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### **Approach to Pediatric Vitiligo**

Developed by Dr. Harry Liu, Sara Choi, and Dr. Wingfield Rehmus for PedsCases.com.

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### **Introduction:**

Welcome to “Approach to Pediatric Vitiligo”, a podcast made for PedsCases.com at the University of Alberta. I am Dr. Harry Liu, a dermatology resident doctor at the University of British Columbia, and I am Sara Choi, a medical student at the University of British Columbia. This podcast will provide an organized approach to understand pediatric vitiligo, a very common pediatric skin condition. We would like to thank Dr. Wingfield Rehmus for developing this podcast with us! Dr. Rehmus is a pediatric dermatologist from BC Children’s Hospital and also a professor in the Department of Dermatology and Skin Science at the University of British Columbia in Vancouver, Canada.

### **Learning Objectives**

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

- 1) Describe the typical clinical presentation of pediatric vitiligo including key features on history and physical examination
- 2) Discuss the underlying pathophysiology of vitiligo and recall its common subtypes
- 3) Generate a differential diagnosis for pediatric vitiligo
- 4) Discuss the psychosocial impact of vitiligo
- 5) List available resources for patients
- 6) Review various treatment modalities for pediatric vitiligo and determine the factors that may influence treatment choice

### **Case**

Let’s start our discussion with a case. You are a third-year medical student on your pediatric outpatient rotation. Your first patient of the day is Anika who is a 6-year-old girl and a new immigrant originally from Nigeria. Anika’s mother tells you that Anika started having some white

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spots on the dorsal aspects of her hands and jaw about 8 months ago. They did not seek medication attention because Anika was completely asymptomatic without pain or itchiness. Before the rash started, the family was going through a lot of stress with moving to a new country. However, there is no history of skin infection or trauma. Over the past 2 months, the size of those spots has significantly increased. The white spots are very noticeable with Anika's darker complexion. Her mother is extremely worried that they could spread to the rest of the body. She is worried about how Anika will be treated at school since she is going into Grade 1 in a few months.

Upon further history, Anika has no family history of similar skin findings, but her mother has Type 1 diabetes and hypothyroidism from Hashimoto's thyroiditis. Anika is otherwise healthy with a normal birth history, she met all her developmental milestones and is not taking any medications.

On skin examination, there are irregularly shaped, sharply demarcated, milky-white, non-erythematous, and non-scaly patches with convex border lateral to the lower vermilion border, one on each side and symmetrically distributed. The texture of her skin has not changed. The patches on the dorsal aspects of her hands share the same morphology. You do a complete skin examination and do not find other lesions. The rest of the physical examination is also unremarkable. The total area of the rash you estimate is about 2% of total body surface area (TBSA). Being a very astute medical student, you believe that Anika could have vitiligo!

### **Epidemiology and Risk Factors**

Vitiligo is the most common cause for depigmentation and it affects 0.1 to 2.0% of the general population. The prevalence of vitiligo increases with age, and one half of cases will present before the age of 20. The peak incidences are in the second and third decade of life. However, it is important to recognize that vitiligo has no predilection towards a specific gender or ethnicity.

The cause of vitiligo is multifactorial and it is associated with multiple risk factors. First, vitiligo is a polygenic condition and there are approximately 36 gene loci associated with vitiligo involved in melanin biosynthesis and immune regulation or apoptosis. Therefore, a positive family history and the presence of other autoimmune diseases including autoimmune thyroid disease, alopecia areata, psoriasis, and inflammatory bowel disease, are significant risk factors. Vitiligo is also associated with rare genetic conditions in some cases.

The concordance rate of only 23% in monozygotic twins highlights the presence of other non-genetic or environmental factors. Patients have reported associated events before the onset of disease, including physical illness, skin trauma (called Koebner phenomenon), sunburn, or even emotional stress which is relevant for Anika as she was moving from Nigeria to Canada. In adults, pregnancy can also be another triggering event.

## **Pathogenesis**

The current understanding is that there are multiple mechanisms contributing to the development of vitiligo, with autoimmunity being the most important one.

Vitiligo is classified as an autoimmune condition in which predominantly autoreactive cytotoxic CD8+ T-cells target melanocytes which produce melanin, a dark pigment responsible for skin color. Studies have shown an increased level of cytokine expression (TNF-alpha, IL-10, IL-17 and interferon gamma) in depigmented skin areas which further support the role of immune system in vitiligo.

