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Dermatological Manifestations of Down Syndrome

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1. Introduction

Down syndrome (DS) is increased frequency of some common dermatoses and associated with rare dermatological disorders. With the increasing life span and number of DS patients in the population, dermatologists are more likely to encounter skin manifestations associated with DS. Subjects with DS have high rates of infections and autoimmune phenomena. The immunological disturbances in DS (High IgG and low IgM levels, reduced total T-lymphocyte numbers, high CD8+ and low CD4+ count, decreased chemotaxis,...) could be implicated in some higher cutaneous manifestations.

In this chapter, it has been exposed the dermatological disorders associated with DS. Very few studies in the literature have studied dermatological manifestations of DS. Newer reports are mostly in the form of case reports highlighting the rare dermatological findings. Dermatologic manifestation in DS has been studied in 6 major surveys but the results are not concordant. These studies differ in some aspects (age range, living conditions of the study group,...). Daneshpazhooh *et al* studied 100 children with DS with a mean age of 11.2 years; Carter and Jegasothy examined 213 institutionalized patients with ages between 12 and 48 years old; Ercis *et al* studied 71 children who live with their families; Polenghi *et al* observed adults with ages between 14 and 53 years old; Schepis *et al* examined 203 patients from infancy till adulthood with a mean age of 11.7 years; and Sureshbabu *et al* studied 95 patients with a mean age of 11.9 years, ranging from 6 months to 40 years.

These dermatologic disorders can be separated in manifestations that could be, or not, associated to immunological alterations (Table 1).

Associated to immunological alterations	Probably not associated to immunological alterations
<i>Atopic dermatitis</i> <i>Seborrhoeic dermatitis</i> <i>Alopecia areata</i> <i>Vitiligo</i> <i>Infections</i> - <i>Onychomycosis</i> - <i>Scabies</i>	<i>Anetoderma</i> <i>Milia-like calcinosis cutis</i> <i>Acanthosis nigricans</i> <i>Syringomas elastosis perforans serpiginosa</i> <i>Leukaemia cutis</i> <i>Acrocyanosis</i> <i>Cutis marmorata</i> <i>Keratodermatoses</i>

Table 1. Dermatological manifestations of Down's syndrome associates or probably not associated to immunological alterations

2. Dermatological manifestations that could be associated to immunological alterations

2.1 Atopic dermatitis

Atopic dermatitis (AD) is a chronic inflammatory skin condition that appears to involve a genetic defect in the proteins supporting the epidermal barrier. AD affects approximately 5-20% of children worldwide. The incidence of AD appears to be increasing. Onset tends to occur during childhood and gradually diminishes with age, although it can persist or even appear in adults. The term AD was coined by Wise and Sulzberger in 1933 to define an entity characterized by dry skin, pruritus, erythematous lesions, and a chronic recurrent course. Currently, the terms AD and atopic eczema are used and both are acceptable.

Its prevalence has increased 3-fold or 4-fold in recent decades in some countries. According to the International Study of Asthma and Allergies in Childhood, during a minimum period of 1 year, the prevalence of symptoms of AD in 6- or 7-year-old children presented great variability between different geographic areas. Thus, prevalence was almost 20% in England or Australia but less than 2% in China or Iran. There is a higher prevalence in urban areas than in rural ones in developed countries, and higher social classes are more affected. Regarding the disease by sex, a study of 12- to 16-year-olds found a higher prevalence among girls (25.7%) than among boys (17%). The onset of AD occurred during the first 6 months of life in 45% of children, in the first year in 60%, and in the first 5 years in more than 85%.

One study diagnosed AD in 56.5% of DS, and another a prevalence of more than 50%. The high reported prevalence of AD, in some studies, could be an overestimate and isolated signs such as facial dermatitis and generalized xerosis could easily be misinterpreted as AD. Pathogenesis of AD is complex; several factors are involved, many of which are still not well understood. Likewise, it has yet to be determined how these factors might interact with one another. An origin of atopic eczema seems to involve a feedback cycle: pruritus and mechanical damage caused by scratching leads to the production of proinflammatory cytokines (interleukin [IL]-1, IL-18, tumor necrosis factor, granulocyte-macrophage colony stimulating factor) that recruit leukocytes to the skin.

