Oxford Eye Hospital guidelines for management of patients with melanocytic choroidal tumours

Bertil Damato, PhD, FRCOphth
Nuffield Laboratory of Ophthalmology, University of Oxford, and Oxford Eye Hospital, John Radcliffe Hospital, OX3 9DU
https://www.ndcn.ox.ac.uk/team/bertil-damato

Table of Contents

Introduction

Choroidal naevi are found in about 6% of individuals whereas only 6 people per million per year develop melanoma. The author has devised the **MOLES** system to help practitioners estimate risk of malignancy and manage patients accordingly. At Oxford Eye Hospital a diagnostic ocular tumour service has been established to assess electronically submitted images remotely. The aim is to avoid unnecessary hospital visits thereby enhancing the safety of patients and staff during the Covid-19 pandemic as well as minimising the stress and inconvenience caused to patients, not to mention the travel expenses and loss of earnings they may incur.[1] This MOLES system and the diagnostic service should also reduce waiting lists, expediting the care of patients requiring urgent treatment for melanoma and other serious diseases.

MOLES Scoring Chart

Indicator	Finding	Score
Mushroom shape	0 = Absent 1 = Incipient (erosion through RPE) / uncertain) 2 = Present (i.e. definitive mushroom shape with overhang)	
Orange pigment	0 = Absent 1 = Dusting / unsure 2 = Confluent (i.e. easily visible clumps of orange pigment)	
Large size	0 = Flat (<1mm thick) and less than 3 disc diameters (DD) wide 1 = Subtle dome shape (1-2mm thick) AND/OR 3-4DD wide 2 = Significant thickening (>2mm) AND/OR more than 4DD wide	
Enlargement	0 = None (or no baseline photography) 1 = Suspected change on comparing photographs 2 = Definite growth confirmed by sequential imaging	
Subretinal fluid	0 = Nil 1 = Trace (limited retinal detachment seen only with OCT) 2 = Definite subretinal fluid visible with ophthalmoscopy	
	Moles total score =	

Recommended Management

MOLES score	Management (i.e., in Oxfordshire)
0 = Common naevus	Advise usual self-care (i.e., with no surveillance other than usual visits to optometrist every 1-2 yrs). Follow B3 College of Optometrists Clinical Management Guidelines (CMG)
1 = Low-risk naevus	Refer NON_URGENTLY to the Oxford Eye Hospital by completing the Oxford Ocular Oncology Referral Form (downloadable from OEH website) and e-mailing it to OUH-tr.ocularmoles.oxon@nhs.net with attached image(s). [Follow B1 referral protocol of the College of Optometrists CMG]. Give patients the leaflet entitled 'Mole at the back of the eye', downloaded from the Oxford Eye Hospital website.
2 = High-risk naevus	
>2 = Probable melanoma	Refer URGENTLY by e-mailing the Oxford Ocular Oncology Referral Form to Pcc2wwoxford@nhs.net with attached image(s) of the lesion.[Follow Level A3 referral protocol of the College of Optometrists CMG and the NHS FastTrack pathway for suspected cancer. Encourage patients to accept the earliest appointment. Give them the FastTrack patient information sheet

