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Case Report

A Rare Coexistence of Turner Syndrome and Mycosis Fungoides: A Case Report

Bayrak Demirel O et al. Mycosis Fungoides and Turner Syndrome

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What is already known on this topic?
Turner syndrome in females is linked to increased autoimmune diseases and certain cancers, including nervous system and gastrointestinal malignancies. Mycosis fungoides, the most common primary cutaneous T-cell lymphoma, affects adults and children with slow progression that requires careful monitoring.

What this study adds?
This is the first documented case of an 11-year-old girl with both Turner syndrome and mycosis fungoides. It highlights the importance of thorough dermatologic evaluation in Turner syndrome patients, especially for atypical skin lesions, suggesting mycosis fungoides as a potential differential diagnosis.

Abstract
Turner syndrome (TS) is the most common sex chromosome abnormality among females, characterised by short stature, hypergonadotropic hypogonadism, congenital heart anomalies, and an increased risk of autoimmune diseases. Although TS does not typically increase the absolute risk of malignancy, specific cancers, such as those affecting the nervous system and gastrointestinal tract and malignant melanoma, may occur more frequently. Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma, typically affecting adults but also seen in children and adolescents. We report an 11.2-year-old girl with TS presenting with substantial weight gain and short stature. Clinical examination revealed characteristic TS features and karyotype analysis confirmed mosaic TS. Following growth hormone (GH) therapy, the patient developed persistent, erythematous, itchy skin lesions diagnosed as CD4+ MF. GH therapy was discontinued, and topical steroids controlled the skin lesions effectively. MF in TS is rare and unexpected, especially in a child. The coexistence of these conditions suggests a potential link between TS and an increased risk of MF, possibly due to T-cell dysregulation or autoimmune processes. While the clinical course of MF is typically indolent, careful monitoring and annual dermatologic evaluations are recommended for TS patients, particularly when skin lesions are present. This is the first reported case of MF in a child with TS. This case emphasises the importance of carefully evaluating skin lesions in patients with TS and suggests considering MF as a differential diagnosis.
Keywords: Turner syndrome, mycosis fungoides, malignancy, primary cutaneous T-cell lymphoma

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Introduction

Turner syndrome (TS) is the most common sex chromosome abnormality among females, caused by the complete or partial absence of one of the X chromosomes**,** which is characterised by short stature, hypergonadotropic hypogonadism, congenital heart anomalies, and an increased risk of autoimmune disease (1). Although the absolute risk of malignancy has been reported not to increase in TS, some specific types of cancer, such as nervous system malignancies, gastrointestinal tract malignancies, or malignant melanoma, have been suggested to occur more frequently in patients with TS (2, 3).

Mycosis fungoides (MF) represents the most common type of primary cutaneous T-cell lymphoma. Adults in their fifth decade are predominantly affected by the condition, but it should be remembered that MF represents the most common cutaneous lymphoma also in children and adolescents (4). MF typically exhibits an indolent course limited to the skin in the early stages when presenting with skin lesions of patches or plaques. However, it may involve visceral organs in a small number of patients in advanced stages, usually associated with tumoral skin lesions. Epidermotropic tumor infiltration, atypical T-cell proliferation, and a cerebriform appearance are typical histopathologic manifestations (5, 6).

To our knowledge, the coexistence of TS and MF has yet to be reported. We aimed to report the clinical findings and follow-up of an 11-year-old girl with TS who developed MF.

Case Report

An 11.2–year–old girl was admitted to the outpatient clinic due to her parents' concerns about substantial weight gain and short stature. Her family noticed she was shorter than her peers and gained about 10 kg in the last two years. She was born at the 32nd week of gestation, from the first pregnancy of a 31-year-old mother. Her birth measurements were within normal range. The parents were nonconsanguineous, and the family history was uneventful. Her postnatal development had been entirely normal.

At the time of referral, anthropometric measurements and pubertal status were detailed in **Table 1**. A plethoric face and low posterior hairline were observed during the physical examination. Notably, there were acanthosis nigricans on the nape and purple striae on the thigh. Additionally, the shortening of the bilateral 5th metacarpals was remarkable. Apart from these findings, systemic examination was otherwise normal, and blood pressure was within the appropriate range for the patient's gender and height.

