PedsCases Podcast Scripts

This podcast can be accessed at www.pedscases.com, Apple Podcasting, Spotify, or your favourite podcasting app.

Approach to Pigmented Cutaneous and Ocular Lesions and Melanoma

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

Introduction:

Welcome to “Approach to Pigmented Cutaneous and Ocular Lesion and Melanoma”, a podcast made for PedsCases.com at the University of Alberta. I am Dr. Harry Liu, a dermatology resident at the University of British Columbia, and I am Jennifer Ling, a fourth-year medical student at the University of British Columbia. This podcast will provide an organized approach to understand pigmented cutaneous and ocular lesions and melanoma. We would like to thank Dr. Miriam Weinstein and Dr. Conor Mulholland for developing this podcast with us. Dr. Weinstein is a pediatric dermatologist in Toronto at the Hospital for Sick Children (SickKids). Dr. Mulholland is a pediatric ophthalmologist at the BC Children’s Hospital in Vancouver. This podcast is a continuation of a previous podcast on the topic of sun protection. If you haven’t had the chance to listen to that podcast, we recommend you have a listen.

Learning Objectives

After listening to this podcast, we expect the learner to be able to:

1. Generate a differential diagnosis for pigmented lesions on the eye and skin
2. Discuss the key features of common pigmented cutaneous and ocular lesions
3. Describe how cutaneous and ocular melanoma can present in pediatric populations
4. List the treatment options for ocular and cutaneous melanoma

(There was no financial support or any conflict of interests for the development of this podcast.)

Case

First, we’d like to present a case. You are now a fourth-year medical student doing a pediatrics elective. Your first patient is Lucy who you saw last year. Now, she is 17 years old, presenting with a pigmented skin lesion on her right eyelid and she is accompanied by her mother. Upon further history, Lucy had the lesions since birth, when it was barely noticeable. Until about 3 to 4 years ago, the skin lesion had been gradually increasing in size and darkened from light brown to dark brown, with no change in border or shape of the lesion. There is no bleeding or ulceration of the lesion. When asked about any other spots she is worried about, Lucy pointed to the brown lesion on her right conjunctiva. She said it was present at birth and she noticed some darkening from light brown to dark brown as well. It is small, and she didn’t notice appreciable size change. She is otherwise completely asymptomatic and denied any eye discharge, blurry vision, foreign body sensation, or pain.

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

Lucy is otherwise healthy and family history are unremarkable with no known melanoma. She never had any severe or blistering sunburn. She does not drink alcohol or use recreational drugs. Her allergies include peanuts and pollen. On examination, her skin is pale. On the right lower eyelid margin slightly lateral to the medial canthus, there is an approximately 4 x 3 mm symmetric, dark brown, and oval shaped papule with irregular but well-demarcated border. Similarly, there is a well-circumscribed, dark brown 1 x 1 mm limbal lesion at the 9 o'clock position on the right eye. There are no lesions visible on direct ophthalmoscopy. Her visions are 20/20 bilaterally.

What could these lesions be? Are worried about them? Could they be melanoma?

From the physicians' perspective, the biggest fear with sun exposure and pigmented lesions is the occurrence of malignant melanoma. However, it is reassuring that the vast majority of pigmented lesions in children are actually benign and monitoring would be the safe option. Next, we will discuss how to recognize those benign lesions then we will talk about malignant melanoma.

Cutaneous Lesions

Congenital Nevi

A very common pigmented lesion present at birth is congenital melanocytic nevi (CMN), which is a benign proliferation of melanocytes. It is important to keep in mind that the small CMN may be initially noticed by the caregivers sometimes later during the first year of life. CMN can present as macular, papular or mixed lesions and vary in colour substantially. Hair may or may not be present. The lesions tend to become more prominent and typically grow in size proportional to the child's growth. It is crucial to be aware that proliferative nodules can occasionally arise in the lesion in young children and be mistaken for melanoma. CMN is classified by its great greatest diameter. Small CMN is < 1.5 cm, medium if 1.5 to 20 cm, large if 20 to 40 cm, and giant > 40 cm. For large and giant CMN, there may be satellite nevi that may be scattered on the skin and can be in areas distant from the main nevus. For smaller CMN, the risk of melanoma is low and virtually all after puberty. The rate of melanoma was 2 to 2.5% for large CMN and 3.1% for giant CMN. They are called congenital melanocytic nevus-associated melanoma.