Different leukocyte populations are activated through different processes; on induction by dendritic cells, the lymphocytes differentiate via the Th2 pathway; these dendritic cells also show increased antigen-presenting capacity and bind to the IgE-antigen complex. The IgE-antigen complex in turn induces mast cell accumulation and activation. The activated Th2 cells release IL-4 and IL-13, which suppress the production of antimicrobial peptides. Viruses, bacteria, and fungi take advantage of these reduced peptide levels, colonizing the skin and releasing proinflammatory products (superantigens, proteoglycans, and lipoteichoic acid) that amplify leukocyte activation. This activation increases the release of inflammatory mediators, such as proteases and IL-31, which perpetuate pruritus.

Increased prevalence of childhood AD in developed countries has led to the appearance of many theories on the possible involvement of environmental factors. Increases in the prevalence of allergic disease probably depend more on environmental factors than on other individual characteristics.

The diagnosis of AD is based on a constellation of signs and symptoms. There is no laboratory "gold standard" for the diagnosis of AD. In a majority of the cases, the diagnosis is quite easy. Establishing firm diagnostic criteria for all forms of AD is difficult due to the

clinical and pathophysiological heterogeneity. Atopic individuals can also suffer from other dermatitis or dermatoses, and because every dermatitis in an atopic individual need not be AD. Hanifin and Rajka for the first time proposed a systematic approach toward the standardization of the diagnosis of AD by incorporating three major/basic and 23 minor features. They suggested that a diagnosis of AD can be established if 3 of the major and 3 of the minor criteria are present. (Table 2).

Major	Minor
<ol style="list-style-type: none"> 1. <i>Pruritus</i> 2. <i>Typical morphology and distribution:</i> <ul style="list-style-type: none"> - <i>Flexural lichenification or linearity in adults</i> - <i>Facial and extensor involvement in infants and children</i> 3. <i>Chronic or chronically relapsing dermatitis</i> 4. <i>Personal or family history of atopy (asthma, AR, atopic dermatitis)</i> 	<ol style="list-style-type: none"> 1. <i>Xerosis</i> 2. <i>Ichthyosis/palmar hyperlinearity/keratosis pilaris</i> 3. <i>Immediate (type 1) skin test reactivity</i> 4. <i>Elevated serum IgE</i> 5. <i>Early age at onset</i> 6. <i>Tendency toward cutaneous infections (esp. Staph. aureus and Herpes simplex)/impaired cell-mediated immunity</i> 7. <i>Tendency toward nonspecific hand or foot dermatitis</i> 8. <i>Nipple eczema</i> 9. <i>Cheilitis</i> 10. <i>Recurrent conjunctivitis</i> 11. <i>Dennie-Morgan infraorbital folds</i> 12. <i>Keratoconus</i> 13. <i>Anterior subcapsular cataracts</i> 14. <i>Orbital darkening</i> 15. <i>Facial pallor/facial erythema</i> 16. <i>Pityriasis alba</i> 17. <i>Anterior neck folds</i> 18. <i>Itch when sweating</i> 19. <i>Intolerance to wool or lipid solvents</i> 20. <i>Perifollicular accentuation</i> 21. <i>Food intolerance</i> 22. <i>Course influenced by environmental/emotional factors</i> 23. <i>White dermographism/delayed blanch</i>

Table 2. Diagnostic criteria of Hanifin and Rajka Diagnosis of AD can be established if 3 of the major and 3 of the minor criteria are present

In DS, the skin in infancy is usually soft, but soon becomes dry, thick, and rough, with patchy lichenification. The reported frequency of xerosis differs from 9.8 percent to 85 percent in various studies. Sureshbabu *et al* observed disorders lichenification as the most common disorder, seen in 52.6% of DS patients, with a peak incidence in the 5-10 year age group. High incidence of AD reported by Carter *et al* (56.5%) and cited in some major review articles contrast with Sureshbabu *et al* study which none of subjects fulfilled the criteria of Hanifin and Rajka for AD. Two studies observed 3% and 4.9% for the prevalence of AD in

DS using the criteria of Rajka and Hanifin, These results are in favour of the opinion that AD is not as common as previously thought when using the acknowledged diagnostic criteria of Rajka and Hanifin.