Management Tips

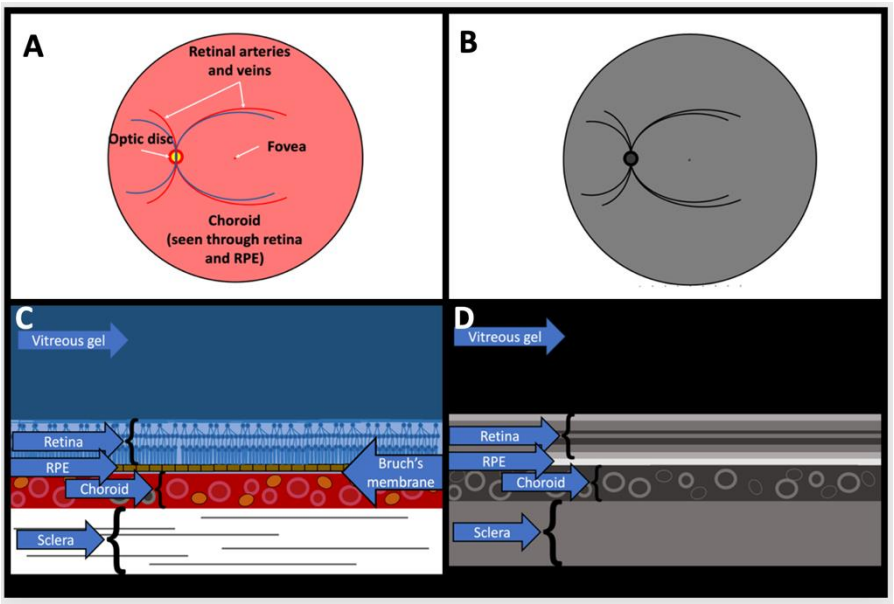
- If possible, include images of the tumour with the referral form, in case diagnosis can be provided remotely.
- Patients referred without attached images are given an appointment at the photography unit at Oxford Eye Hospital. Subsequent management will be planned according to remote review of these images, with a face-to-face meeting with an ophthalmologist only if necessary.
- Baseline imaging should consist of colour photography. Optical coherence tomography (OCT) and/or fundus autofluorescence (FAF) imaging may help but are not essential.
- Ultrasonography is indicated only for large tumours that are too thick or peripheral for OCT.
- Monitoring usually requires only sequential colour photography, with other imaging only if growth is suspected.

Links

- FastTrack info sheet: https://www.oxfordshireccg.nhs.uk/professional-resources/documents/clinical-guidelines/cancer/fast-track-pathway-patient-information-leaflet.pdf
- College of Optometrists CMG: https://www.college-optometrists.org/guidance/clinical-management-guidelines/pigmented-fundus-lesions.html
- Oxford Eye Hospital Ocular oncology referral forms: https://www.ouh.nhs.uk/eye-hospital/work/ocular-moles-guidelines.aspx
- Patient information sheet, 'Mole at the back of the eye': https://www.ouh.nhs.uk/eye-hospital/departments/ophthalmic/ocular-moles/default.aspx

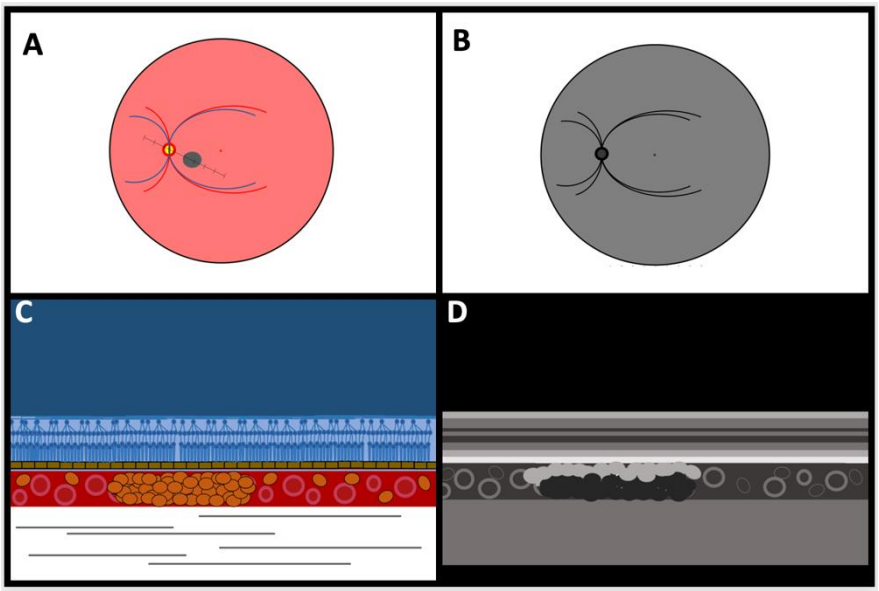
Schematic drawings of melanocytic choroidal tumours

