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Review

Mycosis fungoides in pediatric population: comprehensive review on epidemiology, clinical presentation, and management

Rohit Kothari[1], MD, Jacek C. Szepietowski[2], MD, Martine Bagot[3], MD, Sunmeet Sandhu[4], MD, Anant Patil[5], MD, Stephan Grabbe[6], MD and Mohamad Goldust[6], MD

[1]Department of Dermatology, Armed Forces Medical College, Pune, India, [2]Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wroclaw, Poland, [3]Faculté de Médecine Paris Diderot, AP-HP, Service de Dermatologie, Hôpital Saint-Louis, Paris, France, [4]Department of Dermatology, Command Hospital Air Force, Bangalore, India, [5]Department of Pharmacology, Dr. DY Patil Medical College, Navi Mumbai, India, [6]Department of Dermatology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany

Correspondence
Mohamad Goldust, MD
Department of Dermatology
University Medical Center of the Johannes Gutenberg University
Mainz
Germany
E-mail: mgoldust@uni-mainz.de

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Abstract

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma. However, it is rare in pediatric population. Most of the cases of pediatric MF present with hypopigmented patches and/or various other forms, which may often mimic common childhood dermatoses, thereby causing a delay in the diagnosis. There are no established treatment guidelines for pediatric MF. As the progression of childhood MF is extremely rare and it has an indolent course, it is usually diagnosed at an early stage (IA, IB, IIA), and hence phototherapy with a response rate of >80% is a well-established effective treatment in children. However, as recurrences are frequently seen on stopping the therapies, a maintenance regimen and long-term follow-up is equally important. This article reviews the epidemiological factors, clinical presentations, diagnosis, and various treatment modalities used in pediatric MF. We analyzed and compared the data of almost 616 childhood MF cases from various studies undertaken from 1988 to 2021.

Introduction

Primary cutaneous lymphomas are a heterogenous group of non-Hodgkin extranodal lymphomas arising from either T- or B-lymphocytes. Cutaneous T-cell lymphomas (CTCL) are the most common, and the incidence increases with age with an average age of 50 years at diagnosis.[1] However, they are rare in pediatric population. Mycosis fungoides (MF), the most frequent type of CTCL, accounts for 38.7–65% of all primary cutaneous lymphomas in children[2,3] and comprises almost 18% of the total MF cases including the adults.[4] Due to the rarity, heterogeneous presentation, lack of standardized treatment guidelines, and at times morphology similar to common benign childhood dermatoses, it is often diagnosed late in children. This review attempts to give an overview and update on various epidemiological factors, clinical presentations, diagnostic features, and management of pediatric MF.

Epidemiology

Incidence

The incidence of MF varies widely with the geographic location and age group of the population. It has an estimated incidence of around six cases per million per year in Europe and the United States, which accounts for 4% of all non-Hodgkin lymphomas,[5] and pediatric MF accounts for almost 4–5% of the total MF cases.[6,7]

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Age

MF can affect any age group, but the average age at disease diagnosis is 50–60 years.[8] Pediatric age group represents a rare subset with most of the cases having onset between 6–8 years of age[7,9] and diagnosed at a mean age of 9–11 years[10] illustrating a delay in diagnosis of approximately 1–5 years for many patients, however, may at times be up to 14–24 years in rare cases.[11,12] The delay in diagnosis of pediatric MF may be due to avoidance of skin biopsy in children in addition to resemblance of MF lesions to various benign dermatoses in childhood like pityriasis alba, eczema, psoriasis, and vitiligo.[13] Hence, MF was aptly called the "great imitator" by Zackheim et al.[14]

Sex

Slight male preponderance is seen in childhood MF, however, many studies reported a ratio between males and females close to 1 : 1[15] as compared to 2 : 1 seen in adults.[4,11,16,17] Only few studies showed an increased incidence in female children with one of them reporting a ratio as high as 1 : 9 (M : F).[18,19]

