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CASE REPORT

Dress Syndrome Induced by Antifimics Drugs: Literature Review and Case Report

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Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is an uncommon but potentially life-threatening adverse response to specific medications. Typical clinical features include fever, exanthema, lymphadenopathy, and eosinophilia, with possible involvement of vital organs. Adverse reactions may also result from antituberculosis drugs, presenting a risk to patients due to the potential necessity of temporarily discontinuing therapy. Such interruptions can compromise the efficacy of treatment and subsequently hinder patient recovery. We report a rare case of DRESS syndrome in a 16-year-old, triggered by first-line antituberculosis drugs, a rare case in pediatric population. Therapy was continued, and the patient's condition resolved following the suspension of causal drugs and implementation of a modified therapeutic scheme.

Keywords: Antituberculosis Drugs, Drug Reaction with Eosinophilia and Systemic Symptoms (Dress), Tuberculosis.

1. Introduction

Tuberculosis (TB) continues to represent a significant source of global morbidity and mortality, despite substantial progress in diagnostic and therapeutic approaches.[1]

Although there have been developments in anti-tuberculosis drugs (ATDs), the standard first-line treatment for non-resistant TB continues to be the RIPE regimen, which includes rifampicin (R), isoniazid (I), pyrazinamide (P), and ethambutol (E).[1]

Adverse Drug Reactions (ADRs) represent a significant cause of hospital admissions and may result in serious outcomes, including temporary or permanent complications and, in severe cases, death

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due to multiple organ dysfunctions such as liver failure, pulmonary hemorrhage, necrosis, and sepsis. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, also referred to as Drug-Induced Hypersensitivity syndrome, was initially described in 1950 by physician Bernard H. Chaiken in a patient using anticonvulsants.[2]

DRESS syndrome (DS) is a rare hypersensitivity reaction associated with over 50 different drugs, including antipsychotics such as clozapine; antibiotics like azithromycin, beta-lactams, dapsone, levofloxacin, minocycline, sulfonamides, and vancomycin; antiepileptics such as carbamazepine, phenobarbital, phenytoin, lamotrigine, and oxcarbazepine; and antiretrovirals including abacavir and nevirapine. [2, 4] An incidence rate between 1 in 1,000 and 1 in 10,000 drug exposures has been reported, with estimates varying from 0.9 to 10 cases per 100,000 individuals. The associated mortality rate is approximately 10% to 20%. [3, 4] DS typically appears two weeks to three months after starting the medication and mainly presents as fever, rash, lymphadenopathy, eosinophilia, facial swelling, and rarely, vital organ involvement.[3, 4, 5]

The precise pathological mechanisms underlying this disorder remain undetermined. Some researchers attribute this phenomenon to an accumulation of toxic metabolites resulting from genetic or environmental alterations affecting the drug detoxification pathway. The cytochrome P450 (CYP450) enzyme system plays a key role in metabolizing anticonvulsant agents into toxic metabolites, while the epoxide hydrolase enzyme is responsible for their subsequent detoxification. Individuals with certain genetic susceptibilities may exhibit reduced activity of this enzyme.[5]

DS occurs as a delayed-type hypersensitivity response involving lymphocytes. During the initial stage, antigen-presenting cells previously exposed to the antigen (such as a drug or its metabolites) activate both CD4+ and CD8+ lymphocytes. This process results in the production of cytokines such as IL-4 and IL-5, which contribute to skin inflammation. The pathophysiology of DS involves impairments in drug detoxification mechanisms, such as slow acetylation, resulting in the buildup of reactive metabolites that can initiate immunological responses. [5]

The development of this condition involves a complex interaction of factors, including drug exposure, immune dysfunction, viral reactivation (particularly human herpesvirus 6, HHV-6), and genetic predispositions, such as HLA-B58:01 for allopurinol and HLA-A32:01 for vancomycin. [3, 4]