Acquired Nevi

Nevi that tend to appear after the first 6 months of life is called acquired nevi. They can have a wide range of clinical presentation but most commonly they are symmetric, round or oval shape, evenly pigmented with sharp and regular outline and homogenous surface. They are usually < 6 mm in diameter and they sometimes can have perifollicular hypopigmentation or pigmentary stippling. The number and size of acquired nevi can increase in number and size during childhood and adolescence, peaking in the third decade and slowly regressing with age afterward. A subtype of acquired nevi are called "atypical nevi". Atypical nevi often have a particular morphology of slightly larger size, with a less distinct border and often more prominent centre with less prominent periphery. It is important to understand that atypical nevi are not "pre-melanoma" but markers for increased risk of developing melanoma. One single atypical nevus

increases the risk of melanoma by 1.5 times; having 5 of them increases the risk by approximately 6 times.

There are some more rare types of acquired nevi that you should be familiar about. Spitz nevus, formerly known as benign juvenile melanoma, is a distinct subtype of melanocytic nevus usually occurring on the face. It usually presents as a pigmented or pink, smooth-surfaced, hairless, dome-shaped papule or nodule with sharp demarcation. It is symmetric and the usual size is from 0.6 to 1 cm in diameter. If the lesion has one or more atypical features of larger size (> 1 cm), irregular borders, irregular topography, or ulceration, they are called atypical Spitz nevus. In general, those with clinically unusual, changing, or concerning features should be biopsied. Last one is Reed nevus. It tends to be seen most often in children and presents as a symmetric dark brown to black papule most commonly on the extremity. As the lesion grows, it can develop the classic starburst pattern which refers to central blue-black pigmentation with regular radial projections at the periphery. Later on, those radial projections may disappear, and the color can become lighter. The lesion may even completely involute sometimes.

Pediatric Melanoma

Melanoma is rare in children, representing 1-4% of all melanomas, but the incidence is increasing at an estimated 1-4% per year. 79% pf pediatric cases diagnosed at the ages of 15 to 19. Pediatric melanoma often has atypical clinical presentation. Particularly in prepubertal children, melanoma can present as a symmetric pigmented lesion with regular border or as a reddish pink, symmetric dome-shaped papule. This is very different from what we see in adults. One prominent of pediatric melanoma is lesion evolution with rapid growth. Patients or caregivers may report bleeding or ulceration of the lesions, and patients may experience discomfort, pain, or pruritus. There are three main types of melanoma in the pediatric population. The first is conventional melanoma mostly among adolescents which is UV-associated with UV-damaged mutations (e.g., BRAF mutation). Spitz melanomas are predominantly seen in preadolescent children. They share some features with atypical Spitz nevus, and it can be difficult to differentiate them apart clinically, pathologically, and genetically. Approximately, one-half to 65% of melanoma arises in a pre-existing nevus, and the last type is the congenital melanocytic nevus-associated melanoma as we discussed early.

Differential Diagnosis of Melanoma

There are a few conditions more common in the pediatric population that you should be familiar with, and they should be differentiated from melanoma. They are

- Vascular lesions, particularly pyogenic granulomas
- Blue nevus
- Café-au-lait macules, which can be confused with nevi but usually not with melanoma

Some vascular lesions (e.g., angiokeratoma, and thrombosed lymphangioma) can look black to mimic melanoma but they are actually not pigmented. Pyogenic granulomas, as known as lobular capillary hemangioma, is an acquired vascular tumor of the skin and mucous membranes that can bleed, simulating amelanotic melanoma. It presents as a bright red to red-brown, raised, slightly pedunculated or sessile papulonodule. Next on the differential is blue nevus, which is a heterogeneous group of congenital and more often acquired melanocytic benign tumors. The melanocytes are deeper in the dermis than other nevi and it represents arrested melanocytic migration in which the melanoblasts remain in the dermis. They appear as

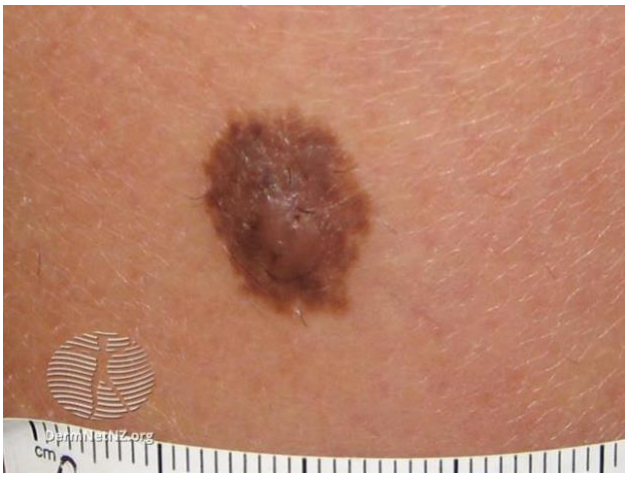
blue-gray macules or papules because of the Tyndall effect, which is selective absorption of longer wavelength components of light by melanin with reflection of the shorter blue components. Café-au-lait macules are flat pigmented lesions that may be present at birth or appear during early childhood, and more prominent after sun exposure. They represent localized areas of increased melanogenesis. The size can range from a few millimetres to > 15 cm in size and they can enlarge in proportion to the growth of the child. The color can be from tan to dark brown and usually uniform, but a few darker macules may appear within the lesions.

