Morphea

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Introduction

Hello everyone, and welcome to the podcast on morphea for PedsCases.com. My name is Amir Pourghadiri, and I am a fourth-year medical student at the University of British Columbia. My name is Jeffrey Toy, and I am a dermatology resident at the University of British Columbia. In this podcast, we will learn about morphea, an autoinflammatory sclerosing cutaneous disorder. We would like to thank Dr. Joseph Lam for developing this podcast with us. Dr. Joseph Lam is a pediatric dermatologist at BC Children's Hospital.

Objectives

After listening to this podcast, learners should be empowered to:

1. Define morphea and discuss its epidemiology.
2. Explain the pathogenesis of morphea through its three overlapping phases.
3. Classify the spectrum of sclerotic disorders that fall under morphea.
4. Discuss the clinical presentation, differential diagnosis, and extracutaneous manifestations of morphea.
5. Identify key management strategies for morphea.

Before we dive in, let's clarify some terminology. Morphea is another term for localized scleroderma. Systemic sclerosis (SSc), sometimes referred to as scleroderma, is a different entity that often involves internal organs. For simplicity, we will focus on pediatric morphea and use the term "morphea."

What is morphea?

Morphea is a group of autoinflammatory sclerosing cutaneous disorders affecting the dermis and hypodermis, and it can also impact muscles, joints, and bones (1). The prevalence varies, with recent studies estimating an annual prevalence of 3.2-3.6 per 10,000 children per year (2). Females are more commonly affected, with a ratio of 2.4-5:1 compared to males (3). The mean age of onset is 10 years for children and 45 years for adults (4). There's often a delay of about 1.5 years in diagnosing morphea, and disease activity usually stabilizes over five years, though certain subtypes like linear morphea may persist longer (5).

Genetic and Environmental Associations

The overall genetic picture of morphea is not well understood. However, certain human leukocyte antigen (HLA) class I and II alleles have been strongly linked to morphea, providing support for this disease as a distinct entity compared to systemic sclerosis (SSc) (6). Like other autoimmune and autoinflammatory conditions, morphea may be triggered by trauma, infections, drugs, vaccinations, and radiation therapy (7).

Pathogenesis

The underlying pathogenesis of morphea is constantly evolving with new studies. In general, the pathogenesis of morphea can be divided into three overlapping phases, referred to as the inflammatory, sclerotic, and atrophic phase (4). To summarize:

1. In the inflammatory phase, Th1/Th17 cells and pro-inflammatory cytokines like interferon-γ (IFN-γ), IFN-α, and TNF-α, damage blood and lymphatic vessels.
2. During the sclerotic Phase, there is a shift to a Th2-mediated response, leading to fibroblast proliferation and the release of profibrotic cytokines, such as IL-4, IL-6, and TGF-β. This results in increased collagen production, decreased collagen breakdown, and the differentiation of fibroblasts into myofibroblasts, causing skin tightening and sclerosis.
3. The molecular pathway of the atrophic phase is not well understood. However, atrophy within the dermis, hypodermis, and underlying muscle tissue has been reported (4,5,8).

Case

Before we dive further, let's start with a case to probe our thinking. The case presented in this podcast was adapted from the Pediatric Autoimmunity and Transplantation textbook (9).

Sarah is a 7-year-old otherwise healthy girl who presents with a 2-year history of slowly progressing skin changes on the right side of her face, and partial loss of her right eyebrow and right frontal scalp hair. She denies vision changes and neurologic symptoms. On physical examination, she has an elevation of her right upper eyelid, a poorly developed right nasal rim, and visible facial asymmetry. An atrophic, shiny white plaque extends from the right parietal scalp to the right nasal bridge. There were no signs of atrophy or similar skin changes in her extremities. CRP is in the normal range.

We will discuss the diagnosis near the end of the podcast!

Morphology

First, let's learn about morphology by revisiting the three phases of morphea:

- Early in the inflammatory phase, lesions are erythematous to violaceous patches or plaques, similar to a bruise, with color varying from pink to red, and violaceous or hyperpigmented in dark skin tones (4).

- In the sclerotic phase, lesions form a violaceous ring with a central induration or thickening that is yellow to white. These are more commonly observed clinically due to diagnostic delays (5).
- Lastly, in the atrophic phase, lesions appear shiny with visible underlying vessels, indicating epidermal atrophy, along with potential loss of hair follicles, adnexal structures, subcutaneous fat, and muscle (7).