## **Clinical Presentation and Diagnosis**

Vitiligo is a heterogeneous condition that can have variable presentations. The most common initial presentation is flat white macules and patches in periorificial areas including the mouth, eyes, nostrils, umbilicus, and genital area. The macules and patches appear milky white with well-defined convex borders, surrounded by normal skin. **It is important to note that vitiligo may show more than one shade of color. Although the location, size, and shape of depigmentation vary, it is often bilateral and asymptomatic. Depigmentation defines total loss of melanin caused by melanocyte destruction, whereas hypopigmentation defines partial loss of melanin pigment.** It can sometimes be challenging to clinically differentiate depigmentation from hypopigmentation in patients with pale skin. However, there are tools, like Wood's lamp, that we can use to aid in diagnosis (which will be discussed later). Besides color change, inflammation is rare therefore should not be associated with changes in skin texture. Other commonly affected sites include extensor surfaces, sun-exposed areas and areas of frequent cutaneous trauma such as the elbows, knees and shins (Koebner phenomenon as mentioned earlier). Areas of depigmentation can expand overtime. Leukotrichia (depigmented hairs) can also be seen in the affected skin, which is a poor prognostic sign.

Vitiligo can be broadly classified into non-segmental and segmental vitiligo. Non-segmental vitiligo is more common and comprises 80% of total cases. The classifying feature being that the white patches of depigmentation are seen all over the body and often in a symmetrical pattern. Non-segmental vitiligo is further broken down into five subcategories.

- 1) Generalized vitiligo involves symmetrical and bilateral depigmented patches of skin in multiple areas of the body. Onset usually before age 30.
- 2) Acral or acrofacial vitiligo defines a pattern of lesions that are on the face or at distal extremities.
- 3) Focal vitiligo refers to isolated area of skin depigmentation.
- 4) Mucosal vitiligo indicates an involvement of the oral or genital mucosa.
- 5) Universal vitiligo defines cases in which there is almost complete depigmentation of over 60-90% of the body.

Segmental vitiligo often presents in childhood and is classified as asymmetrical and distributed in a true or pseudo dermatome pattern, most commonly along the distribution of the trigeminal nerve. Segmental vitiligo is unique in the case that the isolated areas of depigmentation stop growing within one year and the risk of expansion is low. It is essential to recognize and identify different types of vitiligo because it may alter the course of management.

Vitiligo is usually a clinical diagnosis with proper history and characteristic morphology. A Wood's lamp emitting UVA light at 365 nm wavelength can be used to confirm the diagnosis, especially useful for patients with pale skin. You will see vitiligo lesions fluoresce blue and white with well demarcated borders. It will be helpful to physically demonstrate this to patients and make sure they are aware that the same phenomenon will occur when they are under blacklight in different settings including glow-bowling, laser tag, and so on.

Under dermoscopy, you might see residual perifollicular pigmentation and telangiectasia in the depigmented area. A skin biopsy is not routinely done but can be performed to differentiate vitiligo from other depigmentation conditions if necessary. If laboratory confirmation is needed, you want to biopsy the border of the lesion to include both normal and depigmented skin. Biopsy for vitiligo will reveal complete absence of melanocytes and the loss of melanin pigment. Furthermore, immunohistochemistry will show increased CD8+ staining in lesional areas.

Approximately 15-25% of patients with vitiligo are affected by at least one other autoimmune condition. Screening for thyroid disease is recommended for all patients due to its prevalence. It is important to watch out for symptoms of other associated autoimmune disease including pernicious anemia, Addison's disease and Type I Diabetes.

There are significant psychological impacts associated with vitiligo. Patients may experience stigmatization and isolation, which significantly impact the patient's quality of life. It is important to consider and explore the psychosocial impacts of vitiligo at the time of diagnosis with regular follow up onwards. This will be discussed in the later sections.

### **Differential Diagnosis**

Although vitiligo is the most common diagnosis for white macule/patch, there is a list of differential diagnoses you need to consider. We will talk about them one by one.

- **Nevus depigmentosus** is a congenital hypopigmentation condition. Associated skin lesions are nonprogressive and benign and usually present at birth.
- **Pityriasis alba** presents with hypopigmented areas that appear to have a scaly texture. Most lesions are found on the face but sun-exposed areas are also commonly affected sites.

- **Post-inflammatory hypopigmentation** is acquired after inflammation or trauma to the skin. There is a temporary decrease in pigmentation in these areas due to melanocyte damage or changes in melanin production. Abnormal pigmentation can occur after wound healing as scar repigmentation is unpredictable.
- **Scars**, especially from chronic excoriation can sometimes become depigmented due to the constant physical trauma to melanocytes. This can be delineated from the history.
- **Halo nevus** is a melanocytic nevus (commonly known as a mole) that is surrounded by a round or oval area of depigmentation.
- **Tinea versicolor** presents with pale scaly macules caused by superficial yeast infections. Tinea versicolor often presents in the chest and upper trunk. The rash has seasonal variation and is exacerbated by sweat. Under a Wood's lamp, the skin areas will appear golden yellow.
- **Piebaldism** is a rare congenital depigmentation disorder. It is characteristic for localized midline depigmentation on the forehead and the forelock (which is the hair just above the forehead).