Genetics

Several human leukocyte antigen (HLA) alleles have been associated with MF in adult population, namely HLA-DQB1 and HLA-DRB1, however, no statistically significant association was found between pediatric MF and any of these HLA alleles except HLA-B*73, the biological significance of which remains questionable due to its low frequency.[20] Certain rare cases of familial MF have higher frequency of HLA-DQB1*03 as compared to controls (66.7% vs. 33%, respectively), which may support an association of this allele with the familial form of MF.[21]

Associated diseases

Pediatric MF has been reported in few cases to be associated with pityriasis lichenoides, atopic dermatitis, lymphomatoid papulosis, Wiskott-Aldrich syndrome, follicular mucinosis, and other malignancies.[22–28]

Clinical presentation

The classical presentation of MF in adults is gradually progressive asymptomatic scaly erythematous patches and plaques usually in the sun protected areas, which may progress to nodules/tumors over a period of several years.[29] MF is typically characterized by a course in three stages: erythema/patch, plaque, and tumor stage. As children mainly show early forms of MF, patch stage is primarily observed. Most of the studies report hypopigmented MF as the predominant variant accounting for almost 55–100% of the cases.[11,15,20,30–33] Other common variants reported are the classical MF, which may account for 15–40% of the cases,[4,9,10,34,35] folliculotropic variant (3–36%),[4,9,11,34] and poikilodermatous MF (5–26%).[16,36]

There are few uncommon variants which have been reported in children including pityriasis lichenoides chronica-like (PLC) MF, unilesional MF, pigmented purpuric dermatosis-like MF, granulomatous MF, ichthyosiform MF, hyperpigmented and intraoral presentation, inflammatory linear verrucous epidermal nevus-like MF, and pagetoid reticulosis, which may at times be difficult to diagnose at the initial presentation.[20,37–44] Few rare cases of familial MF and MF post organ transplant have also been reported[21,45,46] (Table 1). Mycosis fungoides with large-cell transformation in children is extremely rare and hence lacks a standardized therapeutic regimen. It is defined when the lymphoid infiltrate has more than 25% large cells with nuclei more than four times the normal size. It may present with erythematous patches, plaques, tumors, or nodules and has an aggressive course.[47,48]

Hypopigmented MF in childhood

The hypopigmented variant of MF in childhood is overrepresented and involves usually the trunk and extremities with lesions predominantly located on the sun protected sites. However, any site may be involved, and pruritus is a variable feature.[49] It may be diagnosed late as it resembles many benign dermatoses in childhood like pityriasis alba, atopic dermatitis, tinea versicolor, post-inflammatory hypopigmentation, or other conditions like vitiligo, leprosy, sarcoidosis, hypopigmented parapsoriasis en plaque, and progressive macular hypomelanosis.[48,50] Among Fitzpatrick skin type IV to VI, hypopigmented MF is more commonly seen in children, and it usually presents at a younger age as compared to children with other variants of MF.[8,30,51]

Stage

The majority of childhood MF cases are diagnosed at an early stage (IA, IB, IIA)[4,15,31,34] while advanced disease like stage IIB and beyond is rare and carries a poor prognosis[11,30] as they may end up reaching after a significant delay to the dermatologist or may be treated initially with some other close differential diagnosis as reported in one of the studies by Dulmage et al.

Table 1 Various forms of mycosis fungoides seen in pediatric population

Common	Uncommon
1. Hypopigmented MF (55–100%)	1. Pityriasis lichenoides-like MF
2. Classical MF (15–40%)	2. Unilesional MF
3. Folliculotropic MF (3–36%)	3. PPD-like (pigmented purpuric dermatosis) MF
4. Poikilodermatous MF (5–26%)	4. Granulomatous MF
	5. Ichthyosiform MF
	6. Hyperpigmented MF
	7. Intraoral MF
	8. MF with large cell transformation
	9. MF post organ transplant

MF, mycosis fungoides.

wherein a tumor stage of childhood MF was initially managed with incision & drainage.[52]

