TSC Alliance Webinar: What’s Facial Angiofibroma Associated With TSC and How Can It Be Managed
Housekeeping

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• Talk to your doctor about what treatment options might be right for you.

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• Nobelpharma America, LLC is sponsoring this event and has provided financial support for the speakers to participate

• Employees of Nobelpharma are attending and participating in this event

• Dr. Joyce Teng is a consultant for Nobelpharma America and a scientific advisor for the TSC Alliance
Today’s Agenda

• Welcome & Introductions – Eric Beresford, VP, Head of Medical Affairs at Nobelpharma America
• What Is Facial Angiofibroma Associated with TSC
• Social and Psychological Impact of Facial Angiofibroma
• Take Care of Your Skin
• What to Know About Treatments
• Q&A
What Is Facial Angiofibroma Associated with TSC
Social and Psychological Impact of Facial Angiofibroma
Take Care of Your Skin
What to Know About Treatments

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What is Facial Angiofibroma Associated with TSC
TSC Can Affect Any Organ System

TSC affects ~50,000 people in the US1-4:

- **Occurs in all races and ethnicities**
- **No variation** based on sex
- **Usually diagnosed in children and infants** (>50% of patients diagnosed by age 17 years)

**Brain**
- 90% epilepsy
- 80–90% SEN
- 10–15% SEG A
- 90% TAND
- 50% intellectual disability
- 40% autism spectrum disorder

**Heart**
- Infants
  - 90% cardiac rhabdomyoma
- Adults
  - 20% cardiac rhabdomyoma

**Kidney**
- 70% angiomyolipoma
- 35% simple multiple cysts
- 5% polycystic kidney disease
- 2–3% renal cell carcinoma

**Skin**
- 90% hypomelanotic macules
- 75–93% facial angiofibroma
- 23% to ~50% shagreen patches
- 15–80% ungual fibroma
- 25% fibrous cephalic plaques

**Other**
- 50% oral fibromas
- 50% retinal astrocytic hamartomas

**Lung**
- Women
  - 80% asymptomatic LAM
  - 5–10% symptomatic LAM, can lead to respiratory failure
- Men and women
  - 10% MMPH

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Education Purposes Related to the TSC Alliance Webinar Only
# Major and Minor Diagnostic Criteria

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
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<tr>
<td>Hypomelanotic macules (≥3; at least 5 mm diameter)</td>
<td>“Confetti” skin lesions</td>
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<tr>
<td>Angiofibroma (≥3) or fibrous cephalic plaque</td>
<td>Dental enamel pits (≥3)</td>
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<tr>
<td>Ungual fibromas (≥2)</td>
<td>Intraoral fibromas (≥2)</td>
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<tr>
<td>Shagreen patch</td>
<td>Retinal achromic patch</td>
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<tr>
<td>Multiple retinal hamartomas</td>
<td>Multiple renal cysts</td>
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<td>Multiple cortical tubers and/or radial migration lines</td>
<td>Nonrenal hamartomas</td>
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<tr>
<td>Subependymal nodule (≥2)</td>
<td>Sclerotic bone lesions</td>
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<tr>
<td>Subependymal giant cell astrocytoma</td>
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<tr>
<td>Cardiac rhabdomyoma</td>
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<tr>
<td>LAM*</td>
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<tr>
<td>Angiomyolipomas (≥2)*</td>
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*A combination of the 2 major clinical features LAM and angiomyolipomas without other features does not meet criteria for a definite diagnosis.

Facial Angiofibroma Is One of the Most Common Skin Conditions Associated With TSC

- Skin conditions appear in almost all (>90%) people with TSC
- Facial angiofibromas are benign tumors found on between 75% to 93% of people with TSC
  - Typically present as pinkish or reddish bumps on nose and cheeks
  - Usually develop at ages 2-5 years
  - Present in ~80% of TSC patients by the time they reach adolescence
  - Proliferate and grow in size gradually (to ≥ 3 mm in diameter)
  - Vary in color depending on fibrous tissue and blood vessel density
  - Presence of ≥ 3 tumors is one of major TSC diagnostic features
Social and Psychological Impact of Facial Angiofibroma
Impact of Facial Angiofibroma

Facial angiofibromas can bleed easily, become infected, and impair function.

They may also cause pain and, if left untreated, may result in disfigurement, and increased psychosocial distress.

These tumors may also be a psychological and social burden for people living with this condition.