Regarding the suspicion of Cushing's disease, the results of the dexamethasone suppression test, 24-hour urinary cortisol, and midnight salivary cortisol levels were all found to be normal. However, impaired glucose tolerance was detected during the oral glucose tolerance test, leading to the administration of metformin treatment. Furthermore, other laboratory examinations, including luteinising hormone (LH), follicle-stimulating hormone (FSH), and estradiol, were 2.21 mIU/mL, 12.18 mIU/mL, and 12.43 pg/mL, respectively (**Table 1**). These results may indicate a diagnosis of TS. The karyotype analysis supported our suspicion, revealing compatibility with mosaic TS (45, X/46, X,i(Xq)/46, XX[8/3/49]). Following the diagnosis, growth hormone (GH) therapy was initiated. However, in the third month of GH treatment, the patient developed persistent, erythematous, itchy skin lesions on her back, chest, axilla, and nape of the neck (**Fig. 1**). It was learned that these lesions had irregularly recurred over the last 3 years and had improved with the use of short-term topical corticosteroid creams, as suggested by a dermatologist. There was no aggravation of the lesions following GH therapy. Aside from these skin lesions, the patient had no personal history of atopy, and familial atopy history was also unremarkable. Following a dermatology consultation, a skin biopsy was performed. The pathological examination revealed CD4+ MF with epidermotropic and adnexotropic characteristics (**Fig. 2**). GH therapy was discontinued and topical steroid therapy was initiated. No additional treatment was required during the follow-up period as the lesions remained well-controlled with topical steroids.

Discussion

MF has been reported to affect adults around 50 years old, with a male predominance (7). However, we described a rare case of MF, a skin cancer uncommon in childhood, developing in an 11-year-old patient with TS. A wide variety of clinical presentations in patients with MF have been reported, including follicular papules, follicle-based patches, indurated plaques, hypopigmented, hyperpigmented, acneiform (comedones, cysts), or keratosis pilaris-like lesions (8). On the other hand, it has been reported that conditions such as hypopigmentation, hyperpigmentation, and alopecia accompany TS with a frequency of 5% (1), which may also be challenging to diagnose in its early stages, as the symptoms can mimic various benign skin lesions like eczema, psoriasis, or other non-cancerous skin disorders. Therefore, the diagnosis of MF, in such a case with TS, was surprising and unexpected. Yet, the clinical course of MF is usually indolent, characterised by a slow and gradual progression over years or even decades, from patches to more infiltrated plaques and then to tumors (7).

MF may simulate a diverse range of benign inflammatory skin disorders both clinically and histopathologically (9). The differential diagnosis of the patient's skin lesions initially included psoriasis and pityriasis rosea; in lesions with follicular accentuation, keratosis pilaris, pityriasis rubra pilaris, follicular mucinosis, and MF were considered. Histopathological examination revealed a thick band-like lymphocytic infiltrate in the superficial dermis and the presence of nonspongiotic epidermotropism, which is typically described in MF, helping to exclude other dermatoses **(Fig. 2a)**. The predominance of CD4 positive lymphocytes in both intraepidermal and dermal lymphocytes further supported the diagnosis of MF **(Fig. 2b and e)** (9). Additionally, biopsies taken from the patient's trunk showed not only epidermotropism but also folliculotropism.

Due to the presence of recurrent lesions over the last three years, we didn't consider that the 3-month GH treatment might be related to MF in our patient. However, given the possibility of increased Insulin-like growth factor-1 receptor (IGF-1R) expression with GH treatment (9), we decided to discontinue the therapy.

It is known that TS patients have a higher incidence of autoimmune diseases than the general population. Recent research has indicated an increased prevalence of autoimmune disorders, including inflammatory bowel disease, systemic lupus erythematosus, and type 1 diabetes mellitus, among individuals with MF. This association is believed to come from the T-cell dysregulation (10). The etiology of MF in TS may be associated with autoimmune processes.

The hormonal abnormalities and treatments associated with TS may influence the risk of hormone-related malignancies, and the chromosomal abnormality itself may also affect cancer risk (11). Ji et al. reported that patients with TS have an increased risk of solid tumors, particularly malignant melanoma and central nervous system tumors (12). Another study by Viuff et al. has stated that patients with the 45, X karyotype had a two to fivefold increased risk of benign CNS tumors, colorectal malignancies, and malignant melanoma, while TS women with the 45,X/46,XX karyotype had an increased risk of tongue cancer (3). In the latest guideline, the International Turner Syndrome Consensus Group recommends an annual skin assessment to identify dangerous lymphoedema, dermatitis, infections, autoimmune skin conditions and skin neoplasms, and appropriate evaluation and treatment by a dermatologist if indicated (13). We also believe that an annual assessment by a dermatology specialist may be beneficial, especially for the presence of skin lesions in cases with TS.

The present study, which addresses the management of MF in a girl with TS, makes an important contribution to the existing literature because, to our knowledge, the coexistence of MF and TS has yet to be reported. MF was treated successfully with topical steroids in this patient. After 12 months of follow-up, MF lesions were under control.

Conclusion

In conclusion, we presented a case of an 11-year-old girl with MF and mosaic TS. To our knowledge, this is the first reported instance of this rare combination. Considering the increased risk for malignancy in patients with TS, a thorough evaluation of skin lesions is crucial. Additionally, MF should also be considered as a possible differential diagnosis. A dermatologic assessment may be necessary to confirm the diagnosis and guide appropriate treatment.