Management

Diagnosis

In children, poor response to treatment with the persistence of hypopigmented, papulosquamous, and purpuric lesions should raise a suspicion with MF as a differential diagnosis.[30] The diagnosis of MF in children is thus based on the correlation of clinical, pathological, and, if necessary, additional tests such as radiology, flow cytometry, and molecular biological methods are useful. Invasive measures such as skin biopsy in case of children due to small age cause diagnostic difficulty and hence require a high degree of suspicion. Skin biopsy alone should not be used for the diagnosis of MF.[4,6]

Histopathology

Most cases of pediatric MF have epidermotropism, atypical lymphocytes (82–100%), and haloed lymphoid cells in the epidermis and intraepidermal lymphocytes that are larger than dermal lymphocytes.[3,10,19,31] Pautrier's microabscess may be seen in 16–60% of the cases.[10,13,31,49] Other features seen on histopathology include perivascular and periadnexal infiltrate, patchy lichenoid infiltrate, and psoriasiform epidermal hyperplasia. Epidermal atrophy is usually not seen (except in poikilodermatous MF)[53] (Table 2).

Histopathology in hypopigmented MF

Along with epidermotropism, it shows minimal dermal involvement or fibroplasia of the reticular dermis.[53,54] Also, unlike classic MF, which has a predominantly $CD4^+$ phenotype, hypopigmented MF often displays a $CD8^+$ T-suppressor phenotype. Hypopigmentation may be considered a good prognostic marker.[55]

Table 2 Skin biopsy, immunohistochemistry, and T-cell receptor gene rearrangement findings in pediatric mycosis fungoides

1. Epidermotropism (82–100%)
2. Atypical lymphocytes (82–100%)
3. Haloed lymphoid cells (86%)
4. Pautrier's microabscess (16–60%)
5. Perivascular and periadnexal infiltrate, patchy lichenoid infiltrate, psoriasiform epidermal hyperplasia (variable)
6. $CD4^+$ T cells phenotype (50–70%)
7. $CD8^+$ T cells phenotype (20–67%; more common in hypopigmented MF)
8. Clonal T-cell receptor gene rearrangements (variable; 17–21% and 70–83%)

IHC, immunohistochemistry; MF, mycosis fungoides; TCR, T-cell receptor.

Immunohistochemistry

Epidermotropic peripheral T lymphocytes with phenotypes $CD2^+$, $CD3^+$, $CD4^+$, and $CD5^+$ are the characteristic findings of MF tumor cells. The most consistent finding on immunochemistry is loss or reduced number of $CD7^+$ lymphocytes, which may be seen in 70–90% of the cases even in early phases of the disease.[9,13,19,53] Predominance of $CD4^+$ T lymphocytes may be seen in 50–70% of cases[11,13,36,53] while $CD8^+$ T lymphocytes are seen in 20–67% of cases, more commonly in the hypopigmented variant (up to 100%).[3,11,13,36,49,53] An overrepresentation of cytotoxic phenotype in children compared to adults has been previously observed in previous studies.[42,56]

Clonal T-cell receptor gene rearrangements

Clonal T-cell receptor gene rearrangements are common in cases of adult MF patients, however, the data in pediatric cases is ambiguous with some studies showing no or lesser clonality ranging from 17–21%,[7,13,48] while others showed a higher percentage of T cell clonality in almost 70–83% of cases.[11,16,36]

Treatment

The treatment of childhood MF differs from that of adult cases in the form that almost all cases are diagnosed at an early stage (stage IA, IB, IIA) and they have less propensity to progress[4]; hence, more amenable to treatment by skin directed therapies which include phototherapy which is the commonest modality used[15] and topical corticosteroids (TCS), bexarotene, nitrogen mustard, vitamin D analogues, carmustine, pimecrolimus. Less commonly used therapies include interferon alpha (IFN), radiation therapy, acitretin and excimer laser, and extracorporeal photophoresis (ECP). ECP is used as a second line or rescue therapy in treatment-refractory MF.[57] The studies on excimer 308 nm therapy in childhood MF are scarce and require further research, however, it may be beneficial in limited distribution cases.[58]

