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Can J Ophthalmol 2016;51:e81–e84
0008-4182/16/$-see front matter
http://dx.doi.org/10.1016/j.jcjo.2016.01.001

Eyebrow madarosis reflecting an intradermal neoplasm: pleomorphic adenoma, a rare brow tumour

Pleomorphic adenoma is a neoplasm named for its mixture of disparate tissue elements, including branching double-layered ductules within a fibroid, myxoid, cartilaginoid, and (rarely) adipocytic stroma.[1] A rare cutaneous tumour presumably arising from apocrine or eccrine sweat ducts, it has been described in the eyelid, where it may occupy various locations, including the sub-brow region.[1,2] Well-recognized tumours with identical histology may arise from the ductules of the major salivary glands and all portions of the lacrimal gland.[3] We report a pleomorphic adenoma of the brow that presented with the unusual symptom of focal brow loss.

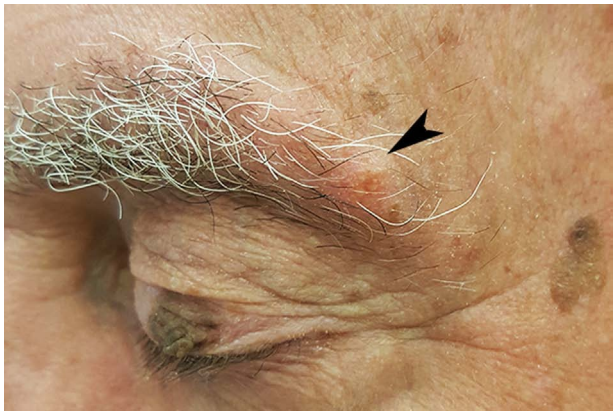

Fig. 1—Hair loss and tumour of the temporal portion of the left brow (arrow). The pigmented eyelid lesion is a seborrheic keratosis.

A healthy 77-year-old male complained of hair loss on the temporal third of the left eyebrow. Examination disclosed a subtly elevated, nontender, faintly erythematous subcutaneous mass in that location (Fig. 1). Excisional biopsy including overlying skin yielded a mass measuring 0.7 cm × 0.2 cm × 0.3 cm. Histology showed a well-circumscribed, nonencapsulated intradermal tumour consisting of branching and nonbranching strands of tubuloalveolar structures arranged among chondroid and adipocytic zones (Fig. 2A). The tubules were composed of a double layer of epithelial cells, the inner layer of which stained positively with epithelial immunostains AE1/AE3, EMA, and CAM5.2 (spotty) as well as gross cystic fluid disease protein (GCDFP-15), an apocrine marker. The outer layer was positive for S100 and NSE but not SMA or GFAP. Ki67 showed a low proliferative rate (<5%).

Formerly designated "chondroid syringoma" and "cutaneous benign mixed tumour," the current preferred terminology of this rare cutaneous neoplasm is "pleomorphic adenoma" implying morphologic variety that includes epithelial and mesenchymal portions.[1] Histology