Figure 1. Normal fundus



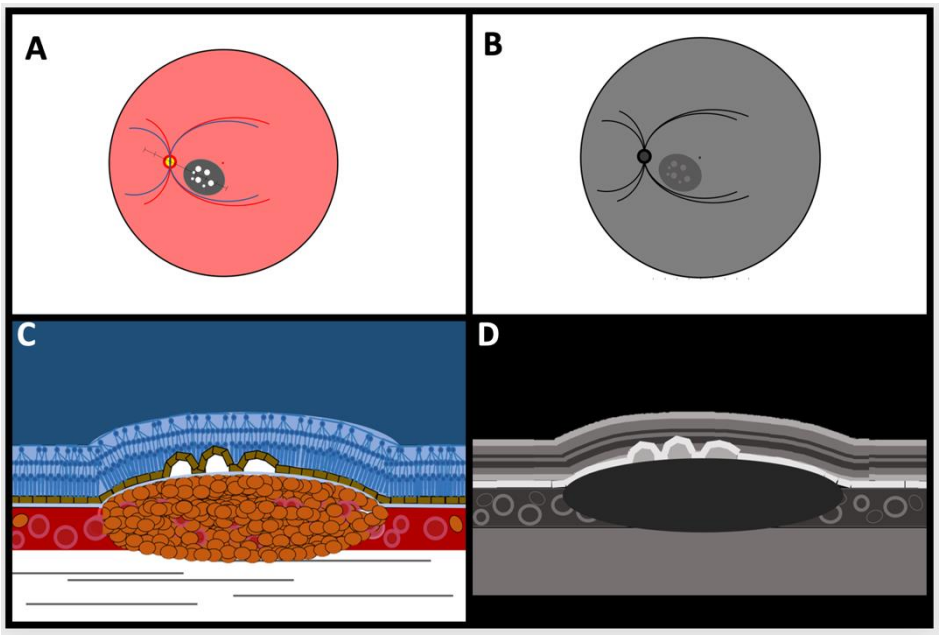
Normal fundus. (A) colour photograph, showing optic disc, retinal blood vessels, fovea and choroid, which is visible through the retina and retinal pigment epithelium; (B) autofluorescence imaging, showing optic disc and retinal vessels silhouetted against a grey background; (C) histology, showing vitreous, retina, retinal pigment epithelium, Bruch's membrane, choroid and sclera; and (D) optical coherence tomography (OCT) showing these layers (Schematic)

Figure 2. MOLES Score = 00000 = 0 = Common naevus



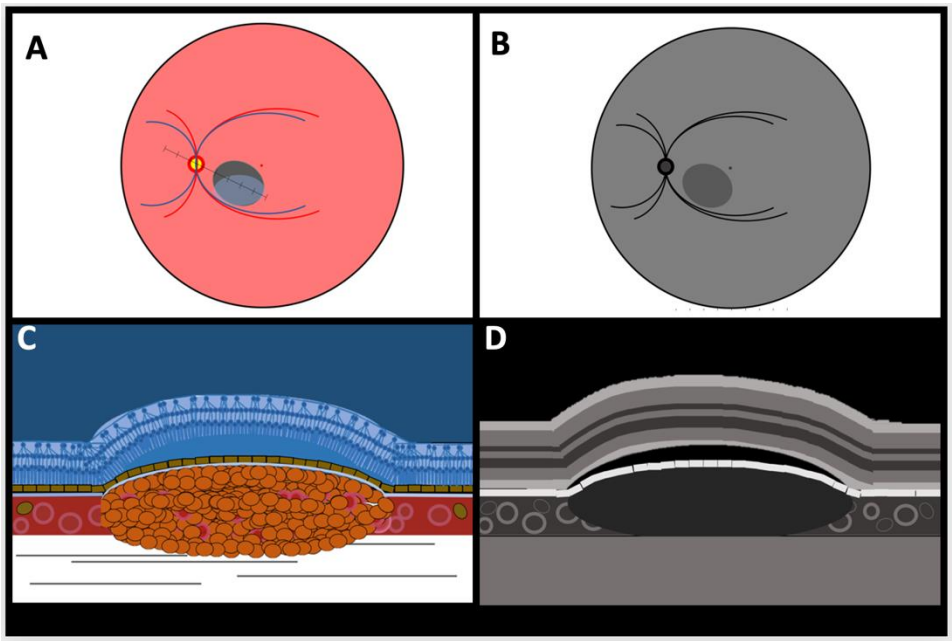
(A) Colour photograph showing a small, flat, grey, and featureless spot. Proximity to disc is NOT a risk factor for malignancy; (B) Autofluorescence image, which shows no abnormalities because the RPE over common naevi is normal; (C) Histology, which shows a small tumour composed of melanocytes with normal RPE and retina; and (D) OCT appearance. Naevi can be hyper- or hypo-fluorescent, depending on their degree of melanin pigmentation. (Schematic)