Assessment Tools for Suspected Melanoma

In terms of assessment tools, we have the conventional ABCDE criteria, which stands for asymmetry, border irregularity, color variegation, large diameter (> 6 mm), and evolving lesion. Given the atypical presentation of melanoma in children, the pediatric ABCD and CUP criteria were developed and can be used, and they stand for:

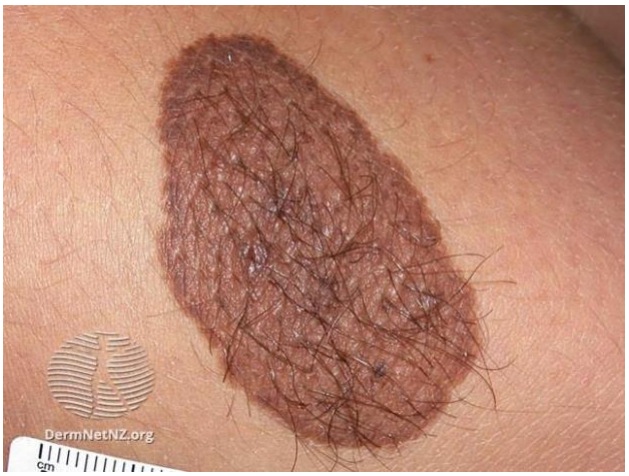
- Amelanotic
- Bleeding, bump
- Color uniformity
- De novo and any diameter
- Color (pink/red), changing
- Ulceration, upward thickening
- Pyogenic granuloma-like lesions, pop-up of new lesions

The bottom line is to have high clinical suspicion for melanoma because the diagnosis can be challenging in children given its rarity and atypical presentation. If melanoma is suspected, referral to the a clinician experienced in management of pediatric pigmented lesions, including pediatric dermatologists, general dermatologists, surgeon, and plastic surgeons. is essential. An excisional biopsy deep to the subcutaneous tissue is needed to confirm histologic diagnosis.

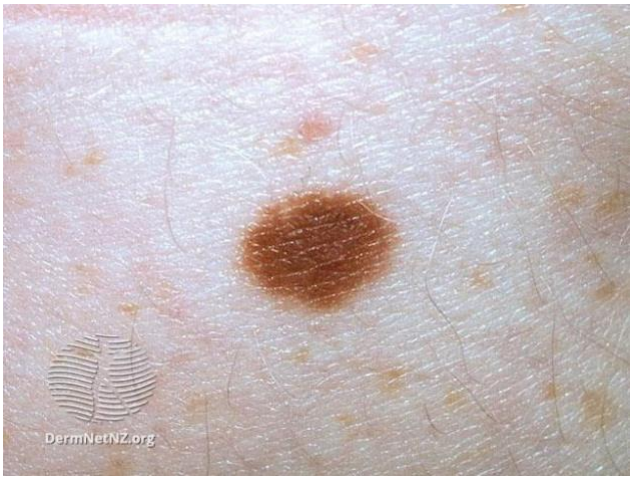


(Small Congenital Nevus)

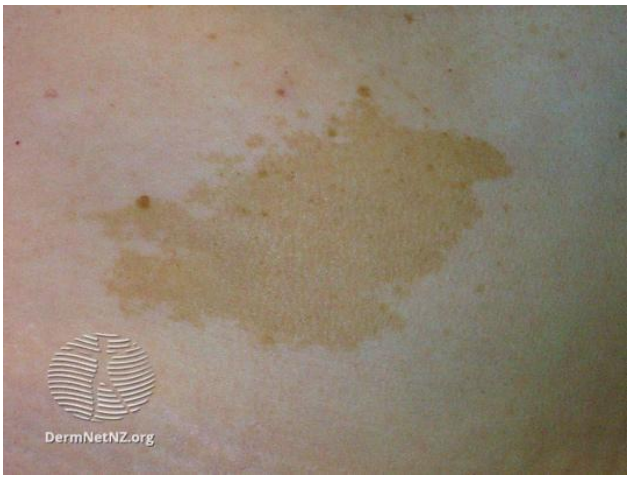
Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021



(Medium Congenital Nevus)