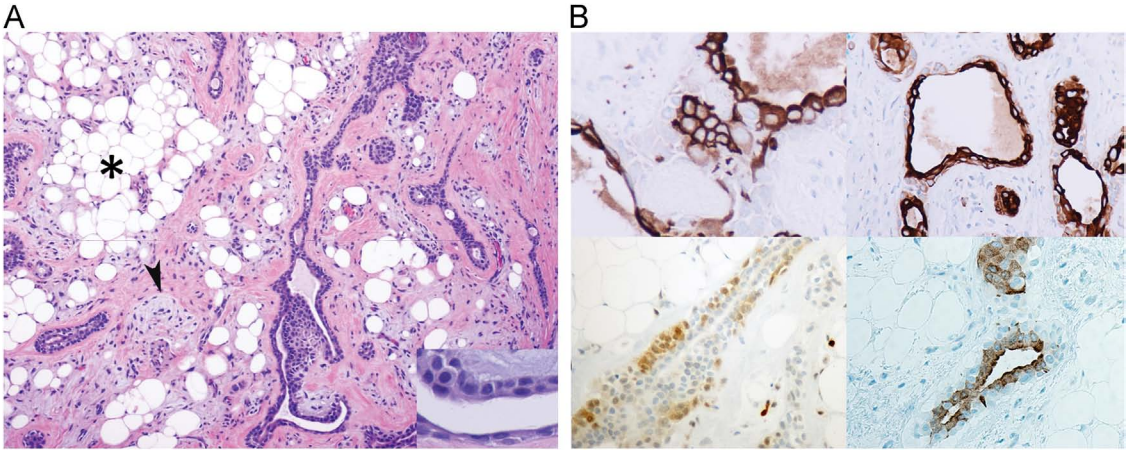

Fig. 2—(A) Tumour consists of branching, double-layered tubuloalveolar structures amidst adipose tissue (asterisk) and chrondroid tissue (arrowhead). Inset shows a double layer of cuboidal cells (hematoxylin–eosin, original magnification ×200, inset ×400). (B) Immunohistochemistry highlights adluminal layer of tubules for AE1/AE3 pancytokeratin stain (upper left) and CAM 5.2 low-molecular-weight keratin (upper right). Outer layer of cuboidal cells stains positively for neuron-specific enolase (NSE) (lower left). Inner layer is positive for gross cystic disease fluid protein-15 (GCDFP-15) (lower right) (immunperoxidase reaction, diaminobenzidine chromogen, ×400).

shows a biphasic, variable architecture containing epithelial tubules set in a fibrous, myxoid, cartilaginoid, and even an unusual adipocytic stroma as in the current case. Immunohistochemisty shows a different staining pattern for the inner tubular cells compared with the outer layer. As there are no characteristic clinical features, diagnosis relies upon excisional biopsy. Malignant transformation has been described, especially after incomplete excision, paralleling the experience in the lacrimal and salivary glands.[4]

The differential diagnosis of eyebrow madarosis is extensive, including common localized disorders such as seborrheic dermatitis, malignancies (basal and squamous cell carcinoma), or components of systemic diseases (alopecia areata, discoid lupus erythematosis, Vogt–Koyanagi–Harada syndrome, sarcoidosis, leprosy, syphilis, cutaneous T-cell lymphoma).[5] Focal brow infarction may provide a clue to the diagnosis of giant cell arteritis. Drugs such as retinoids, heparin, anticonvulsants, angiotensin-converting enzyme (ACE) inhibitors, and androgens may trigger telogen hair shedding and madarosis.[6] Hair loss after systemic chemotherapy is well known. Patients may not admit to trichotillomania, a disorder involving the plucking of hairs.[7]

The approach to brow loss may be challenging and should involve consideration of the systemic medical status, including medication usage, and possible psychiatric evaluation. Focal and asymmetric brow loss merits suspicion for an underlying tumour[8] as in the current case. Complete surgical excision should always be attempted.

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Can J Ophthalmol 2016;51:e84–e85

http://dx.doi.org/10.1016/j.jcjo.2016.01.013

Brothers with ocular motor apraxia, juvenile nephronophthisis, and mild cerebellar defects

Ocular motor apraxia (OMA) is a disorder of absent or flawed horizontal eye movements. Head thrusts compensate for poor saccades.[1] These signs usually improve with time. Although most cases are sporadic, familial cases suggest either an autosomal dominant or recessive inheritance pattern.[2] A small subset have extraocular findings, including Joubert syndrome with or without juvenile nephronophthisis.

Nephronophthisis is a cystic renal disease and the most frequent cause of end-stage renal disease (ESRD) in the first 3 decades of life. Nephronophthisis can be further categorized by the mean age (in years) of onset: infantile (1), juvenile (13), and adolescent (19).[3] Initial symptoms are relatively mild, including polyuria, polydipsia, secondary enuresis, and anaemia. By the average age of 9 years, a slightly increased serum creatinine can be detected, preceding the expected development of ESRD. Cysts seen by ultrasonography begin to appear at the corticomedullary junction after ESRD. Kidneys can be normal or reduced in size.[3,4]

Juvenile nephronophthisis is the most common form of nephronophthisis, accounting for 5–10% of childhood ESRD; its incidence is approximately 1 in 50,000 live births in Canada and 9 in 8.3 million in the United States.[4,5] Nephronophthisis generally follows an autosomal recessive inheritance pattern.[1,6]

Mutation in 8 genes (*NPHP1, 3, 4, 5, 6, 7, 8,* and *9*) can cause juvenile nephronophthisis.[4] Approximately 85% of patients with juvenile nephronophthisis type 1 (NPH1) have a large homozygous deletion of ~290 kb (originally thought to be ~250 kb) spanning the *NPHP1* gene; 15% of patients are heterozygous for this large deletion and a point mutation in this gene. Breakpoints for this common deletion are thought to be located within a 45 kb sequence located 20 kb upstream of the *NPHP1* gene and directly repeated 250 kb