While the same pharmacological agents may trigger DS, Stevens-Johnson syndrome, toxic epidermal necrolysis, Sézary syndrome, systemic lupus erythematosus, staphylococcal scalded skin syndrome, among others, each condition exhibits distinct clinical features that aid in differentiation. Accurate diagnosis requires that healthcare professionals possess comprehensive knowledge of these disorders to ensure effective identification and management. [2, 4, 5]

ATDs rarely cause DS. The primary culprits are first-line drugs: rifampin, isoniazid, pyrazinamide, and ethambutol. DS from ATDs occurs more often in adults than children and affects both sexes, with about 95% of cases linked to these first-line agents, including the RIPE regimen. [3] DRESS syndrome from antituberculosis drugs (DS-ATDs) is rare but increasingly recognized. Over 75% of cases involve first-line ATDs, with up to 48.1% linked to multiple drugs. Group A drugs like quinolones and linezolid (LZD) account for less than 2% of cases, and only three LZD-related cases have been reported. [3, 6] In recent years, reports of DS-ATDs cases have increased. This issue affects public health, as discontinuing first-line medications may reduce treatment effectiveness, raise therapeutic costs, extend treatment duration, increase the likelihood of drug resistance, and affect adherence. As a result, desensitization is considered an important strategy for facilitating the reintroduction of ATDs that have previously caused hypersensitivity. [6]

DS-ATDs is a rare condition, with only a limited number of cases reported in the pediatric population in medical literature. Early diagnosis in this age group requires careful consideration, as timely identification may help reduce morbidity and mortality. [7] Diagnosing DS is challenging. Criteria include acute rash, fever over 38°C, at least one lab abnormality (e.g., abnormal lymphocyte count, low platelets, or eosinophilia), involvement of multiple organs, enlarged lymph nodes in more than two areas, and hospitalization. [2, 4] A significant majority (97%) of patients have skin rash. Among these individuals, 60% exhibit a maculopapular rash, 54% demonstrate a generalized erythematous rash, and facial edema—most prominent in the periorbital region—is observed alongside a 39% incidence of cheilitis. The maculopapular rash typically manifests as pruritic and may advance to erythroderma accompanied by scaling. Additional findings can include sterile pustules, either follicular or non-follicular, bullae, and in certain cases, mucosal involvement. Initial areas affected generally include the face, trunk, and upper extremities, with subsequent involvement of the lower extremities. Notably,

all patients presenting with a skin rash experience involvement of more than 50% of their total body surface area. [5] However, diagnostic difficulty arises when there are systemic symptoms without cutaneous manifestations. [7]

Renal manifestations occur in up to 8% of individuals with DS, with acute interstitial nephritis (AIN) identified as the most commonly observed condition. The co-occurrence of NIA and acute pyelonephritis (PNA) in DS has not been reported in the medical literature. [2, 4, 5] In DS, 94% of patients show liver involvement, with 59% having elevated transaminases and 12% presenting hepatomegaly. Liver effects range from mild to severe damage or failure, making this a key diagnostic feature due to the organ's frequent involvement in the hypersensitivity reaction. [4, 5] ATDs-induced hepatitis is defined according to the following criteria:

1. Normal liver chemistry before starting treatment.
2. The patient was receiving isoniazid, rifampin, pyrazinamide, or ethambutol, alone or in combination, for at least 5 days before developing an abnormal liver function test.
3. *An increase in ALT and/or AST up to 3 times the upper limit of normal with symptoms or an increase in ALT and/or AST up to 5 times the upper limit of normal without symptoms.*
4. Elevated liver function tests without other apparent cause (primarily rule out acute infectious hepatitis).
5. Normalization of liver function tests, or at least 50% improvement from previously abnormal values, upon discontinuation of ATDs. [1]

1.1 Degrees of Hepatotoxicity (according to WHO)[1]

MILD. Elevation of AST and/or ALT of 3–5 times the upper limit of normal (121 to 200 U/L).

MODERATE. Elevation of AST and/or ALT of 5–10 times the upper limit of normal (201 to 400 U/L).

SEVERE. Elevation of AST and/or ALT more than 10 times the upper limit of normal (More than 400 U/L).