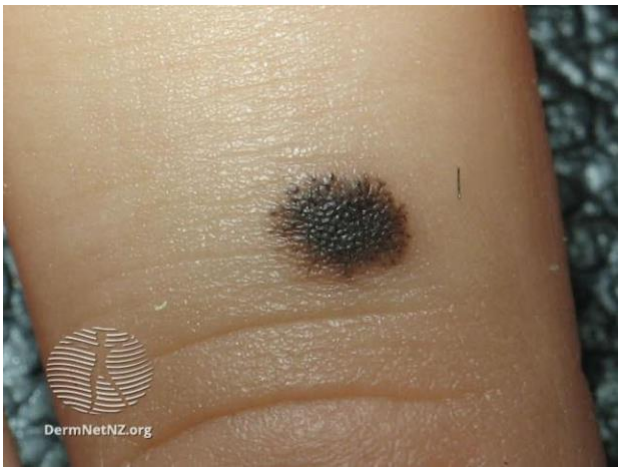


(Acquired Nevus)

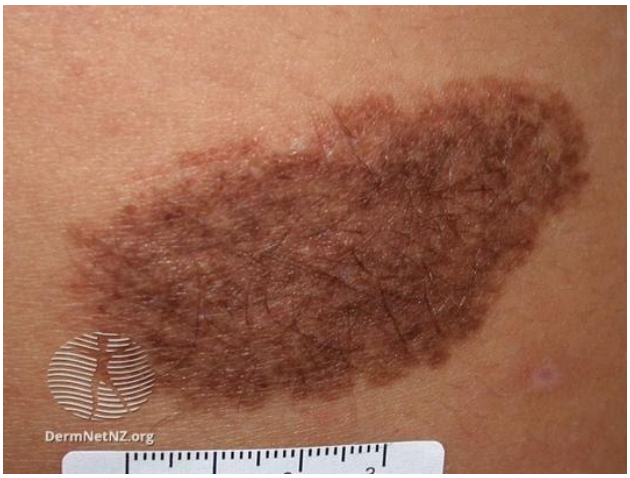


(Café-au-lait Macule)

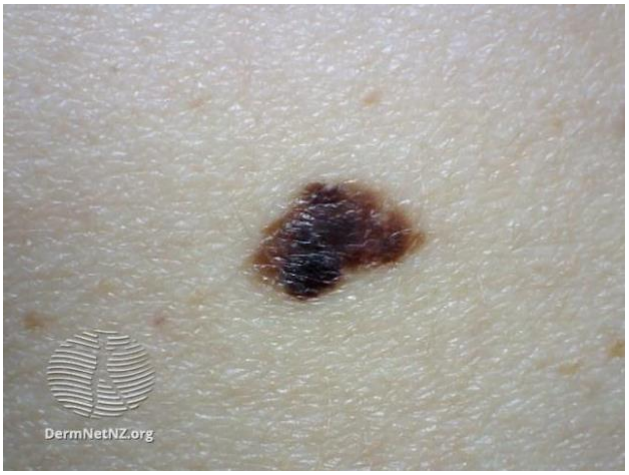
Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021



(Reed Nevus)

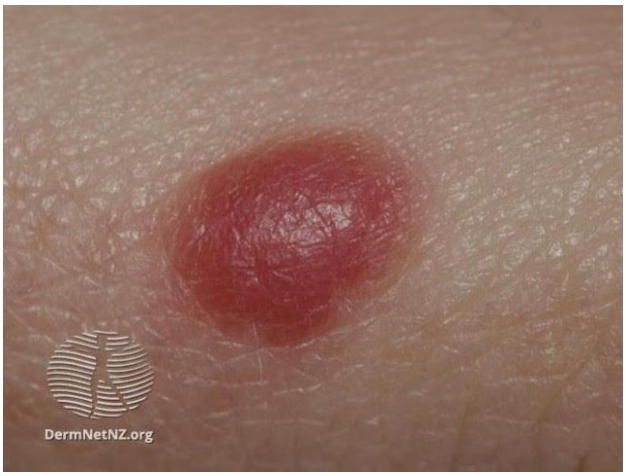


(Congenital Melanocytic Nevus)

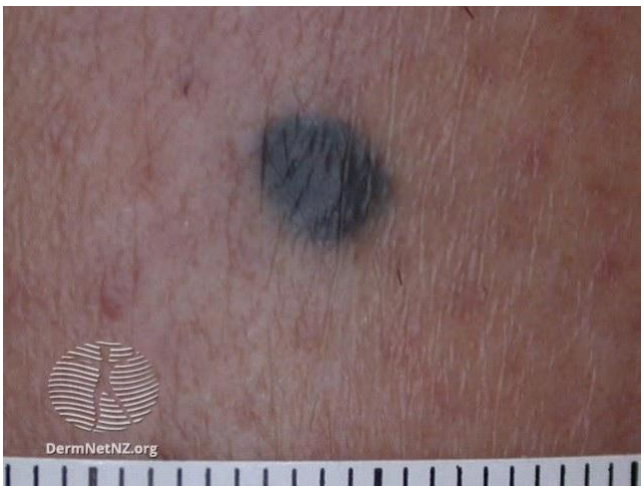


(Atypical Acquired Melanocytic Nevus)