Patients have reported that facial angiofibroma can have negative effects on appearance and self-image, causing some people to avoid social situations.
Significant Psychosocial Impacts of Acne Vulgaris

- Work/social situations
- Questions, concerns, and advice from others
- Developmental delays
- Fear of school
- Bullying
- Behavioral issues/adjustment disorders
- Confidence
- Appearance/self-image

In a study evaluating young adolescents with acne vulgaris:
- Moderate/severe experienced greater psychosocial and emotional impairment
- Body image modified proportionally to the severity of acne
- Girls and boys are equally affected
- Impact is proportional to severity
- More severe disease associated with greater effect on QoL with implications for:
  - Self-esteem
  - Body image
  - Relationships with others
Care Prevention of Facial Angiofibroma
Sun Exposure May Have a Role in the Development of Facial Angiofibroma

Increased sun exposure → AF development


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Sun Protection Is Important To Help Prevent Angiofibroma

Avoid mid day sun exposure
Wear protective clothing
Wide-brimmed hat
Wrap around sunglasses

Germline Mutation → Angiofibroma

Follow Guidelines and Use Sunscreen To Protect Yourself

https://www.aad.org/public/everyday-care/sun-protection

• Broad-spectrum (UVA/UVB protection)
• SPF 30 or higher
• Water resistance
• Barriers
  • Cost
  • Cosmetic elegance
  • Effectiveness

SPF 100+ sunscreen is more protective against sunburn than SPF 50+ in actual use: Results of a randomized, double-blind, split-face, natural sunlight exposure clinical trial

Williams et al. JAAD Vol 78, (5). May 2018, P 902-910, e2

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Sun Protection Is Critical for Children As Well

- Physical sunscreen in children 6-months to 2-years old
  - Safety concern
    - High body surface to body mass ratio
    - Immature skin with increase absorption
    - Increased skin sensitivity
- Other physical protection
  - Hats
  - Sun protective clothing
Treatment Options for Facial Angiofibroma
Challenges in the Diagnosis and Treatment of Facial Angiofibroma

• Who diagnoses? Who prescribes?
  • Pediatricians/neurologists often may be the first to see patients with TSC, and they may see patients more frequently. Therefore, they often collaborate with dermatologists to manage patients’ facial angiofibroma.
  • Dermatologists, especially pediatric dermatologists likely will be more up to date on potential treatment options and manage problematic or symptomatic facial angiofibromas.
  • Facial angiofibroma can be misdiagnosed as acne in young children and adolescents.
Treatment Considerations

• Age
• Severity
• Symptoms: i.e. bleeding
• Comorbid medical risks
• Newly suspected or diagnosed patients with TSC should be re-evaluated every six months

How well does it work?
How safe is the treatment?
Newly suspected or diagnosed patients with TSC: All patients should undergo a detailed dermatologic and dental exam to be evaluated for facial angiofibromas, fibrous cephalic plaques, and hypomelanotic macules or confetti lesions.

For already diagnosed patients with definite or possible TSC: Provide ongoing education on sun protection. Watch for improvement in skin lesions over several months. If lesions do not improve, or if earlier intervention is indicated, then consider use of surgical approaches. For protuberant lesions, consider surgical approaches (e.g., excision, lasers). Skin lesions that are smaller and flatter appear to respond better to topical sirolimus than bulky lesions, so early treatment is recommended. For flat or minimally elevated lesions, topical mTOR inhibitor treatment is recommended.

Treatment Received by People With Facial Angiofibroma

![Bar chart showing the proportion of patients receiving different treatments.]

- **No Treatment:** 45.2%
- **Topical mTOR Inhibitor:** 24.8%
- **Laser:** 17.1%
- **Systemic mTOR Inhibitor:** 12.3%
- **Abrasive:** 2.6%

*Source: TSC Alliance Natural History Database*
Surgical Removal of Angiofibromas

PHYSICAL REMOVAL\(^1\,\,3\)

- May include surgical removal, laser therapy, dermabrasion
- Can be invasive and painful; with the risk of scarring, dyspigmentation, and post-procedure infection
- Recurrence rates are ≤80% and follow-up treatment is frequently required
- May require anesthesia, which may be associated with risks and complications, particularly in children
- Can be costly
Medications

MTOR INHIBITORS¹-⁶

- Both oral and topical formulations of mTOR inhibitors (e.g., sirolimus, everolimus) are used to treat TSC-related complications but may not be indicated for facial angiofibroma.
- Oral mTOR inhibitors have been shown to improve facial angiofibroma but their use is generally restricted due to concerns around systemic side effects (e.g., stomatitis, mouth ulcers, marrow suppression, infections).
- International consensus recommendations suggest topical mTOR inhibitors be used for flat or minimally elevated angiofibromas¹.

Possible Adverse Reactions From Topical mTOR Inhibitors

• Application site irritation / Acne / Rash
• Dry skin / Itching
• Photosensitivity
• Eye redness
• Skin bleeding / Skin irritation
Key Takeaways To Manage Facial Angiofibroma

• Baseline comprehensive exam
• Subsequent skin exam
  • Annually or every 3 to 6 months
• Consider biopsy when appropriate
• Early intervention
• Sun protection
• Choice of treatment varies among the patients.
  • Surgical approaches may be preferable for symptomatic large tumors
• Patient will benefit from collaborative multidisciplinary care