## Management

Before discussing treatment options, it is very important to know there is no cure for vitiligo and the main goals of treatment are to slow down progression, promote repigmentation and minimize the visible changes in skin color. It is very important to have an honest discussion with the patient about the nature of the disease and their expectations so you can work together to determine what is the most optimal treatment option. Some patients may choose to not treat vitiligo.

Most cases of pediatric vitiligo are managed by family physicians. However, a dermatology referral should be considered in the following cases:

- Diagnosis in question.
- Family physician does not have sufficient experience to treat vitiligo.
- Rapidly progressive disease.
- Significant involvement of TBSA.
- Lack of satisfactory response to treatment after a reasonable amount of time (usually 3 months).

Now let's move on to the discussion of what treatment options are available for vitiligo.

## Patient Education

A diagnosis of vitiligo can have significant lifelong impact on patients as it is associated with increased stigma and significant emotional and psychological distress. Patients may experience shame, low self-esteem and social isolation. Putting the condition into cultural context, some cultures believed it was a form of punishment or white leprosy. It is important to recognize and

acknowledge the possibility of psychosocial impact when planning management. Going back to our case, Anika's mother is already worried about how the condition can impact her general well-being. As Anika has a darker skin complexion, depigmented lesions will be more noticeable than in a patient with lighter complexion. It is more important to discuss the implication of the diagnosis and connect them with patient advocacy and support programs. Some of them include:

- Changing Faces (<https://www.changingfaces.org.uk/>) is the UK's leading charity for everyone with a scar, mark, or condition on their face or body that makes them look different.
- Vitiligo Support International (<https://vitigosupport.org/>) is a patient driven nonprofit organization offering a comprehensive resource of vitiligo education, research, and awareness for those whose lives have been affected by vitiligo.
- Vitiligo Research Foundation (<https://vrfoundation.org/>) is a registered non-profit organization, funding fast-tracking medical research globally to develop effective treatments for millions of people around the world who suffer from vitiligo.

There has been increased exposure and awareness of vitiligo in current media. For example, Canadian fashion model Winnie Harlow is recognized internationally as a vocal advocate of body confidence. She frequently provides honest and inspiring accounts of living with vitiligo. This can be very powerful story to be shared with teenage patients and their caregivers.

### Sun protection

First and foremost, sun protection or sun avoidance is crucial. Melanin serves an important photoprotective role against DNA-damage by absorbing ultraviolet (UV) radiation. Thus, depigmented areas of skin are at higher risk for sunburn and skin cancer. Additionally, sun protection prevents increased pigmentation of unaffected area and thus reduces the contrast between affected and unaffected skin. Sunscreen, sunglasses, hats, and clothing protection are effective methods of sun safety. Broad spectrum sunscreens with a high sun protection factor (SPF) of at least 30 is strongly recommended for patients with vitiligo. It may seem counterintuitive, but a little bit of sun can actually be helpful in stimulating repigmentation in lesional areas. When prescription light source is not available for treatment, some physicians may recommend sunlight. However, the overall risk of skin cancers with sun exposure still outweighs its benefit and it is important to educate patients about sun protection.

### Cosmetic makeup and camouflage

There are various cosmetic camouflage products on the market such as Dermablend or Covermark. Products range from self-tanners containing dihydroxyacetone (DHA) to concealers to highly pigmented creams and powders. DHA-based products can provide lasting color up to several days. Cosmetic camouflage is offered in a wide array of shades and colors to match the patient's natural skin color. It is important to note that these methods are temporary and must be reapplied frequently. Some cosmetic camouflages wash away with water, perspiration and have the potential to stain clothing. Parents and children should be encouraged to learn proper

techniques of cosmetics application if it is something that they are interested in. This could be a great option for our patient Anika because her lesions are present in exposed areas including her face and hands.