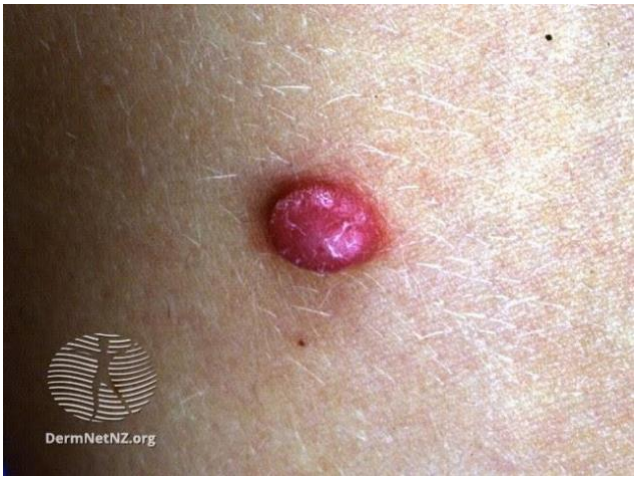
Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021



(Spitz Nevus)



(Blue Nevus)



(Pyogenic Granuloma)

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

Pigmented Ocular Lesions

Before we discuss pigmented ocular lesions, we'd like to acknowledge that they are a small fraction of ocular diseases that have been linked to ultraviolet radiation. Acute exposures, due to the high intensity sun exposure or arc welding, can lead to photokeratitis. Over time, UV exposure can lead to droplet keratopathy, cataracts, pterygiums, and ocular malignancies. The Beaver Dam Eye Study, which examined the incidence of macular degeneration over 15 years, showed an association with childhood ultraviolet radiation exposure and the development of macular degeneration.

Pigmented lesions can occur on a number of ocular structures, including the conjunctiva and uveal tract. A pigmented lesion on the conjunctiva could be a nevus, primary acquired melanosis (PAM), complexion-associated melanosis (CAM) or malignant melanoma.
While this podcast is focused on anterior segment pigmented lesions, we will briefly discuss pigmented lesions of the posterior segment. The uveal tract consists of the choroid, ciliary body, and iris. A pigmented lesion of the uveal tract could be a nevus, Lisch nodules, melanocytoma, congenital hypertrophy of the retinal pigment epithelium or melanoma.

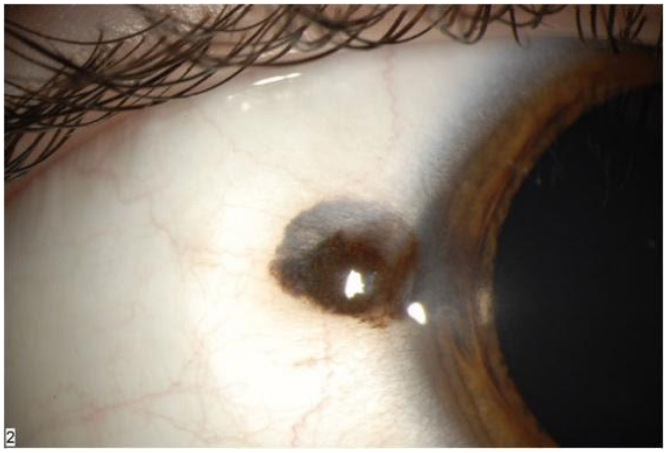
Assessing Pigmented Ocular Lesions

Patients should be asked when they first noticed the lesion, any changes they have noticed with the lesion, their sun exposure history, and their person and family history of any skin cancers.
A thorough slit lamp exam by an ophthalmologist is important to characterize the lesion. The lesion's shape, colour, size, thickness and location are important in determining the diagnosis and prognosis. It's particularly important to evert the eyelids to ensure no lesions are missed.
Additional tests, such as optical coherence tomography (OCT) and ultrasound may be needed to further characterize the lesion, such as its depth.