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Table 1: Clinical and laboratory findings of the patient

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	At time of referral	**Last examination**
Anthropometric measurements		
Age (years)	11.2	12.2
Weight kg/(SDS)	40.5/(0.2)	53.6/(0.9)
Height cm/(SDS)	132.8/(-2.1)	138.1/(-2.5)
BMI kg/m^2/(SDS)	22.8/(1.4)	28.1/(2.3)
Puberty stage (Tanner)	B2P1	B3P2
Bone age (year)	12	12.5
PAH cm (SDS)	144	146,6
Target height cm (SDS)	159 cm (-0.69)	
Hormonal profile		
LH (mIU/mL)	2.2	5.9
FSH (mIU/mL)	12.2	12.2
E2 (pg/mL)	12.4	14
AMH (ng/mL) (n.r. 0.62-11)	0.36	
HbA1C (%)	5.1	5.2
	OGTT- glucose (mg/dL) 0.': 116 30.': 131 60.': 125 90.': 121 120.': 144	**OGTT- insulin (µU/mL)** 0.': 29 30.': 168 60.': 6 90.': 9 120.': 36
Imaging		
Echocardiogram	Bicuspid aorta	
Renal US	Normal	
Pelvic US	R ovary 2.1 mL, L ovary 1.2 mL, uterus 3.8 mL	

Figure 1: Erythematous rash in **(a)** the nape of the neck and **(b)** the axilla

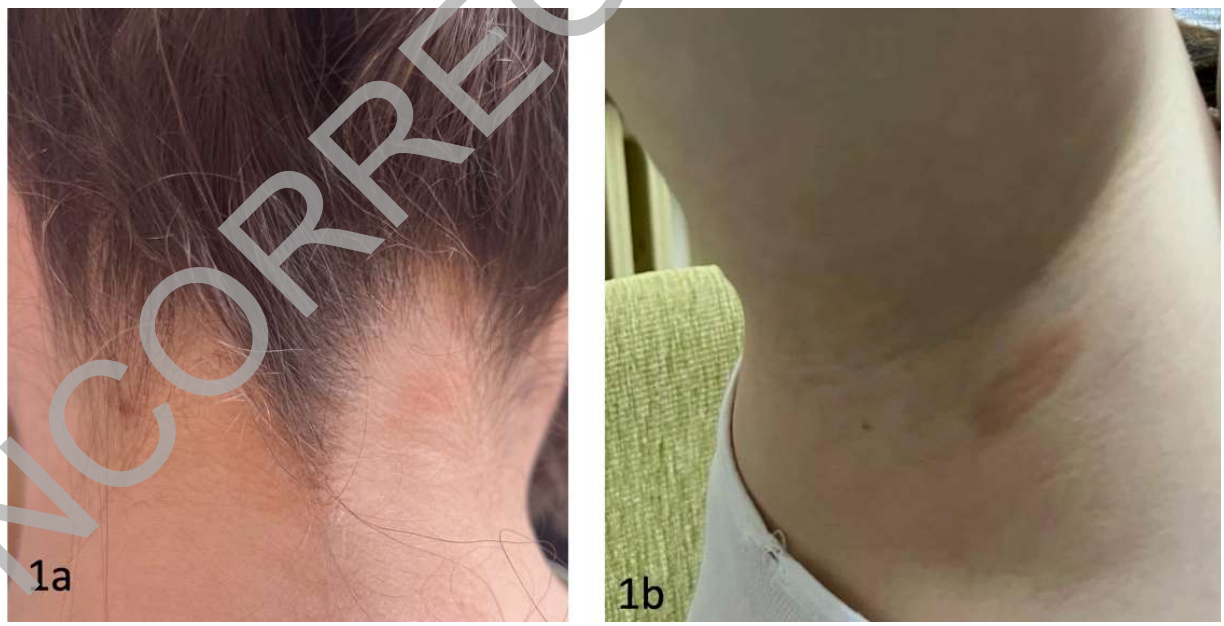

Figure 2: **(a)** Lymphocytic infiltration in the superficial dermis, with a band-like pattern, intermittently contacting the epidermis, in the biopsy taken from the left axilla (HEX50), **(b)** Predominance of CD4 staining within the infiltration (CD4X50), **(c)** CD8 staining of the same specimen (CD8X50), **(d)** In the biopsy taken from the left side of the trunk, a weaker infiltration is observed in the superficial dermis, while a lymphocytic infiltration around follicles and skin appendages is noticeable in the deeper layers. (HEX50), **(e)** Predominant CD4 positivity within the infiltration (CDX50), **(f)** Sparse reaction of CD8 staining in dermal lymphocytes (CD8X50)