Figure 3. MOLES Score = 00100 = 1 = Low-risk naevus



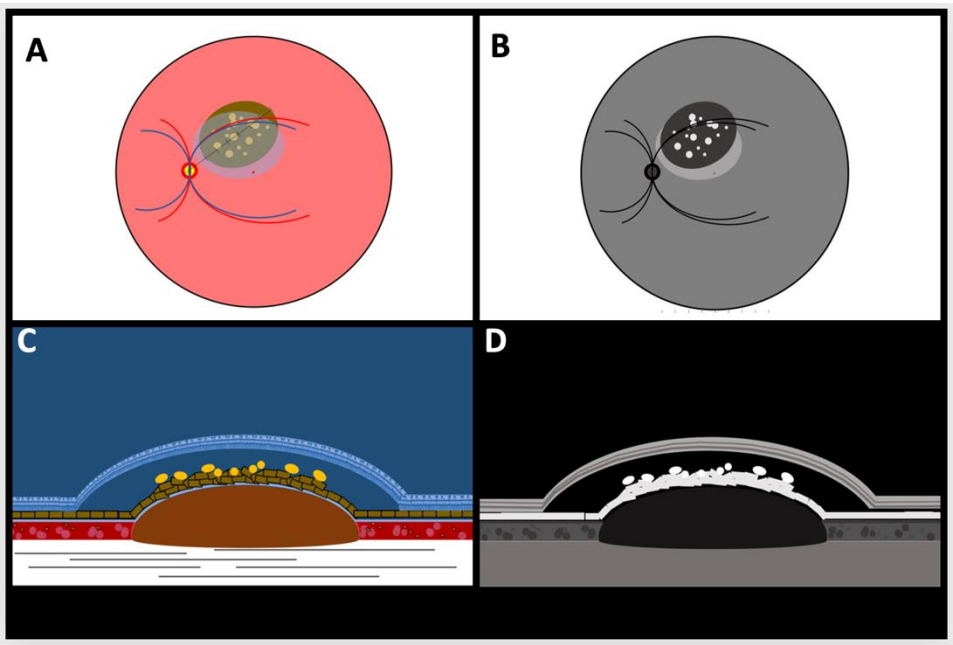
(A) Colour photograph showing that naevus is slightly larger than usual (i.e., 3-4 DD) without any other suspicious features and with waxy, white drusen on its surface; (B) Fundus autofluorescence imaging shows the naevus to be darker than the surrounding choroid. Any drusen tend to autofluoresce only dimly or not at all; (C) Histology shows swelling of the choroid by the naevus. Any drusen develop between the RPE and Bruch's membrane; and (D) OCT shows the naevus to be darker than the surrounding tissues. The RPE appears as a thick, white line and is draped over any drusen. (Schematic)