In the treatment of AD, topical corticosteroids are considered the gold standard for assessment of other treatments. The potency and formulation employed depends on the area to be treated and the chronicity of the lesions. Areas with have undergone lichenification requiring stronger formulations. One application per day is sufficient, as treatment twice a day confers no advantage while increasing the likelihood of adverse reactions. Adverse reactions are well known and frequently overestimated by patients and their family members, even though the new formulations have a demonstrated lower risk of causing cutaneous atrophy than the older ones and that several studies have found a far lower incidence of local and systemic complications.

Application of topical antibiotics in combination with corticosteroid therapy has advantages compared to topical corticosteroids. Fusidic acid appears to be the topical antibacterial treatment of choice, due to its low minimum inhibitory concentration and its good penetration.

Topical calcineurin inhibitors have proven to be effective in the treatment of AD. Topical tacrolimus seems to have an efficacy similar to high-potency corticosteroids, whereas pimecrolimus is substantially weaker. Controlled pediatric studies have confirmed the superior efficacy of topical tacrolimus compared to pimecrolimus and hydrocortisone. There appear to be no significant differences between the response of children to concentrations of 0.03% and 0.1%. Neither tacrolimus nor pimecrolimus cause cutaneous atrophy, but they can cause other adverse reactions such as local itching-burning sensation when being applied, which is an added discomfort for the skin of children with AD.

Use of emollients is widely recognized as a basic measure in the treatment and prevention of flares of AD. It has been shown that their use in combination with topical corticosteroids accelerates healing and decreases the total dose of corticosteroids required to resolve the flare.

Dietary restrictions have proven effective in the case of children with egg-specific IgE, but not for other foods which have the same effect. It seems reasonable to establish diets that avoid food proven to cause an allergic response using the radioallergosorbent test, although the most relevant test would be the challenge test, which in many cases cannot be performed. Psychological care is recommended to help deal with the emotional needs of patients with atopic dermatitis, and should be based on providing education and information on the clinical and preventable aspects of the disease. One study found that this type of intervention reduced anxiety scores.

Short-course systemic corticosteroids are recommended to control acute flares of AD, taking into account that new flares are frequent after stopping treatment. Their long term use in children is not recommended. Little evidence exists to support using oral antihistamines in AD. Other systemic treatments to AD are: Cyclosporine A, azathioprine, interferon, light therapy or intravenous immunoglobulins. Biologic treatment has recently appeared in the field of dermatology and has shown some potential.

2.2 Seborrhoeic dermatitis

Seborrhoeic dermatitis (SD) is a common, chronic dermatoses of unknown aetiology, characterized by scaling and redness occurring primarily in the areas with the highest

concentration of sebaceous glands such as the scalp, face (mid-facial region), and certain areas of the trunk, such as the mid-thoracic and interscapular areas and the area around the buttocks. On the scalp, it generally appears first as small patches of scales, progressing to involve the entire scalp with exfoliation of excessive amounts of dry scales.

It affects around 1% to 3% of the immunocompetent adult population, with a higher prevalence in men than women. Although it can appear at any age, the highest prevalence is observed in individuals aged 30 to 60 years and in the first 3 months of life in the infantile form of the disease.

Clinically, the disease is characterized by erythema and flaking of the skin in the affected area. Lesions are well delimited, reddish, and covered with oily yellowish-white scales. On the scalp, in the milder form of the disease, the scales are small, dry, and whitish, and they detach easily and spontaneously in steady amounts. In the more severe form of the disease, plaques are observed that range in size from a few centimeters to areas covering a large part of the scalp; they are made up of thick dry scales. On the face they are found in the eyebrows, around the nose, at the edge of the scalp, and on the inner surface of the auricle. In the thorax, the lesions are rounded, well delimited, and reddish brown; they are located on the medial part of the chest and on the back, between the shoulder blades. All of these forms are associated with varying degrees of itching. In adults, the course of SD involves periods of remission and exacerbation, irrespective of the treatments administered. Outbreaks are common under conditions of emotional stress, fatigue, and depression.