Juvenile-onset MF generally has a comparably good prognosis and responds well to treatment; however, due to the potential long-term therapy in children, the treatments need to be chosen with care.[15] Recurrences are frequently seen on discontinuing therapies, which signifies the importance of maintenance therapy and a long-term follow up.[4,6] Treatment strategies for pediatric MF needs to be tailored on a case-by-case basis, and multiple factors should govern the choice of therapy including the age, stage, variant of MF, expectations of patient and the family and various adverse events associated with the therapy. Life expectancy in stage IA or IB disease of childhood MF has not shown any significant difference from that of general population, hence any intervention must have a favorable safety profile.[19]

Phototherapy

Phototherapy treatment options include broadband UVB (BBUVB), narrowband UVB (NBUVB) (311 nm), psoralen with

Table 3 Various studies (sample size ≥3) and the response to common treatment modalities

Study	Total cases	Age	Presentation	Stage	Therapy	Response	Remark
Ocampo OV et al. (2020)[4]	23	4–18 years; mean:11 years; (10 F, 13 M)	Classic MF (26.1%), hypopigmented (52.2%), folliculotropic (17.4%), classic MF with capillaritis (4.3%)	IA (26.1%); IB (73.9)	Phototherapy: 22 1. PUVA: 14 (PUVA bath: 4, PUVA+IFN: 1) 2. NBUVB: 8 (with chemotherapy: 1) 3. TCS alone: 1	CR: 14 (64%), PR:8 (36%) 1. CR: 8 (57%) PR: 6 (43%) (CR : PR with PUVA bath = 2 : 2) (CR: with PUVA+IFN) 2. CR: 6 (75%) PR: 2 (25%) (PR: with chemothaerapy) 3. PR with TCS alone➔subsequently given NBUVB+UVA1 due to active disease	All received mid-potent to potent TCS alongside phototherapy Chemotherapy used: methotrexate, cytarabine and vorinostat
Kalay et al. (2020)[63]	4 (n = 29; four cases were children <20 years)	6–19 years; mean: 13 years (2 F, 2 M)	Erythematous/hyperpigmented (25%), erythematous/ hypopigmented (25%), hypopigmented (25%), hypopigmented with follicular hyperkeratosis (25%)	IA (50%), IB (25%), IIA (25%)	1. TCS, topical bexarotene NBUVB: 1 2. Topical bexarotene gel: 1 3. PUVA with TCS: 1 4. PUVA with IFN: 1	CR: 2 (50%) PR: 2 (50%) (all cases treated with PUVA)	All except 1 (treated with topical bexarotene gel) had relapses during follow-up (3–7 years) period
Nasimi M et al. (2019)[30]	30	2–17 years; mean:11 years (13 F, 17 M)	Hypopigmented (56.6%), patchy (20%) PPD-like (13.3%), PLC-like (3.3%), hyperpigmented (3.3%), tumoral (3.3%)	IA and IB (96.6%); IIB (3.3%)	All treated with NBUVB	No clearance (43.3%); partial or total clearance (56.7%)	>80 sessions of NBUVB had more chance of a totally or partially clearance
Amorim GM et al. hypopigmented MF (2018)[64]	3 (n = 20; 3 were children)	10–17 years; mean: 12.6 years (3 M)	Hypopigmented in all (100%)	IA (67%), IB (33%)	1. NBUVB: 2 (67%) 2. PUVA: 1 (33%)	1. PR: 2 (NBUVB) 2. CR: 1 (PUVA)	TCS was given to 1 case with NBUVB; ≥100 sessions given to all
Virmani P et al. (2017)[34]	23 (n = 74 with age < 30 years; 23 were children <20 years)	6–20 years; Median: 17 years (11F, 12 M)	Hypopigmented (65.2%), classic (26%), folliculotropic (8.7%)	IA (30.4), IB (61%), I* not otherwise specified (8.7)	1. All early stage cases were treated with NBUVB, PUVA, UVA1 2. Topical agents (mid- & high-potent TCS, topical nitrogen mustard bexarotene)	Among early disease 44.1% achieved CR and 47.1% remained stable or had PR with NBUVB which was the main treatment modality used	
Cervini AB et al. (2017)[10]	14	8–15 years: mean: 11.23 years (8 F, 6 M)	Hypopigmented (100%), concomitant/subsequent classical MF (42.8%)	IA (14.3%), IB (78.5%), IVA2 (7.2%)	1. CHOP QT & EBT (stage IVA2 case): 1 (7.2%) 2. PUVA+TCS+NBUVB: 1 (7.2%) 3. PUVA+TCS: 1 (7.2%) 4. NBUVB+TCS: 1 (7.2%)	1. Stage IVA2 case had recurrence after initial clearance 2. CR: 3 (21.4%)	Those still undergoing treatment were excluded
Jang MS et al. (2016)[41]	3 (n = 10; 3 cases were children < 18 years)	8–17 years; mean: 13.3 years (2F, 1 M)	Ichthyosiform MF in all (100%)	IB (100%)	1. PUVA: 1 2. PUVA: 1 3. PUVA, acitretin: 1	PR, 6 years later relapse, NBUVB → CR 2. PR: 1 3. PR: 1	No new lesions thereafter Responded to treatment but lesions remained
Alikhan et al. (2014)[26]	3 (n = 11 children; 3 had MF)	11–19 years; mean: 14.9 years (3 M)	Folliculotropic (100%)	IA (100%)	1. NBUVB: 2 (67%) 2. Topical bexarotene gel: 2 (67%) 3. Minocycline 100 mg BD: 1 (33%) 4. Excimer laser: 1 (33%)	1. NBUVB: CR 2. Bexarotene: CR when combined with excimer laser or NBUVB although flares noted intermittently 3. Minocycline: CR when combined with NBUVB	