Figure 4. MOLES Score = 00101 = 1 = High-risk naevus



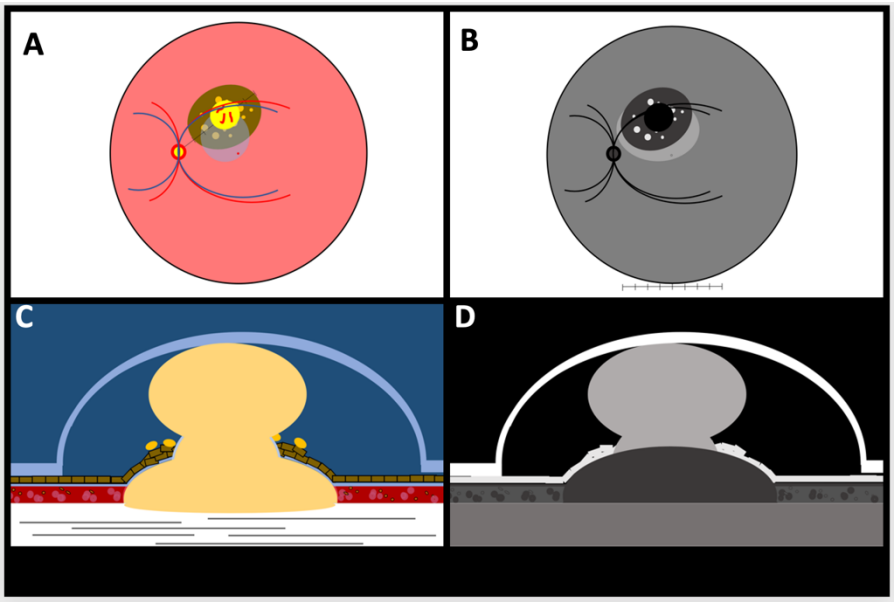
(A) Colour photography shows this naevus to be slightly larger than usual, with a small trace of subretinal fluid, which is not visible except with OCT; (B) Autofluorescence imaging does not show the retinal detachment; (C) Histology shows swelling of the choroid by the naevus and a small amount of subretinal fluid detaching the retina slightly over a limited area. This occurs because the function of the RPE is impaired by the naevus; (D) OCT shows the retina to be slightly detached by a small collection of subretinal fluid

Figure 5. MOLES Score = 02202 = 6 = Probable melanoma



(A) Colour photography shows that this tumour is larger than most naevi, with clumps of orange pigment and subretinal fluid that is abundant enough for the retinal detachment to be seen with an ophthalmoscope; (B) Autofluorescdnce imaging shows the lipofuscin clumps to auto-fluoresce brightly. The subretinal fluid gravitating from the tumour has damaged the RPE and retina inferior to the tumour so these are hyper-auto-fluorescentn; (C) Histology shows serous retinal detachment and clumps of lipofuscin on the retinal surface of the RPE; (D) OCT shows fluffy lipofuscin deposits and retinal detachment.

Figure 6. MOLES Score = 22202 = 8 = Probable melanoma



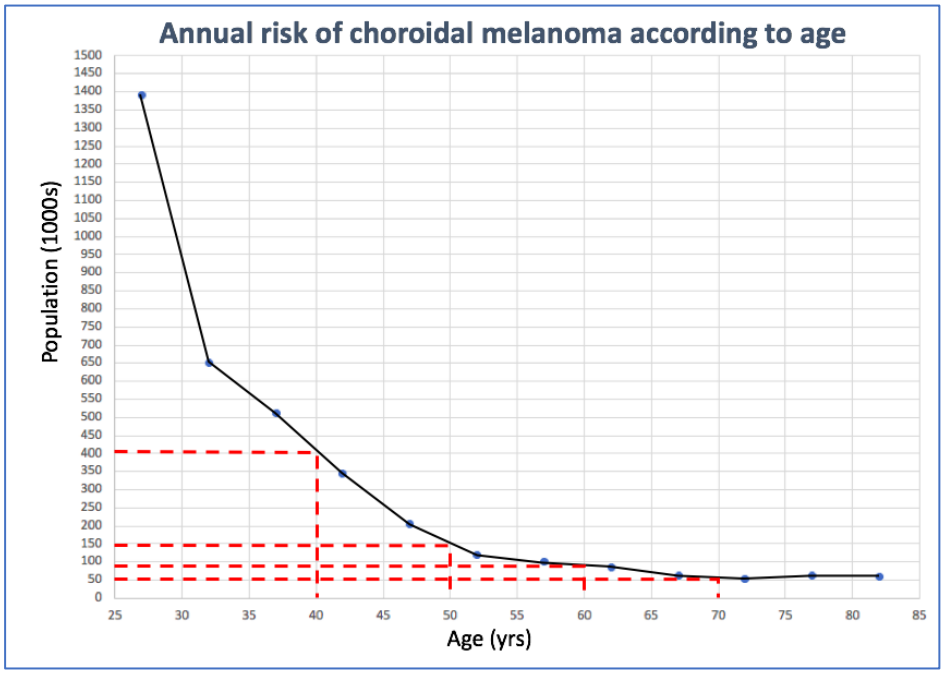
(A) Colour photography shows that this melanoma has grown through the RPE so that its true colour is apparent. This tumour is tan in colour because it has little melanin pigment. Congested blood vessels are seen in apical part of the tumour; (B) Autofluorescence imaging shows no autofluorescence in the area where the tumour has grown through the RPE. The RPE inferior to the tumour is hyper-autofluorescent where it is damaged by retinal detachment; (C) Histology would show growth of the tumour through Bruch's membrane, which strangulates the tumour so that it becomes oedematous and swollen, to form a mushroom shape; (D) Ultrasonography is required to assess this tumour, which is too thick for OCT. The oedematous tumour within the retina is highly reflective whereas the compact basal part of the tumour shows low reflectivity

