



Figure 1 (a) Clinical appearance of the cystic lesion along the medial aspect of the left upper eyelid with a flesh-colored base and a deep purple hue at the apex. A horizontal, linear demarcation within the cyst was observed, representing layered hemorrhage. (b) Histologic analysis of the cyst in panel a demonstrated an inner layer of eosinophilic cuboidal to columnar epithelium showing focal decapitation type secretion, consistent with apocrine hidrocystoma, while the lumen contained abundant hemosiderin-laden histiocytes and degenerated erythrocytes. (c) Clinical appearance of the cystic lesion along the medial aspect of the right upper eyelid. (d) Histologic analysis of the cyst in panel c demonstrated eosinophilic columnar cells lining of the cystic lesion. The inner layer of columnar cells showed decapitation secretion, focal lipofuscin pigment deposition and focal ciliary processes, all consistent with apocrine hidrocystoma, while the cyst lumen contained degenerated and intact erythrocytes.

degenerated red blood cells consistent with recent and old hemorrhage, respectively.

We suggest that hemorrhagic apocrine hidrocystomas of the eyelid are more common than previously reported, and may be seen in the setting of minimal systemic anticoagulation, including aspirin use alone.

Conflict of interest

The authors declare no conflict of interest.

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Reference

- Novitskaya E, Rene C, Dean A. Spontaneous haemorrhage in an eyelid hidrocystoma in a patient treated with clopidogrel. *Eye (Lond)* 2013; **27**(6): 782–783.

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Sir,
'Spontaneous haemorrhage in an eyelid hidrocystoma in a patient treated with clopidogrel' by Tehrani *et al*

We thank Tehrani *et al*¹ for their interest in our article² and for sharing their experience of two cases of spontaneous hemorrhage in an apocrine hidrocystoma in patients on antiplatelet therapy.

We challenge their assertion that spontaneous bleeding within a hidrocystoma may occur even in the absence of clopidogrel use, because both of their patients were on clopidogrel, as in our case. Furthermore, they have provided no references to support that view. Although this is difficult to prove, we believe that the antiplatelet activity of clopidogrel contributed to the spontaneous bleeding within the hidrocystoma in our patient, as well as their two cases. However, the risk of spontaneous

bleeding within a hidrocystoma may not be unique to clopidogrel, and could apply to other antiplatelet agents. Interestingly, one of their patients was on concurrent aspirin therapy but there are no reports to date of spontaneous hemorrhage in a hidrocystoma related solely to aspirin use.

We have no reason to believe that spontaneous bleeding within an eyelid hidrocystoma is a common phenomenon, as there are no other reports in the medical literature. Tehrani *et al*'s report of two additional cases does nothing to alter the fact that this is a rare phenomenon.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Tehrani S, Rozelle C, Solomon A, Steele E. Comment on 'Spontaneous haemorrhage in an eyelid hidrocystoma in a patient treated with clopidogrel'. *Eye (Lond)* 2013; **27**(11): 1326–1327.
- 2 Novitskaya E, Rene C, Dean A. Spontaneous haemorrhage in an eyelid hidrocystoma in a patient treated with clopidogrel. *Eye (Lond)* 2013; **27**: 782–783.

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Sir,

Pseudoexfoliation syndrome and cardiovascular disease: studies must control for all cardiovascular risk factors

I read with interest the case–control study by Gonen *et al*¹ who sought to identify the incidence of renal artery stenosis (RAS) and abdominal aortic aneurysm (AAA) in patients with pseudoexfoliation syndrome (PXE).

PXE affects 30% of patients over 60 years of age;¹ not all can undergo ultrasonographic screening. Elucidating the quantitative contribution—or relative risk—of PXE to cardiovascular disease is critical in identifying patients at significant cardiovascular risk who can be referred from ophthalmic clinics for further management. Any study seeking to evaluate the significance of a candidate cardiovascular risk factor must therefore identify and control all other established cardiovascular risk factors (Table 1).

Gonen *et al*¹ did not account for serum cholesterol and urinary albumin excretion—two major independent cardiovascular risk factors associated with AAA and RAS—which may have conceivably contributed to their development. These were not obviously examined as

Table 1 Cardiovascular risk factors

Non-modifiable risk factors

Age
Gender
Family history^a

Modifiable risk factors

Hypertension
Diabetes
Hypercholesterolaemia
Microalbuminuria^b
Smoking
Obesity (body mass index >30 kg/m²)
Diet
Sedentary lifestyle
Hyperhomocystinaemia

^a Positive family history is a cardiovascular event before 55 years of age in males and 65 years of age in females in a first-degree relative.

^b Urinary albumin excretion >30 mg/24 h.

explicit parameters, nor proven statistically equivalent between PEX cases and controls.

Hypercholesterolaemia has been demonstrated as an independent risk factor for both RAS and AAA. Overall, 33% of patients with heterozygous familial hypercholesterolaemia have RAS on formal renal angiography, predominantly proximal in location.² Meta-analysis of pooled data from eight studies identified significantly lower HDL and higher LDL cholesterol in patients with AAA compared to controls.³

Microalbuminuria (>30 mg/24 h) is an independent cardiovascular risk factor and predictive of all-cause cardiovascular mortality (relative risk of 3.2).⁴ Microalbuminuria is associated with increased renovascular resistance and reduced aortic compliance in diabetic subjects, after adjustment for other cardiovascular risk factors.⁵ Microalbuminuria may conceivably influence renal artery peak systolic velocity parameters used as an end point in this study.

A prospective longitudinal cohort study is required in patients with PXE to determine the relative risk of serious cardiovascular events in relation to other risk factors. Alternatively, ocular examination of subjects in large existing population-based studies such as the Framingham Heart Study may help to identify the contribution of PXE to cardiovascular risk.

Urinary albumin estimation and serum cholesterol assays may have added further value to this study by excluding potentially confounding variables on the expressions of cardiovascular disease in PXE.

Conflict of interest

The author declares no conflict of interest.

References

- 1 Gonen KA, Gonen T, Gumus B. Renal artery stenosis and abdominal aorta aneurysm in patients with pseudoexfoliation syndrome. *Eye (Lond)* 2013; **27**: 735–741.