Ocular Nevus

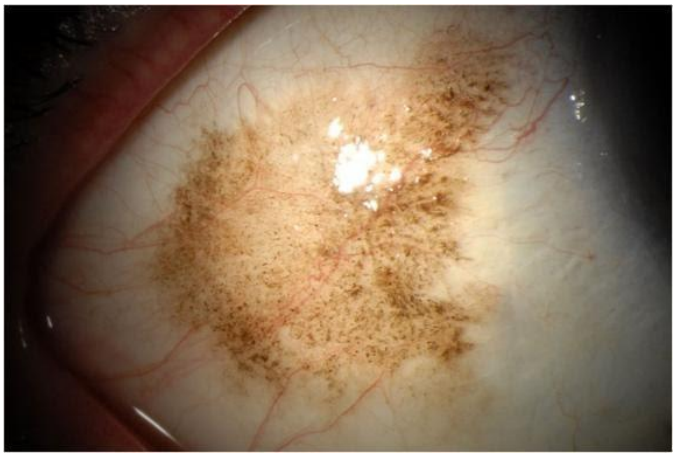
Nevi are common, benign conjunctival lesions, and are the most common conjunctival lesion. Just like skin nevi, conjunctival nevi may be junctional, compound or subepithelial. On examination, they are mobile over the sclera, and appear cystic, with well-circumscribed margins. Typically, they are unilateral, at the interpalpebral fissure, and at the limbus. Their colour can range from pale yellow to dark brown. They are relatively stable throughout life, but may darker with puberty or pregnancy, giving the appearance of growth. If the nevus is stable, it should be monitored every 6-12 months and photographs should be taken at each point. More frequent examination is required if the nevus is changing. Enlargement, colour changes or increases in vascularity should prompt evaluation and possibly removal. Each nevus carries a <1% chance of evolving into melanoma.

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021



Primary Acquire Melanosis (PAM)

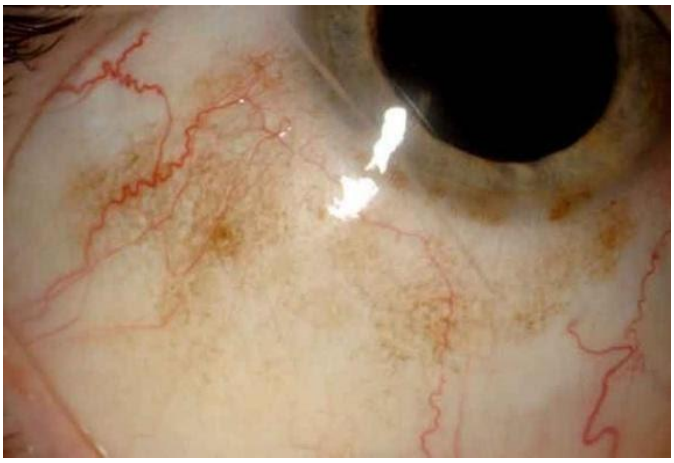
PAM is most common in fair-skinned middle-aged or older patients, and very uncommon in young patients. It appears as a flat, unilateral patch of yellow to brown pigment. On exam, they are flat, diffuse and not well-circumscribed. Typically, they are unilateral, and may have a waxing and waning nature of their size and pigment. Small lesions less than two clock-hours should receive yearly follow up. Concerning features include increased nodularity, vascularity, and thickening, for which a full excisional resection should be done. Larger lesions and lesions with cellular atypia require wide excision with cryotherapy, with a 4-5mm margin. Mitomycin C is often used as adjuvant chemotherapy. Depending on the cellular atypia, up to 50% may evolve into melanoma.



Complexion-Associated Melanosis

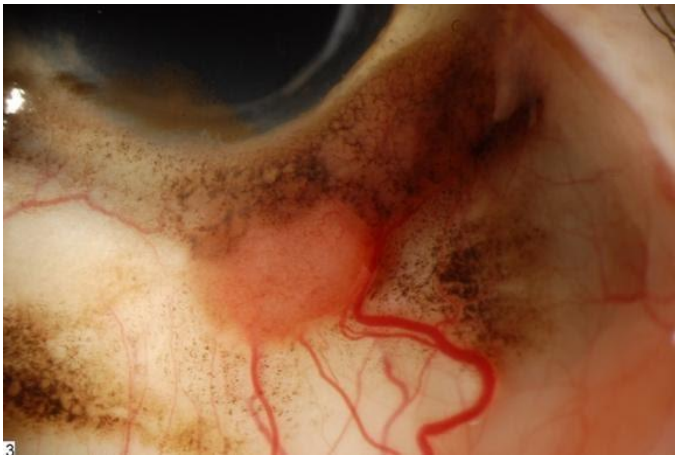
CAM, also known as racial melanosis, is a benign lesion in people with deeper skin colours. It is most common around the limbus and appears flat and noncystic on exam. It is often bilateral and increases with age. While CAM does not become melanoma, people with deeper skin colours are not immune to melanoma and should have yearly surveillance.

