciliary body and choroidal involvement with metastases from medullary thyroid carcinoma.3 One patient had a solitary iris metastasis from mixed papillary and follicular thyroid carcinoma.3 Only 1 patient had a highly differentiated follicular thyroid carcinoma metastatic to the iris.4 These cancers were excluded in our patient, as neither a primary tumor nor secondary tumors were detected at subsequent follow-up. Malignancy was also unlikely because of a negative family history for thyroid cancer, the young age of the patient, the lack of mitotic activity, and negative Ki-67 labeling within the lesion. Because primary thyroid carcinoma may be very small (microcarcinoma) and difficult to detect, we monitored the patient to promptly identify any sign of tumor within the thyroid gland.
and in other parts of the body. Once no primary or secondary tumors were detected after more than a year of follow-up, we concluded that the thyroid tissue in the iris of our patient was ectopic.

Ectopic thyroid tissue outside the normal migration path of the thyroid has previously been found in the submandibular region, parotid salivary gland, mediastinum, trachea, carotid, heart, lung, duodenum, adrenal gland, gallbladder, skin, and liver, but not in the eye. The intraocular thyroid tissue cannot be explained by embryogenesis. We hypothesize that heterotopic thyroid tissue in the iris might be the result of aberrant differentiation of local tissues by heteroplasia or metaplasia. Recently, mutations of the thyroid transcription factor 1 gene or of genes regulating thyroid transcription factor 1 expression were implicated in ectopic thyroid development. A somatic mutation in genes that suppress inappropriate thyroid differentiation in nonthyroid embryonic tissues could explain this condition.

In conclusion, although it is extremely rare, ectopic thyroid tissue should be considered in the differential diagnosis of iris nonpigmented lesions. Complete surgical excision and systemic follow-up are advisable to achieve a definitive diagnosis and to prevent malignant transformation, which has been reported in a few cases of ectopic thyroid tissue.

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Ligneous Conjunctivitis in a Mexican Patient With a Mutation in the Plasminogen (PLG) Gene

Ligneous conjunctivitis is an autosomal recessive inherited disease caused by mutations in the plasminogen (PLG) gene. Herein, we report a girl affected by this disorder, caused by a homozygous deletion of 14 base pairs in exon 5 of the PLG gene.

Report of a Case. A 2-year-old Mexican girl, product of the fourth pregnancy of second-grade consanguineous parents with no relevant family history, was cared for at the Service of Ophthalmology of the University Hospital, Universidad Autónoma de Nuevo León, because of a refractory bilateral conjunctivitis noticed when she was 2 months of age. The physical examination revealed chronic inflammation of the eyelids and synchiae of the tarsal and bulbar conjunctivae with hard pseudomembranes in both eyes; the rest of the examination results were normal. The parents did not show any abnormality in the eyes or facial mucous epithelia. The patient required surgical removal of the pseudomembranes after failing medical treatments with topical antibiotics and corticosteroids.

The evaluation of the fibrinolytic route demonstrated very low concentration of plasminogen (<1 mg/dL; <0.113 mmol/L); reference range, 7-17 mg/dL [0.791-1.921 mmol/L]) and plasminogen functional activity (6%; reference range, 75%-140%), confirming the diagnosis of ligneous conjunctivitis. The patient and her parents were studied for abnormalities in the PLG gene located at 6q26. Genomic DNA were isolated from peripheral blood and DNA samples were amplified by polymerase chain reaction using different sets of primer pairs designed in the Department of Biochemistry for analysis of exons 2, 5, 7, 10, 13, 14, 15, and 17 of the PLG gene. All amplicons included exon-intron boundaries. Polymerase chain reaction products were purified and sequenced in an automated DNA sequencer (Li-Cor DNA 4200; Li-Cor Inc, Lincoln, Neb) and confirmed by restriction fragment length polymorphism analysis. This study showed a homozygous nucleotide deletion of 14 base pairs in exon 5 of the PLG gene in the patient, which creates a stop codon at position 145 of the protein. The deletion eliminates a restriction site for PstI present in the wild-type allele. After digestion with PstI (New England Biolabs, Inc, Ipswich, Mass), amplicons were electrophoresed in 2.5% agarose gel and visualized by ethidium bromide staining. Both parents were heterozygous for the mutation (Figure).

Comment. Ligneous conjunctivitis is a rare disorder characterized by re-