### Topical Therapies

Topical therapy is the first-line therapy for vitiligo involving < 10% of TBSA, specifically localized non-segmental stable vitiligo and segmental vitiligo. The main classes of topical medications include mid- to high-potency topical steroids and topical calcineurin inhibitors. They aim to repigment the affected areas via modulation of the immune system. The frequency and duration of therapy should be individualized. Some common regimen includes clobetasol applied twice daily for two months, stopped for the following two months and then repeated on a cycle. Side effects include thinning of skin, mild atrophy, telangiectasia, folliculitis, or even hypertrichosis. On the other hand, for tacrolimus which is a calcineurin inhibitor blocking the activation of T cells, it can be applied continuously twice a day until satisfactory outcome has been reached. Calcineurin inhibitors are preferred for the face, neck and groin, and areas where adverse effects are more common with topical steroids. It is important to note that repigmentation is a slow process and commonly originates from the hair follicles as there is a reservoir of melanocytes in this location. This also explains why leukotrichia is a poor prognostic sign. Repigmentation from treatment will often look uneven and speckled. Make sure to explain this to patients and their caregivers so they have realistic expectations of the treatment regimen.

### Phototherapy (UVB) Ultraviolet light

Phototherapy (most commonly narrowband UVB) involves exposing the patient's skin to controlled UV light on a 2-3 times weekly basis for a trial of several months. If repigmentation is noted, UVB therapy can be continued for 1-2 years. It is considered first line therapy for older pediatric patients with extensive vitiligo (10-40% TBSA) as it helps with both the repigmentation and stabilization of disease. The clinical course of vitiligo can be unpredictable. Stabilization is especially important as it gains control of the condition at its early stages before widespread distribution occurs. Therefore, UVB is considered a cornerstone treatment for vitiligo. In addition, phototherapy can also be used in disseminated disease and localized recalcitrant vitiligo. Treatment is well tolerated in older children, but side effects may include erythema, pruritus and phototoxicity. The 308-nm excimer laser provides targeted laser treatment for localized vitiligo. To our knowledge, there is currently little evidence in support of laser over phototherapy, but it could alter the course of treatment of vitiligo in the future.

### Systemic Therapy

Low dose oral steroids including prednisolone, betamethasone, and dexamethasone can be used in the stabilization of rapidly worsening disease, but the current evidence is limited. It is not a repigmentation therapy therefore it is often used in combination with narrow band UVB therapy.

Since vitiligo is difficult to treat and can have significant impacts on patients, it is not uncommon to see caregivers seeking complementary and alternative therapies, including vitamins, alpha-lipoid acid, Ginkgo biloba, or Polypodium leucotomos. However, the current evidence for those therapies are very limited. An open discussion of the potential risks and benefits of those therapies with patients and their caregivers is very important.

### **Surgical Grafting**

Autologous skin grafting is a surgical therapy in which a skin tissue graft is transferred from an unaffected area of the body to the site of vitiligo. There are various grafting techniques including tissue and cellular grafting. Complications include cobblestoning of the skin graft, potential scarring, and pain. Surgical grafting is typically reserved for a specific cohort of patients. A suitable candidate would be a patient with stable and localized lesions (unchanged for 12 months) that have been resistant to other methods of therapy. It is often contraindicated in pediatric vitiligo because lesions are more likely to progress during childhood and there is a risk associated with general anesthesia in children, which would be required for this procedure in young children.

### **Psychological Impact**

There is strong evidence suggesting the association of vitiligo with anxiety, depression and other psychiatric conditions. Patients may face long-term social discrimination and be in constant fear of disease progression. These factors contribute to decreased quality of life and a significant psychosocial burden. Children, especially adolescents, should be screened for mood disorders and psychological symptoms and referrals to relevant specialists should be made when appropriate. In terms of treatment, psychotherapy, such as cognitive behavioral therapy, has shown to be effective at relieving the psychosocial stress. Counselling can also help patients better control their anxiety symptoms. The overarching goal is to improve patient quality of life and help build resilience.

### **Take Home Points**

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

- 1) Vitiligo is the most common depigmentation skin condition affecting 0.1-2.0% of the general population, with half of the cases presenting during childhood.
- 2) Vitiligo is an acquired autoimmune condition that leads to the destruction of melanocytes; the common risk factors include family history of vitiligo and other autoimmune conditions as well as other environmental factors like skin trauma, sunburn, and emotional stress.



- 3) There are many subtypes of vitiligo and the most common form is non-segmental vitiligo which presents with bilateral white patches of skin in many areas of the body and makes up 80% of total vitiligo cases.
- 4) The diagnosis of vitiligo can be made clinically with thorough history, skin exam, and Wood's lamp, and a skin biopsy is rarely required. It is important to screen for other autoimmune conditions and psychosocial impacts.
- 5) Treatment options for pediatric vitiligo include cosmetic camouflage, topical steroids or calcineurin inhibitor, phototherapy, oral steroids, and rarely surgical grafting.

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

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