While the disease rarely causes serious complications, it always leads to a marked esthetic deterioration that leads to emotional and social difficulties for the affected individual.

The etiology of seborrheic dermatitis is not fully understood but is known to involve various factors. Increased secretion by the sebaceous glands favours the development of microorganisms of the genus *Malassezia*, which are responsible for the symptoms.

It appears more frequently in patients with neurological disorders such as Parkinson disease, in those suffering from depression, and in patients with AIDS. One study, by Carter and Jegasothy, found a 36% prevalence of SD in DS patients and another was found a similar prevalence (Ercis *et al.* 31%; mostly during the first year of life). SD was seen in 4.2% of DS by Sureshababu *et al.* SD is commonly seen in patients with immunodeficiency. High prevalence of *pityrosporum folliculitis* in DS patients could have a pathogenic role.

A diet rich in animal fats and lacking in vegetables, as well as alcohol consumption can also potentiate the appearance of lesions. Topical corticosteroids are the first choice treatment for SD. Others drugs can currently be used to minimize the effects of this dermatologic disease: antifungals, keratolytics, tar or pyrithione derivatives, and selenium sulfate. Many of these treatments have been tested as both monotherapy and in combination.

2.3 Alopecia areata

Alopecia areata (AA) is a recurrent nonscarring type of hair loss that can affect any hair-bearing area. Clinically, AA can manifest many different patterns. Although medically benign, AA can cause tremendous emotional and psychosocial distress in affected patients and their families.

AA is a genetically determined, immune-mediated disorder of the hair follicle with an estimated lifetime risk of approximately 2%, making it one of the most common autoimmune diseases

AA is characterized by patchy hair loss on the scalp, which can eventually involve the entire scalp (*alopecia totalis*) or the entire body (*alopecia universalis*). The onset of the disease can be sudden, its progression is unpredictable, and it can be recurrent throughout life. It is thought that AA represents a breakdown in immune privilege with the subsequent inability to function of the hair follicle by T lymphocytes. AA has a deeply disturbing psychological impact on affected individuals. It shows a spectrum of severity that ranges from patchy localized hair loss on the scalp to the complete absence of hair everywhere on the body.

Treatment of AA may induce hair growth, but usually does not change the course of the disease. When treatment is stopped, hair loss recurs. Many patients with one or two small patches can be managed without treatment and with reassurance of the benign nature of the condition. Treatment with topical and oral steroids, topical minoxidil, topical cyclosporine, and photo-dynamic therapy has been found to have no long-term benefit of these interventions. In patients with persistent hair loss and less than 50% scalp involvement, intralesional corticosteroid therapy is the first-line treatment. Patients with more than 50% hair loss can be treated with topical immunotherapy using diphenyl-cyclopropenone or squaric acid. *Alopecia totalis* and *alopecia universalis* have the worst prognosis, with fewer than 10% of patients recovering.

AA occurs in approximately 0.1% of the general population but a recognized association of AA with DS exists and it was reported between 20% to 1.4% prevalence. Sureshbabu *et al* saw in 9.4% of DS with AA. Female predilection was observed by Carter and Jegasothy but not in other studies. AA was observed in 3% of DS patients in the study of Schepis *et al*, with the usual age of onset in middle childhood (5-10 years). AA, in DS patients, is usually severe and refractory to the standard treatments.

2.4 Vitiligo

Vitiligo is a hypopigmentation disorder where the loss of functioning melanocytes causes the appearance of white patches on the skin. It occurs when melanocytes, the cells responsible for skin pigmentation, die or are unable to function. The cause of vitiligo is unknown, but research suggests that it may arise from autoimmune, genetic, oxidative stress, neural, or viral causes. Vitiligo is an autoimmune disease characterized by melanocyte loss, which results in patchy depigmentation of skin and hair, and is associated with an elevated risk of other autoimmune diseases. It is a genetically complex disorder involving multiple susceptibility genes and unknown environmental triggers. Recent data provide strong evidence supporting an autoimmune pathogenesis of vitiligo. Genetic factors also appear to play a role in the etiopathogenesis of vitiligo as 20% to 30% of patients have a family history of the disorder. Vitiligo is associated with other autoimmune diseases (Addison's disease, hyperthyroidism and pernicious anemia).