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021



Conjunctival Melanoma

Malignant melanoma of the conjunctiva may arise de novo, from a nevus, or from primary acquired melanosis. It is most common at the limbus, though non-limbal lesions, such as those in the caruncle, tarsus and fornix, carry a worse prognosis. It often appears as an elevated lesion with vascularity.



Uveal Nevus

Uveal nevi usually appear as flat or elevated lesions with variable pigment, and they should be observed lifelong with photographs. Iris freckles are superficial lesions that have no elevation or distortion. They are typically nonprogressive, though malignant transformation is possible and rare.

Melanocytoma of the Optic Nerve

Melanocytoma of the optic nerve is a darkly pigmented congenital tumor over at least part of the optic nerve. It occurs with equal frequency across all races.

Lisch Nodules

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

Lisch nodules are small, well-defined nodules in patients with neurofibromatosis-1. They usually become apparent by age 5. Approximately 85% of uveal melanomas are within the choroid posterior to the equator of the globe, while the rest occur within the anterior choroid, iris, and ciliary body.

Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE)

CHRPE is typically flat, well-circumscribed, and pigmented. Sometimes within the lesion are depigmented lacunae with pale haloes. It may be solitary or grouped in a 'bear tracks' pattern. Four or more of these lesions in a patient is linked to adenomatous polyposis of the colon or Gardner's syndrome. Malignant transformation of CHRPE lesions has been reported previously.

Uveal Melanomas

Uveal melanomas appear as pigmented or nonpigmented lesions. They typically present during adolescence. Iris melanomas usually at least 3 mm in diameter and 1 mm thick, and usually in the inferior half of the iris and associated with blood vessels. The pigment is often variable and the tumor progresses slowly. Most advanced tumors are treated with enucleation, while radiotherapy and local resection may be used for smaller, less advanced tumors.

Treatment for Cutaneous Melanoma

Similar to adults, the first-line treatment for pediatric melanoma is a wide local decision to the deep fascia. The margin size of excision is less defined in pediatric patients but mostly depends on the depth of invasion and the location of the tumor. Lymphatic mapping and sentinel lymph node biopsy (SLNB) are controversial in pediatric melanoma and the clinical decision should be made on a case-by-case basis. Adjuvant therapy has been used for localized disease with high risk of metastasis and systemic therapy for advanced melanoma. However, the data is very limited regarding their efficacy.

Treatment for Ocular melanoma

Conjunctival lesions that appear suspicious for ocular melanoma require an incisional biopsy to prevent tumor seeding. Once melanoma is confirmed, excision with a dry, no touch technique and 4-6 mm margins is the standard of practice. Afterwards, a double cycle of cryotherapy is applied to the margins, and alcohol is used to debride abnormal corneal cells. Sclerotomy may be needed when the lesion involves underlying sclera. A 4-6mm tumor-free margin is required. For melanomas greater than 2 mm or with high-risk features, sentinel lymph node biopsy is needed. De novo melanomas have the worst prognosis, and local recurrence is quite common.

Uveal melanomas have historically been treated with enucleation, though recent advancements have now allowed treatment with proton beam or plaque brachytherapy to be reasonably effective. However, vision loss or decreased vision continue to be side effects.

Case

Now we have reviewed pigmented lesions. Let's go back to the case to see what we would recommend for our patient Lucy. To recap, Lucy is a 17-year-old girl who presents with a 4 x 3

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

mm symmetric, oval shaped papule with irregular but well-demarcated border on her right lower eyelid, and a 1 x 1 mm darkly pigmented cystic lesion on the right temporal conjunctiva at the limbus. There are no lesions on direct ophthalmoscopy.

For the skin lesion, it was present at birth and had been gradually increasing in size until about 3 to 4 years ago, with no change in border or shape of the lesion. Otherwise, asymptomatic. As you may already guessed, the skin lesion described is most likely congenital melanocytic nevus. Most congenital melanocytic nevi have irregular borders as in the case for Lucy. However, it is important to know that irregular border might be a concerning feature for an acquired nevus, so you should always confirm if a pigmented lesion was present at birth. For Lucy's skin lesion, its increase in pigmentation and size proportional to her growth until the end of puberty is a part of its natural course. The pediatric ABCD and CUP criteria are negative for the lesion. The risk of melanoma in the future is also low given its size.