MOLES rationale

Introduction

Choroidal melanomas threaten patients with visual handicap, loss of the eye, and death from metastatic disease. Early diagnosis and treatment maximise any opportunities for preventing these outcomes.

Small melanomas can be difficult to distinguish from naevi. Such benign 'moles' are common, with a prevalence of approximately 6% (i.e., 1 in 17 adults).[2] In contrast, choroidal melanomas are rare, with an annual incidence of approximately 1 in 400,000 at around the age of 40 years, increasing to almost 1 in 100,000 at 60 years and to 1 in 50,000 over the age of 65 years (Fig. 7).[2]



(Graph derived from data by Singh, Kalyani and Topham (2005)

These rates are lower in individuals having a dark complexion.[1] For these reasons, patient care needs to be individualised according to clinical features indicating any increased risk of malignancy. The author has devised the MOLES protocol to help clinicians remember these clinical signs and to plan patient care accordingly. Other systems, such as TFSOM-DIM (To find small ocular melanoma doing imaging) require ultrasonography to assess internal acoustic reflectivity[3]; however, such scanning not widely available in the community in the UK. The MOLES system can be based on ophthalmoscopy alone, ideally with colour fundus photography. Here, the MOLES rationale is discussed.

MOLES scoring system

Mushroom shape (i.e., with overhang) is almost pathognomonic for choroidal melanoma. It occurs when the tumour extends through Bruch's membrane and retinal pigment epithelium (RPE). When this happens, the tumour thickness increases so that the MOLES score exceeds 2. A score of 1 indicates that the tumour bulges slightly through a defect in Bruch's membrane and RPE.

'Orange pigment', consisting of lipofuscin, accumulates on the retinal surface of the RPE, usually overlying rapidly growing tumours. Light dusting of orange pigment can occur over choroidal naevi and is given a MOLES score of 1; however, clumps of confluent orange pigment indicate more severe RPE dysfunction, which tends to occur with melanomas, hence the score of 2. Over amelanotic tumours, lipofuscin can appear brown. This pigment is hyper-autofluorescent on fundus autofluorescence (FAF) imaging. On OCT, lipofuscin forms fluffy deposits on the retinal surface of the RPE, unlike drusen, which form discrete lumps between RPE and Bruch's membrane. Note that orange pigment can appear over other tumours, such as metastases and haemangiomas.

Larger size. Choroidal melanomas tend to be wider and thicker than naevi, although there is considerable overlap. A study by Augsburger et al indicates that there are approximately 125 choroidal naevi for every melanoma in the thickness range of 1.5 to 2 mm, 25 naevi for every melanoma in the thickness range of 2 to 2.5 mm, and 5 naevi for every melanoma in the thickness range of 2.5 to 3 mm.[4] Erring on the side of caution, the tumour thickness is given MOLES scores of 0, 1 and 2 if the tumour thickness is <1 mm, 1-2 mm or >2 mm respectively (i.e., 'flat/minimally thickened', 'slightly dome shaped – seen with difficulty on ophthalmoscopy', and 'significantly elevated- easily visible on ophthalmoscopy'). If possible, the thickness of small, posterior lesions should be documented by performing optical coherence tomography (OCT). Ultrasonography may be useful when OCT is not possible because of large tumour size or peripheral location. Augsburger et al also found that there are approximately 70 naevi for every choroidal melanoma in the basal diameter range of 5 to 6 mm, 10 naevi for every melanoma in the range of 6 to 7 mm, and 3 naevi for every melanoma in the range 7 to 8 mm.[4] MOLES therefore scores basal diameter as 0, 1 or 2 if measurements are <3 DD, 3-4 DD, and >4 DD respectively. Tumours rarely become thicker without also increasing in diameter; colour photography should therefore be sufficient to assess size when OCT and ultrasonography are not possible.