Table 3 Continued

Study	Total cases	Age	Presentation	Stage	Therapy	Response	Remark
						4. Excimer laser: CR with intermittent flaring	
Boulos et al. (2014)[11]	34	4–19 years; median: 14 years (16 F, 18 M)	Hypopigmented (53%), hyperpigmented (29%), folliculotropic (3%)	IA (41%), IB (56%), IIB (3%)	1. Phototherapy: 21 (62%) ➔ NBUVB: 14, PUVA:5, natural sunlight alone: 2 2. Nitrogen mustard: 3 (9%) 3. Topical retinoids: 5 (15%) 4. IFN: 6 (18%)	1. Phototherapy: CR (24%), PR (57%); progression: 10% (IA➔IB with natural sunlight alone Stable disease: 10% disease 2. Nitrogen mustard: PR (33%) when combined with phototherapy and 67% had no clinical response 3. Topical tazarotene: CR (60%) in combination with phototherapy and other agents, PR: 20%, no clinical response: 20% 4. IFN: CR (67%) when combined with phototherapy and other agents, no clinical response: 17%, rest lost to follow up	All cases that responded to NBUVB were hypopigmented MF
Heng et al. (2014)[31]	46	Age range not given; mean: 10.3 years (14 F, 32 M)	Hypopigmented (91%), PLC-like (2%), PPD-like (2%), classic MF (2%), solitary MF (2%)	IA (39%), IB (59%), IIA (2%)	1. Phototherapy➔NBUVB: 32 (47%); PUVA: 3 (7%); UVA1: 1 (2%) 2. TCS alone: 8 (17%)	1. Phototherapy➔NBUVB: CR in 15 (50%) with mean of 29.5 session; PUVA: CR in 0%, PR in 3 (100%) 2. TCS: No follow-up data	Two cases chose to be treated at other institutions; 22% (7 patients) relapsed with NBUVB after a mean duration of 14.9 months
Hodak et al. (2014)[9]	50	0.75–18 years; mean: 7.4 (20 F, 30 M)	Hypopigmented (58%), FMF (36%), psoriasiform (20%), classic MF (16%), hyperpigmented (2%), unilesional (6%)	IA (52%), IB (37%), IIA (6%), IIB (2%)	1. Phototherapy ➔ BBUVB: 3 (6%); NBUVB: 13 (26%); PUVA: 9 (18%) 2. Topical nitrogen mustard: 2 (4%) 3. Surgical excision: 1 (2%) 4. Climatotherapy: 2 (4%)	1. Phototherapy for non-FMF disease: CR in 10 (71%) with BB-UVB & NBUVB; for FMF disease: CR in 7 (70%) 2. Topical nitrogen mustard: CR in 1 (50%) in combination with PUVA 3. Surgical excision: no follow-up 4. Climatotherapy: PR in 1 (50%); other was lost to follow-up	
Koh MJ et al. (2014)[32]	9	5–12 y; Mean = 8.8 y (1 F, 8 M)	Hypopigmented (100%) with concomitant pityriasis lichenoides (56%)	IA (22%), IB (67%), IIA (11%)	NBUVB: 9 (100%)	CR in 8 (89%) by 9 months (3 of the 8 had sustained remission, 5 relapsed after 13 months)	Mean number of sessions: 57; 2–3 session/week were given with no difference in response for 2/week versus 3/week treatments
Laws et al. (2014)[19]	28	Age range not given; mean: 11.6 years (15 F, 13 M)	Hypopigmented (79%), classic MF (21%)	IA (36%), IB (61%), not known (4%)	1. NBUVB: 18 (64%) 2. Bath PUVA: 8 (29%)	CR or PR in 86% (collectively for both NBUVB and PUVA)	58% and 50% cases treated with NBUVB and PUVA respectively, required further course of phototherapy after 4 and 45.5 months respectively
Castano et al. (2013)[53]	35	4–20 (20 M, 15 F)	Hypopigmented (100%)	Not reported	1. Phototherapy➔NBUVB: 19 (54%); PUVA: 1 (2%) 2. TCS alone: 6 (17%)	1. Phototherapy: PR in 16 (84%) and recurrence: 7 (20%) after discontinuation of therapy	