Vitiligo affects 1% of the world population, but the prevalence has been reported as high as 4% in some South Asian, Mexican and American populations. Vitiligo can develop at any age, but several studies report that 50% of cases appear before the age of 20 years old. Only one study investigated the association between vitiligo and DS found a prevalence of 1.9%. 75% of this also had AA. However, Sureshbabu *et al* did not observe an incidence significantly higher in DS people.

Flat areas of normal-feeling skin without any pigment appear suddenly or gradually. These areas have a darker border. The edges are well defined but irregular. Vitiligo most often affects the face, elbows and knees, hands and feet, and genitals. It affects both sides of the

body equally. Vitiligo is more noticeable in darker-skinned people because of the contrast of white patches against dark skin. No other skin changes occur. Sometimes, the use of Wood's light can improve to see lesions. In some cases, a skin biopsy may be needed to rule out other causes of pigment loss.

Vitiligo is difficult to treat. As vitiligo can have a major effect on quality of life, treatment can be considered and should preferably begin early when the disease is active. Current treatment modalities are directed towards stopping progression of the disease and achieving repigmentation. Therapies include corticosteroids, topical immunomodulators, phototherapy, surgery, combination therapies and depigmentation of normally pigmented skin. Topical corticosteroids can be used for localized vitiligo. The use of topical immunomodulators seems to be equally effective as topical steroids, especially when used in the face and neck region. Narrowband ultraviolet-B therapy seems to be superior to psoralen ultraviolet-A. Depigmentation therapy can be considered if vitiligo affects more than 60% to 80% of the body.

2.5 Onychomycosis

Onychomycosis is one of the most prevalent fungal infections in the population with a higher rate of treatment failures. Onychomycosis is a frequent nail disease caused by dermatophytes, yeasts, and nondermatophyte molds. *Trichophyton rubrum*, *T mentagrophytes*, and *Epidermophyton floccosum* are the most common etiologic agents worldwide.

Onychomycosis may be classified into several types: distal subungual, white superficial, proximal subungual, endonyx, and total dystrophic. Distal subungual onychomycosis, the most common type, involves the nail bed and, subsequently, the nail plate. White superficial onychomycosis usually manifests as superficial white patches with distinct edges on the surface of the nail plate. Proximal subungual onychomycosis results when the fungal organism enters via the cuticle and the ventral aspect of the proximal nail fold. In endonyx onychomycosis, fungal organisms invade the nail plate without resulting nail bed hyperkeratosis, onycholysis, or nail bed inflammatory changes. In total dystrophic onychomycosis, complete dystrophy of the nail plate occurs; these changes may be primary or secondary.

Diagnosis is corroborated by direct microscopic examination, culture, and histomycology. Treatment is based on oral antifungals. Systemic treatment for onychomycosis includes terbinafine, an allylamine that is primarily fungicidal, and itraconazole, a triazole that is primarily fungistatic. Both represent a major therapeutic advancement over griseofulvin in the treatment of this condition.

For toenail infection, terbinafine is usually taken continuously for 12 weeks, whereas itraconazole is taken either continuously or intermittently that is 1 week in 4 weeks for the same period. Because therapeutic concentration of itraconazole is believed to persist in the nail for a considerable time after systemic treatment is stopped, intermittent therapy with higher daily doses to achieve and maintain therapeutic concentration might be an effective alternative to continuous treatment.

Such intermittent treatment is widely used currently to treat onychomycosis and is claimed to be as effective for this condition as both continuous itraconazole and continuous terbinafine.

Although both itraconazole and terbinafine are well tolerated and highly effective drugs, continuous terbinafine is more effective than intermittent itraconazole at achieving mycological cure of toenail onychomycosis.

There is a higher frequency of onychomycosis in DS patients. It has been reported prevalence of 67,8% to 4,4%. A low incidence of infection was seen in Sureshababu *et al* study in contrast to Carter *et al* who reported a high prevalence of fungal infections. Schepis *et al* also reported a relatively low figure for onychomycosis and tinea corporis. Fungal infections may have been over diagnosed in the past or may be caused by poor hygienic conditions.