Morphea Classification

Now that we have learned about describing lesions in various stages of morphea, let's briefly discuss how morphea is classified. According to the Padua classification scheme, Morphea can be categorized into five types: circumscribed/plaque, linear, generalized, pansclerotic, and mixed morphea (10). Linear morphea accounts for about 65% of cases, followed by circumscribed or plaque morphea at 26%, generalized morphea at 7%, and deep morphea, which affects subcutaneous tissue, at 2% (11). Mixed morphea presents with two or more subtypes and affects about 15% of patients (10,12).

Most of these categories can be further divided into subtypes depending on the anatomical region and extent of tissue involvement. We have included a table in our notes for your reference; however, in this podcast, we will focus on linear morphea, which is most prevalent in pediatric settings.

Subtypes of linear morphea can affect the extremities or the face. These lesions appear band-like and become progressively indurated, with varying degrees of involvement in the dermis, hypodermis, muscles, joints, and bone (4). Linear lesions frequently follow Blaschko's lines, which are developmental growth patterns of cells in the epidermis (13).

Linear morphea affecting the face is further categorized into *en coup de sabre* and progressive facial hemiatrophy. *En coup de sabre* translates to "the strike of a sword" due to the appearance of lesions. Sclerosis of lesions may be seen, or there may be indentations in the skin, indicative of atrophy. Lesions are primarily unilateral and can extend to the scalp, causing scarring alopecia (4). In contrast, progressive hemifacial atrophy has limited involvement of the dermis and epidermis, and primarily affects the regions below the subcutaneous tissue. Therefore, the two subtypes of linear morphea affecting the face are distinguished clinically by thickening in the overlying skin (1).

Extracutaneous Manifestations

Morphea can present with extracutaneous findings, with the most common affecting the musculoskeletal (MSK) system, followed by neurologic and ocular symptoms (14). MSK symptoms include limited range of motion and joint contractures (15,16). These findings are generally not associated with pain (15).

Ocular and neurologic symptoms have also been reported in linear lesions affecting the face (11,14,17). Important neurologic symptoms to note are headaches and seizures.

Differential Diagnosis

Early recognition of morphea is crucial to mitigating potential damage and atrophic features. Therefore, a comprehensive approach to the differential diagnosis of morphea will depend on the disease subtype and whether the disease is in the inflammatory, sclerotic, or atrophic phase. For this podcast, we will briefly review conditions that can mimic morphea.

An important differential diagnosis to consider is lichen sclerosus. Guidelines recommend examining the anogenital region in patients with morphea to screen for genital lichen sclerosus (1). Morphea may also be confused with juvenile idiopathic arthritis (JIA); however, these two conditions can be distinguished by assessing for pain, and if needed, ultrasound findings will show erosive joint disease in JIA, whereas morphea will mainly show fibrotic features (15). Lastly, certain morphea categories with greater tissue involvement may be mistaken for systemic sclerosis. Examining the digits for Raynaud's phenomenon, comparing the distribution pattern of skin lesions, and assessing for internal organ involvement will help distinguish these two conditions (18,19).

Diagnosis

The diagnosis of morphea is based on the 2019 Single Hub and Access point for pediatric Rheumatology in Europe or SHARE guidelines, which is commonly used in Canada (20). We will summarize some of the key recommendations.

Establishing a diagnosis of morphea is largely based on clinical grounds, and there are currently no diagnostic laboratory investigations. Acute phase reactants, such as ESR and CRP are often in the normal range.

Clinically, morphea can be assessed by examining the extent of body surface area involvement, erythema, skin thickness, and the appearance of lesions. These four criteria are useful for assessing the severity and activity of morphea lesions. If there are symptomatic joints, patients should be evaluated with a comprehensive joint examination at diagnosis and follow-up visits. Further, regardless of the presence or absence of neurologic symptoms, patients with linear morphea affecting the face or scalp should obtain a head MRI at the time of diagnosis.

Management

The treatment of morphea includes both topical and systemic therapies, and this choice largely depends on the level of tissue involvement. According to the 2024 S2K guidelines from Germany, for children with limited cutaneous involvement affecting the epidermis and dermis, daily high-potency corticosteroids for one month, or daily mid-potency corticosteroids for three months, is recommended (1). To enhance dermal penetration, occlusive therapy may be considered. If topical corticosteroids are not tolerated, 0.005% calcipotriol or 0.1% tacrolimus can be considered as an alternative to topical corticosteroids in the active phase of the disease.