Enlargement of choroidal naevi is rare after the age of 25 years, and when it occurs it is minimal and slow, developing over many years (i.e., <0.1 mm per year). Fundus photography makes it easier to detect tumour growth. Sequential fundus photography is ideal but not essential as long as a baseline photograph is available. Tumour enlargement confirmed photographically is given a MOLES score of 2. If photography is suggestive of growth but inconclusive, because of poor image quality, a score of 1 is given. A score of 0 is given if a lesion is detected and its absence previously not confirmed photographically. A score of 0 is given also if the patient was not informed of any naevus in previous ocular examinations. This is because the lesion may have been missed or because the clinician did not mention the presence of the lesion to the patient. In the author's opinion, when monitoring suspicious lesions, ultrasonography is not required if sequential colour photography does not suggest growth. This is because it is rare for tumours to grow thicker without becoming wider.

Subretinal fluid (SRF) develops when RPE function is disturbed by an underlying choroidal tumour, as usually happens with melanomas. The retina is flat over common naevi (i.e., MOLES score = 0) but some larger lesions may show minimal or localised detachment; these features are given a score of 1. Cystoid spaces within the retina indicate chronicity so that a score of 0 is given unless SRF is also present. Significant and extensive retinal detachment that is visible ophthalmoscopically is given a MOLES score of 2. Subretinal fluid is best detected with OCT.

Management

In an audit by the author and associates, most choroidal naevi referred to the Oxford Eye Hospital ocular tumour diagnostic clinic were common naevi (i.e., MOLES score of 0), with almost no risk of malignancy. The referral of large numbers of common naevi is placing a burden on hospital resources, possibly delaying the care of patients requiring urgent treatment for diseases such as ocular melanoma. Unnecessary referrals are also causing distress to many patients, who may also incur loss of income and expenses for travel, etc. The Covid-19 pandemic has aggravated these problems.

All patients should be informed of any pigmented fundus lesions and ideally provided with an information sheet and a photograph of the lesion. Patients with a common naevus need no special arrangements (i.e., usual self care, such as review every 2 years, as is recommended by the College of Optometrists for patients without pigmented fundus lesions).

Patients with low-risk and high-risk naevi should be referred non urgently to an ophthalmologist by e-mailing the relevant referral form with attached images to the hospital eye clinic. Such images may enable an expert diagnosis without the patient having to travel to hospital. If adequate images are not received with the referral letter, these will be requested from the optometrist. If adequate images are not available, the patient will need to attend the photography unit at the hospital for imaging studies, which will be reviewed by an ophthalmologist within a few days.

Patients should ideally receive baseline colour photography and, if possible, FAF and OCT (or ultrasonography if a raised lesion is too thick or peripheral for OCT). Long-term surveillance of suspicious naevi is indicated, with follow-up every 6 to 12 months depending on the estimated risk of malignancy. Whereas monitoring of high-risk naevi is best undertaken by an ophthalmologist, monitoring of low-risk naevi by community optometrists would be ideal if NHS funding for this service is provided.

If the MOLES score is more than 2 (i.e., 'probable melanoma'), the patient should be referred urgently to Oxford Eye Hospital to be seen within 2 weeks, according to the NHS FastTrack protocol for suspected cancer. The onus is on the referring practitioner to ensure that relevant guidelines are followed. The ophthalmologist will then decide whether to discharge or monitor the patient or to refer on to a specialist ocular oncology service for definitive diagnosis and treatment.

External validations at Moorfields Eye Hospital have shown MOLES scores to correlate well with expert diagnosis and management.[5, 6]

Conclusions

It is hoped that the MOLES acronym, scoring system and management recommendations will prevent unnecessary referral of patients with choroidal naevi to hospital eye clinics while expediting the care of patients with ocular melanoma.

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