Table 3 Continued

Study	Total cases	Age	Presentation	Stage	Therapy	Response	Remark
					3. Radiation: 1 (3%)	2. TCS: CR in 2 (33%), PR in 2 (33%), mo response in 2 (33%) 3. Radiation: not recorded	
Yazganoglu et al. (2013)[7]	20	2–18 years; mean: 9.20 years (8F, 12 M)	Hypopigmented (45%), unilesional MF (20%)	IA (45%), IB (15%), IIA (15%), IIB (20%)	1. Phototherapy→NBUVB: 6 (30%); PUVA: 3 (15%) 2. TCS alone: 9 (45%) 3. Topical bexarotene: 1 (5%) 4. Topical carmustine: 1 (5%)	1. NBUVB: no recurrence in 4 (67%); PUVA: no recurrence in 1 (33%) 2. TCS: no recurrence in 4 (44%); No response in 1 (11%) and 1 (11%) patient was receiving therapy at time of study 3. Bexarotene: recurrence 4. Carmustine: Recurrence	
Alsuwaidan et al. (2012)[33]	5	6–13 years; mean: 9 years (5 M)	Hypopigmented (80%), classical MF (20%)	IA (80%), IIA (20%)	TCS or NBUVB	All had complete or almost complete response	Data on specific number of patients receiving NBUVB/TCS not given
Kim et al. (2009)[35]	23	4–19 years; mean: 11 years (5 F, 18 M)	Hypopigmented (21%), PLC like (17%), classic MF (35%), other (30%)	IA or IB (100%)	1. Phototherapy→PUVA: 14 (61%); NBUVB: 3 (13%); UVA1: 4 (17%) 2. Retinoic acid: 5 (22%) 3. Calcipotriol: 4 (17%) 4. Topical keratolytic: 2 (9%)	1. Phototherapy→PUVA: CR in 2 (14%) and PR in 12 (86%); NBUVB: CR in 3 (100%); UVA1: CR in 1 (25%) and PR in 3 (75%) 2. Retinoic acid: PR in 5 (100%) 3. Calcipotriol: PR in 4 (100%) 4. Topical keratolytic: PR in 2 (100%)	

CR, complete response; MF, mycosis fungoides; PLC, pityriasis lichenoides chronica; PR, partial response.