2.6 Scabies

Scabies (caused by *Sarcoptes scabiei*) is probably one of the most common parasitic infections, usually spread by bodily contact, though other contaminated objects can also infect. There is severe itching, usually worse at night, with lesions (mostly excoriated burrows) on the fingerwebs, volar wrists, buttocks, Scabies is an infestation caused by human itch mite, *Sarcoptes scabiei*, which infests some 300 million persons each year and is one of the most common causes of itching dermatoses throughout the world. Gravid female mite measuring 0.3 to 0.4 mm in length burrows superficially beneath the stratum corneum for a month, depositing two or three eggs a day. Nymphs that hatch from these eggs mature in about 2 weeks through a series of molts and then emerge as adults to the surface of the skin, where they mate and subsequently reinvade the skin of the same or another host. Transfer of newly fertilized female mites from person to person occurs by intimate personal contact and is facilitated by crowding, uncleanliness and sexual promiscuity.

The most commonly used to treatment scabies is permethrin 5% cream which applied all over the body. The whole family or sexual partners of infected people should be treated, even if they do not have symptoms. Creams are applied as a one-time treatment or they may be repeated in 1 week. Wash underwear, towels, and sleepwear in hot water. Vacuum the carpets and upholstered furniture. For difficult cases, oral Ivermectin 200-400 µgr/Kg may be used.

Other creams include benzyl benzoate, sulfur in petrolatum, and crotamiton. Lindane is rarely used because of its side effects.

Itching may continue for 2 weeks or more after treatment begins, but it will disappear if the infection is over.

Patients with DS seem predisposed to crusted scabies. Immunological dysfunction has been proposed as one factor for this propensity. However, Norwegian scabies can appear as isolated or epidemic conditions but no cases were recorded in some studies

3. Other dermatological manifestations that would not be associated to immunological alterations

3.1 Anetoderma

Anetoderma is a rare benign dermatosis caused by a loss of mid-dermal elastic tissue resulting in well-circumscribed areas of pouchlike herniations of flaccid skin. It has been hypothesized that a congenital malformation of elastic fibres in this population may be responsible for anetoderma.

Sureshababu *et al* observed anetoderma in 3.2% of DS. Schepis *et al* reported 3.9% of patients having anetoderma in their study. It has been hypothesized that a congenital malformation of elastic fibers in this population may be responsible for anetoderma secondary to chronic folliculitis. Anetoderma is due to elastolysis probably induced by leukocytes or bacteria during the recurrent inflammatory events

3.2 Milia-like calcinosis cutis

Milia-like idiopathic calcinosis cutis (MICC) is a rare entity. Only few cases have been reported so far. Two-thirds of these have been associated with Down syndrome.

MICC is a micronodular, whitish, acral, calcified lesion. Laboratory tests are usually within normal range (including serum calcium and phosphate, urinary calcium and parathyroid hormone). The term MICC was introduced in the literature by Smith *et al* who described a 6-year-old child affected by DS. Some additional cases of MICC have been reported in children or adolescents affected by DS.

Milia-like idiopathic calcinosis cutis has long been regarded as a peculiar subtype of idiopathic calcinosis cutis. The pathogenesis of the disorder remains unclear. The pathogenesis of MICC in association with DS is unclear. Higher concentrations of calcium in sweat have been found in DS, which may lead to sweat-duct calcification

3.3 Acanthosis nigricans

Acanthosis nigricans (AN) is a skin disorder in which there is darker, thick, velvety skin in body folds and creases. Obesity can lead to AN, as can some endocrine disorders. It is often found in people with obesity-related diabetes. Some drugs, particularly hormones such as human growth hormone or oral contraceptives, can also cause AN. Because AN usually only changes the skin's appearance, no treatment is needed. It is important, however, to treat any underlying medical problem that may be causing these skin changes. When AN is related to obesity, losing weight often improves the condition.

AN was seen by Sureshbabu *et al* in 8,4% of DS. The increased incidence of AN in adults is more than in children, but this fact may be attributed to the fact that all these patients were obese with a high BMI (> 30).