Similarly, the eye lesion was also present at birth with some noticeable hyperpigmentation with no change in size. Based on the history and physical examination, the most likely diagnosis is also congenital melanocytic nevus. The risk of ocular melanoma is low, but you should carefully photograph the lesion and book a 6-12 month follow up appointment. You refer Lucy to an ophthalmologist for a comprehensive eye exam to ensure there are no other lesions involving the anterior and posterior segments of the eye. You counsel the patient on continuing to use sun protection, and returning if there are concerning signs, such as bleeding, ulceration, pain, and so on. Lucy and her mother are grateful for your expertise and thank you for your time.

Take Home Points

We hope you found our podcast helpful and learned something new. Here are some quick take home messages for you:

1. Pigmented lesions on the eye and skin should be observed carefully and biopsied if there are high risk features or changes.
2. Pediatric melanoma is rare and can have atypical presentations, especially in prepubertal children. The pediatric ABCD and CUP criteria could be used clinically for skin lesions.
3. A thorough eye exam with photographs should be performed by an ophthalmologist to characterize each lesion and ensure there are no other concerning eye lesions.

This concludes our discussion. Thank you for listening to PedsCases Podcasts!

References

Balzer BW, Cherepanoff S, Joshua AM, Giblin M, Conway RM, Anazodo AC. Conjunctival Melanoma in Childhood and Adolescence: A Systematic Review. Ocular oncology and pathology. 2019;5(6):387-95.

Bartenstein DW, Kelleher CM, Friedmann AM, Duncan LM, Tsao H, Sober AJ, Hawryluk EB. Contrasting features of childhood and adolescent melanomas. Pediatric dermatology. 2018 May;35(3):354-60.

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021

Cordoro KM, Gupta D, Frieden IJ, McCalmont T, Kashani-Sabet M. Pediatric melanoma: results of a large cohort study and proposal for modified ABCD detection criteria for children. Journal of the American Academy of Dermatology. 2013 Jun 1;68(6):913-25.

Herwig, M. and Wells, J., 2020. Conjunctival Melanocytic Tumors - Eyewiki. [online] Eyewiki.aao.org. Available at: <https://eyewiki.aao.org/Conjunctival_Melanocytic_Tumors>

Howman-Giles R, Shaw HM, Scolyer RA, Murali R, Wilmott J, McCarthy SW, Uren RF, Thompson JF. Sentinel lymph node biopsy in pediatric and adolescent cutaneous melanoma patients. Annals of surgical oncology. 2010 Jan 1;17(1):138-43.

Navid F, Furman WL, Fleming M, Rao BN, Kovach S, Billups CA, Cain AM, Amonette R, Jenkins JJ, Pappo AS. The feasibility of adjuvant interferon α-2b in children with high-risk melanoma. Cancer. 2005 Feb 15;103(4):780-7.
Paller A., Mancini AJ, Hurwitz S. Hurwitz clinical pediatric dermatology: A textbook of skin disorders of childhood and adolescence. New York: Elsevier/Saunders, 2011. Chapter 9.

Paller A, Mancini AJ, Hurwitz S. Hurwitz clinical pediatric dermatology: A textbook of skin disorders of childhood and adolescence. 5th ed. New York: Elsevier/Saunders; 2016.

Paradela S, Fonseca E, Prieto VG. Melanoma in children. Archives of pathology & laboratory medicine. 2011 Mar;135(3):307-16.

Sayyad FFE, Karp CL. Conjunctival Pigmented Lesions: Diagnosis and Management. AAO EyeNet Magazine. 2013 Sep; 35-36.

Shields CL, Shields JA. Tumors of the conjunctiva and cornea. Survey of ophthalmology. 2004 Jan 1;49(1):3-24.

Shields CL, Sioufi K, Alset AE, et al. Clinical Features Differentiating Benign From Malignant Conjunctival Tumors in Children. JAMA Ophthalmol. 2017;135(3):215–224.

Shields CL, Swathi K, Sruthi ABA, et al. Uveal Melanoma in Children and Teenagers. Saudi J Ophthalmol. 2013 Sep;27(3):197-201

Shields JA, Eagle RC Jr, Shields CL, Brown GC, Lally SE. Malignant transformation of congenital hypertrophy of the retinal pigment epithelium. *Ophthalmology*. 2009;116(11):2213-2216. doi:10.1016/j.ophtha.2009.04.048

Silverberg NB, McCuaig CC. Melanoma in childhood: changing our mind-set. Cutis. 2013 Nov;92(5):217.

Gandini S, Sera F, Cattaruzza MS, Pasquini P, Abeni D, Boyle P, Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. European journal of cancer. 2005 Jan 1;41(1):28-44.

Wills Eye Hospital. 2020. Conjunctival Primary Acquired Melanosis | Wills Eye Hospital. [online]

Developed by Jennifer Ling and Dr. Harry (Chaocheng) Liu for PedsCases.com.
Published Feb 7, 2021