Phototherapy modalities may be used as monotherapy or in combination with topical therapies. The conceptual basis of phototherapy as a treatment option is based on the anti-fibrotic and anti-inflammatory effects of phototherapy. Modalities for phototherapy include

UVA1, Psoralen combined with UVA (PUVA), and narrow-band UVB (NBUVB), which is most readily available in Canada.

In patients with morphea extending beyond the dermis, methotrexate is supported as first-line therapy. The guidelines recommend a treatment duration of at least one year after achieving remission. Due to potential hepatotoxicity, the Canadian Rheumatology Association recommends folate supplementation and screening patients for Hepatitis B and C, and HIV prior to initiating methotrexate (21). Methotrexate can be used as monotherapy or combination therapy with intravenous (IV) methylprednisolone or oral prednisone.

As you can see from the above, treatment for morphea is not curative. Given that this is an active area of research, newer agents may be available with ongoing clinical trials, so be sure to keep up to date with the literature and review guidelines for the latest therapies!

Sarah's case

Let's remind ourselves of Sarah's case:

Sarah is a 7-year-old otherwise healthy girl who presents with a 2-year history of slowly progressing skin changes on the right side of her face, and partial loss of her right eyebrow and right frontal scalp hair. She denies vision changes and neurologic symptoms. On physical exam, she has an elevation of her right upper eyelid, a poorly developed right nasal rim, and visible facial asymmetry. An atrophic, shiny white plaque extends from the right parietal scalp to the right nasal bridge. There were no signs of atrophy or similar skin changes in her extremities. CRP is in the normal range.

What is the diagnosis?

If you guessed *en coupe de sabre*, you are right! There is no sign of hemifacial atrophy, and the presence of sclerotic plaques suggests extensive involvement of the dermis, decreasing the clinical suspicion of progressive hemifacial atrophy.

This concludes our podcast. Here are some key points to take away from this podcast:

1. Morphea, also known as localized scleroderma, is an autoinflammatory sclerosing cutaneous disorder that affects the dermis and hypodermis and can extend to muscles, joints, and bones. Linear scleroderma is the most prevalent category in pediatric cohorts, and females are more commonly affected.
2. Morphea progresses through three overlapping phases: inflammatory, sclerotic, and atrophic phase. The inflammatory phase involves Th1/Th17 cells and pro-inflammatory cytokines, the sclerotic phase features a shift to a Th2-mediated response with increased collagen production, and the atrophic phase can cause atrophy of cutaneous and subcutaneous tissue.
3. Morphea can be categorized into five types: circumscribed or plaque, linear, generalized, pansclerotic, and mixed. Linear morphea is the most prevalent in pediatric cases and includes subtypes *en coup de sabre* and progressive facial hemiatrophy.
4. The diagnosis of morphea is clinical, with no specific diagnostic laboratory tests. The assessment involves examining body surface area involvement, erythema, skin

thickness, and lesion appearance. Imaging, such as head MRI, is recommended for patients with linear morphea affecting the face or scalp.

5. Treatment options depend on the level of tissue involvement and includes topical and systemic therapies. For limited cutaneous involvement, high-potency corticosteroids or mid-potency corticosteroids are recommended. Phototherapy can be used alone or with topical therapies. If there is extensive tissue involvement, Methotrexate is the first-line therapy.

Table 1- Classification of Morphea subtypes (10).

Category	**Subtype**	**Description**
Circumscribed or plaque morphea	Superficial	≤3 oval or round indurated, edematous, firm, and indurated plaques, measuring up to 3 cm, and limited to the epidermis and dermis. plaques are typically located on trunk and may also be present in the extremities.
	Deep	Single or multiple lesions extending into the subcutaneous tissue, fascia, with possible involvement of the muscles. In certain cases, there is only subcutaneous tissue inolvement without affecting the dermis and epidermis.
Linear morphea	Trunk/limbs	Linear indurations involving the dermis, subcutaneous tissue, and possible involvement of the muscle and bone.

	Head	*En coup de sabre* (ECDS): appearance of a “sword strike” in the forehead region. Linear induration affects the face and/or scalp, with potential involvement of muscle and bone. Progressive hemifacial atrophy (PHA): decreased tissue on one side of the face; may involve the dermis (limited), hypodermis, muscle, and bone.
Generalized morphea		≥ 4 coalescing plaques involving ≥ 2 of seven anatomical sites: head-neck, right & left upper extremity, right & left lower extremity, anterior & posterior trunk.
Pansclerotic morphea		Circumferential involvement of the extremities, affecting the dermis, subcutaneous tissue, muscle, and bone. Excludes external organs.
Mixed morphea		A combination of two or more subtypes.

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