Key Points for Clinical Practice

Dermatological Pathologies Often Associated With Trisomy 21 : Part 1

Hidradenitis Suppurativa (HS):

- Hidradenitis Suppurativa (HS) is a chronic, recurrent, and debilitating inflammatory follicular disease that progresses with typically suppurative, intermittent and painful flare-ups, or with a constant presence of symptoms.
- In Trisomy 21, the prevalence of HS is about 10 times higher than in the general population.
- The triplication of the amyloid precursor protein (APP) gene present on HSA21 stimulates the adhesion, migration, and proliferation of keratinocytes, leading to follicular occlusion and, by acting as a competitive substrate for gamma-secretase, reduces Notch signaling, resulting in the persistence of an autoinflammatory process underlying HS.
- Any nodular or cystic lesion, any abscess located in the axillary, inguinal, perineal, or mammary regions should suggest the diagnosis of HS.
- The age of onset is significantly earlier than in the neurotypical population.
- Disseminate recurrent folliculitis, concentrated on the thighs and buttocks, is often associated with and precedes HS.
- HS is a debilitating disease with major consequences for physical and mental health and quality of life.
- Treatment of HS in Trisomy 21 is difficult, as in the general population, and should be entrusted to specialized multidisciplinary teams.
- In individuals with T21, data on treatment efficacy and potential side effects are extremely limited, particularly for biologic treatments such as adalimumab, and the risks of infection and malignant tumors are concerning.

Ichthyosis vulgaris:

- Ichthyosis vulgaris is the most common and least severe of the hereditary, non-syndromic forms of Ichthyosis.
- Diagnosis is clinical with a scaly, hyperkeratotic, and rough skin appearance on the extensor surfaces of the limbs, particularly the lower limbs. The lesions tend to worsen during winter and improve during summer and in humid climates.
- Often associated with xerosis, keratosis pilaris, and palmar-plantar hyperlinearity, Ichthyosis Vulgaris may be more common and occur later (> 5 years) in individuals with T21 than in the general population.
- Treatment includes the use of emollients at least twice a day, ideally after bathing, and in case of scales or thick hyperkeratosis, keratolytic agents or topical retinoids, observing contraindications (no salicylic acid before age 2).

Dermatological Pathologies

Psoriasis (PSO):

- Psoriasis (PSO) is a chronic inflammatory skin disease that can manifest at any age, with one-third of cases beginning in childhood.
- The course of the disease is unpredictable. It is characterized by flares of variable intensity, interspersed with periods of remission of varying duration.
- The diagnosis is clinical, with the most common form (80-90% of cases) being Psoriasis vulgaris, characterized by well-defined, salmon-pink plaques covered with scales. The symmetrical plaques are typically located on the extensor surfaces of the knees and elbows, the lumbosacral region, and the scalp.
- Recent studies report a higher prevalence of PSO in individuals with T21 than in the general population.
- The frequent association between PSO and Trisomy 21 may be linked to immune dysregulation with basal hyperactivation of IFN-γ expression and hypersensitivity to IFN in Trisomy 21. PSO in Trisomy 21 may be more interferon-dependent than cytokine-dependent.
- The predominant clinical form in Trisomy 21, as in the general population, is Psoriasis vulgaris. Rare cases of annular pustular, linear, or nail PSO have also been reported.
- The association of PSO with Trisomy 21, with chronic inflammatory psoriatic arthritis, Hidradenitis Suppurativa, Alopecia Areata, overweight and obesity, has also been reported.
- All PSO severity stages are encountered in individuals with T21, with a significant impact on quality of life in nearly 80% of cases.
- The treatment of PSO in individuals with T21 is similar to that of the general population. In moderate or severe forms, biologics targeting the stages of the pathophysiological process leading to PSO are increasingly used in individuals with T21. In the most recent findings, IL-12/23 inhibitors, IL-23 inhibitors, and IL-17 inhibitors demonstrated greater efficacy than TNF-α inhibitors, and the authors reported that JAK3 inhibitors such as tofacitinib have an emerging role. The benefit/risk ratio of these biologics is still a subject of research.

Lichen Nitidus (LN)

- Lichen Nitidus (LN) is a rare, benign, chronic inflammatory skin disease. More common in children and young adults, its prevalence remains unclear.
- LN presents as small clusters of many shiny, flat-topped pinpoint papules on the chest, abdomen, genitals (especially the penis), and upper limbs. LN is generally asymptomatic but can sometimes be accompanied by moderate pruritus.
- LN is usually isolated but has been described in association with Niemann-Pick disease, Crohn's disease, HIV, and Trisomy 21, as well as with other skin diseases such as Psoriasis, Lichen Planus, and Vitiligo.
- Although rare, generalized LN is associated with Trisomy 21 (7 of 8 published cases), all pediatric patients, with facial involvement. An association with segmental vitiligo and Hirschsprung's disease has been described.
- LN requires no active treatment except for generalized and pruritic cases, which should be referred to a dermatologist.

Hyperkeratotic (Crusted or Norwegian) Scabies (HKS):

- Scabies is a parasitic skin infestation caused by a mite, Sarcoptes scabiei var. hominis, affecting 150-250 million people worldwide. Scabies is highly contagious and is transmitted through direct skin contact or indirectly through clothing and bedding.
- HKS and profuse scabies are rare but severe forms of scabies characterized by massive parasitic infestation and the development of extensive lesions.
- HKS presents as a rash of hyperkeratotic plaques; the skin is thickened, sometimes cracked, with gray or yellowish scales, which, when scraped off, reveal smooth, erythematous skin. It is commonly observed on the soles of the feet, palms of the hands, ears, and extensor surfaces of the elbows. It is typically minimally pruritic.
- Diagnosis, often delayed by several months, is based on the identification of Sarcoptes scabiei in the scales. Differential diagnosis includes PSO, eczema, palmoplantar hyperkeratosis, etc.
- The association of HKS with Trisomy 21 is robust, based on the presence of primary immune dysregulation facilitating parasitic proliferation, less effective scratching due to intellectual disability, and the common occurrence of institutional living.
- HKS in Trisomy 21 affects children more than adults, both males and females, affects the same areas typically seen in the general population, and generally presents with pruritis.
- HKS should be considered a severe disease with a risk of mortality, and treatment in individuals with T21 is no different from that in the neurotypical population.
- Comprehensive treatment includes treating the infected person, their close contacts, and their environment. Hospitalization is required in 2/3 of cases.
- Currently, treatment consists of a combination of oral ivermectin and 5% permethrin topical cream, along with mechanical removal of hyperkeratotic layers.
- Treatment efficacy is close to 100% in the general population.