3.4 Elastosis perforans serpiginosa

Elastosis perforans serpiginosa (EPS) is characterized clinically by papules and keratotic plaques and histologically by focal elastosis of the dermis and transepidermal elimination of abnormal elastic fibers. It is a rare skin disease classified as a primary perforating dermatosis similar to reactive perforating collagenosis. It was given the current denomination of EPS by Dammert and Putkonen.

The incidence of EPS has yet to be established, although looks like higher in DS people. Around 90% of patients develop symptoms of the disease prior to 30 years of age, the majority between 6 and 20 years of age; however, age at onset may range from 5 to 89 years, as reported in the literature. Approximately 75% of those affected are male.

Etiopathogenesis is as yet unclear. It is believed that the focal inflammation in the dermis, which has a biochemical or mechanical origin, may induce the formation of epidermal and follicular channels to expulse abnormal elastic fibers considered irritants.

The disorder can present with papules and erythematous or normochromic, keratotic, asymptomatic or pruriginous plaques grouped in an annular, arciform or serpiginous pattern, surrounded by satellite lesions. They have umbilicated centers from which dermal material is eliminated. The lesions are characteristically symmetrical except in cases associated with DS.

Various forms of treatment have been indicated; however, management of the disease is difficult and there is no standard treatment. There have been reports of therapeutic success using cryotherapy with liquid nitrogen and oral isotretinoin.

3.5 Others

It also has been reported higher prevalence of other skin alterations in DS patients: syringomas, leukaemia cutis, acrocyanosis and cutis marmorata, keratodermatoses... However, none all studies have observed them; for example Sureshbabu *et al* did not see syringoma, milia-like calcinosis cutis, leukemia cutis, elastosis perforans serpiginosa, carotenemia, or vascular instability; they referred that may relate to the fact that their study was not hospital based, unlike other previous studies. Other miscellaneous cutaneous lesions were probably coincidentally seen in the studies, concordant with that seen in the general population.

4. Conclusions

DS is increased frequency of some common dermatoses. Some dermatologic manifestation in DS can be in relation with their immunological alterations. Skin alterations of DS have been observed by few studies. Their management is equal to rest patient, but they can occasionally be more resistant to conventional treatment, for example AA.

AD is one of the most frequent skin diseases associated a DS. However, perhaps this high association observed in first studies could be overestimated. Newer studies, which have used criteria of Hanifin and Rajka to diagnostic AD, does not show so higher incidence of AD in DS. SD can be more extensive than in other patients.

Some immunologic skin diseases, as vitiligo and AA, have been reported with high incidence in DS. Also, fungal infection and scabies has been observed with higher prevalence in DS than rest population. However, scabies in DS could be overestimated in some studies with patients under epidemic conditions.

MICC y EPS are rare skin alterations observed more frequently in DS. AN, frequently associated to overweight, can usually be observed in patients with IMC>30. Other miscellaneous cutaneous lesions were probably coincidentally seen in every study.

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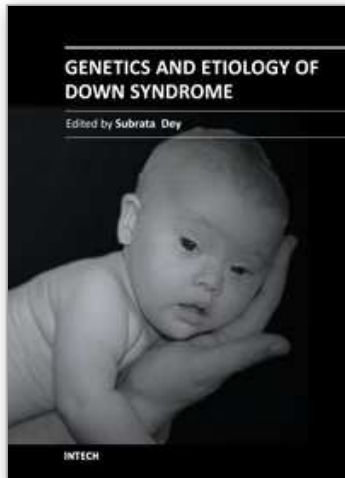
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This book provides a concise yet comprehensive source of current information on Down syndrome. Research workers, scientists, medical graduates and paediatricians will find it an excellent source for reference and review. This book has been divided into four sections, beginning with the Genetics and Etiology and ending with Prenatal Diagnosis and Screening. Inside, you will find state-of-the-art information on: 1. Genetics and Etiology 2. Down syndrome Model 3. Neurologic, Urologic, Dental & Allergic disorders 4. Prenatal Diagnosis and Screening Whilst aimed primarily at research workers on Down syndrome, we hope that the appeal of this book will extend beyond the narrow confines of academic interest and be of interest to a wider audience, especially parents and relatives of Down syndrome patients.

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