UVA (PUVA) and UVA1. NBUVB is commonly used as first-line approach. Phototherapy has an affect on abnormal lymphocytes in MF.[59] There is ample evidence on efficacy of PUVA and NBUVB in the treatment of pediatric MF with a response rate usually >80%. Both these modalities offer favorable outcome; PUVA therapy is penetrating deeper into the dermis compared to UVB therapy. However, the duration of remission may be greater with PUVA (30–87 months) as compared to NBUVB (4–29 months).[19] NBUVB is preferred over PUVA in children due to the adverse effects of systemic psoralen, which may include risk of cataract or secondary skin cancers, while no such events are associated with NBUVB.[19,60,61] The common side effects of both the therapies include erythema, blistering, lentigines, and irritation of varied degree. Oral psoralen should be avoided in children <10 years of age, and hence topical PUVA is a good alternative.[62]

The total number of treatment sessions can have a significant impact on the overall outcome, and a greater number of sessions (induction as well as maintenance) may be associated with prolonged remission and less relapses.[30] Literature review over a period of 16 years (2005–2020) revealed 17 studies on childhood MF with sample size of ≥3 which revealed an overall response rate (complete and partial resolution) of 91% with PUVA and 70% with NBUVB[4,6,10,30,41,63,64] (Table 3). The studies which did not report the specific number of cases who received either NBUVB or PUVA were not included.[26,34]

Topical therapy

It forms an integral part as an adjuvant or in few cases as the sole agent in the management of childhood MF. TCS are the most commonly used agents. TCS used alone in very early disease gave an average overall response of almost 50%.[4,6] Recent studies involving topical bexarotene used as monotherapy in one patient and along with NBUVB and TCS in other achieved complete remission.[63] Topical nitrogen mustard used in MF in 203 adults and children achieved an overall response rate of 83%.[65] The rest of the topical agents are almost always used in conjunction with other therapies.

Systemic therapies

Certain rare presentations of pediatric MF like advanced stage, granulomatous MF, or cases of large cell transformation may need a more aggressive approach with total skin electron beam radiation therapy, methotrexate, oral bexarotene, interferon, liposomal doxorubicine, brentuximab vedotin, ifosfamide, etoposide, gemcitabine, polychemotherapy, and may require allogeneic hematopoietic cell transplant with a myeloablative regimen for a better outcome.[10,48]

Many newer agents like mogamulizumab, alemtuzumab, immune checkpoint inhibitors, histone deacetylase inhibitors (vorinostat, romidepsin, panobinostat, belinostat, and resminostat), pralatrexate, forodesine, denileukin diftitox, duvelisib, lenalidomide, and everolimus may be available, however, these are usually reserved for trials, advanced and refractory cases, and data for use in pediatric MF is lacking. They may form a part of future therapies in pediatric cases once sufficient data is available for each of these agents.[66]

Prognosis

In general, the prognosis of MF is stage dependent as the extent of skin involvement and presence or absence of extracutaneous disease are the main prognostic factors for the course of the disease. The overall prognosis in pediatric MF is good. Progression to advanced-stage MF during childhood seldom occurs (~3.3%).[9] Survival rates at 5 and 10 years follow-up are 95% and 93%, respectively. The hypopigmented and poikilodermatous variant appears to have a better prognosis. $CD8^+$ T cell immunophenotype is also associated with a better prognosis compared to adult-onset MF.[36,63,64]

Conclusion

Mycosis fungoides in the pediatric population is an uncommon disease. Diagnosis, and hence treatment, is usually delayed as it may mimic various common childhood dermatoses. As the majority of the patients has an early-stage disease (IA, IB, IIA) and favorable prognosis, phototherapy as first-line treatment is an effective treatment option for pediatric MF. Juvenile MF patients respond well to conventional therapy. Long-term follow-up and safety considerations of long-term treatment are needed in children. Due to a lack of standard treatment guidelines, there is a need to perform large scale studies to formulate effective and various patient tailored treatment regimens for the management of pediatric MF.

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