Five percent of individuals are affected by lung disease, while two percent have central nervous system disorders, and another two percent experience heart conditions, including pericarditis or myocarditis. [5] Internal organ involvement may include arthritis, myositis, pancreatitis, meningoencephalitis, thyroid conditions such as transient hypothyroidism and thyroiditis, as well as syndrome of inappropriate antidiuretic hormone secretion. [5] Hematologic abnormalities include hypereosinophilia in 66% of patients (average eosinophil counts: 3.5 – 4.1 × 10^9/L), atypical lymphocytes in 27%, lymphopenia in 51.9%, atypical lymphocytosis in 18.5%, and thrombocytopenia in 3.7%. [5] Multiple diagnostic scoring systems exist for the evaluation of DS.

The RegiSCAR (Registry of Severe Cutaneous Adverse Reaction) scoring system is a European registry used to assess the severity of cutaneous adverse reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and DS (**Table 1 and 2**). [5] Like the RegiSCAR diagnostic criteria, the Bocquet and Japanese Consensus Group criteria serve as diagnostic tools for identifying and characterizing DS, and for evaluating drug-related risks (**Tables 3 and 4**). [4, 8, 9]

Table 1. [9]

RegiSCAR study group
Three or more Asterix (*) criteria are required for the diagnosis of DRESS
1. Hospitalization
2. Reaction suspected to be drug related
3. Acute Rash*
4. Fever above 38 °C*
5. Enlarged lymph nodes involving at least two sites*
6. Involvement of at least one internal organ*
7. Blood count abnormalities*
a. Lymphocytes above laboratory limits
b. Eosinophil above laboratory limits(in percentage or absolute count)
c. Platelet count below laboratory limit

The RegiSCAR system categorizes DRESS cases as definite (score ≥6), probable (score 4–5), possible (score 2–3), or not DRESS (score <2). [4, 8, 9]

Table2[8, 9]

RegiSCAR scoring system			
Features	**No**	**Yes**	**Unknown**
• Fever (>38.5°C)	-1	0	-1
• Enlarged lymph nodes (> 2 sites, > 1 cm)	0	1	0
• Atypical lymphocytes	0	1	0
• Eosinophilia			
▪ 700-1499 o 10–19.9%	0	1	
▪ >1500 o >20%		2	
• Skin rash			
▪ Extent >50%	0	1	
▪ At least 2: edema, infiltration, purpura, scaling	-1	1	
▪ Biopsy suggesting DRESS	-1	0	
• Internal organ involvement			
▪ One	0	1	0
▪ Two or more		2	
• Resolution >15 days	-1	0	-1
• ≥3 biological test to exclude alternative diagnosis	0	1	0

Sasidharanpillai et al. evaluated the Japanese criteria and found that it did not identify a considerable number of DS cases, including severe forms. Based on these results, the group recommends using the RegiSCAR scoring system for the diagnosis of DS. [9]

Table 3.[8, 9]

Bocquet et al
DRESS is confirmed by presence of 1 and 2 and 3
1. Cutaneous drug eruption.
2. Adenopathies >2 cm in diameter or hepatitis (liver transaminases > 2 times the upper limit of normal) or interstitial nephritis or interstitial pneumonitis or carditis.
3. Hematological abnormalities: a. Eosinophilia > 1.5 x 10^9/l. b. Atypical lymphocytes.

Evaluation of renal function involves the measurement of serum creatinine, glomerular filtration rate, creatinine clearance, 24-hour urine proteinuria, and urinary sediment. [5]

Table 4.[8]

Japanese consensus group
Typical DRESS (presence of all seven criteria); atypical DRESS (all criteria present except lymphadenopathy and HHV-6 reactivation)
1. Maculopapular rash developing > 3 weeks after starting drug. 2. Prolonged clinical symptoms 2 weeks after discontinuation of causative drug. 3. Fever above 38 °C. 4. Lymphadenopathy. 5. ALT>100 U/l or other organ involvement. 6. HHV-6 reactivation. 7. Leucocyte abnormalities (at least one): a. Leukocytosis (>11 x 10^9 /L) b. Atypical lymphocytosis (>5%) c. Eosinophilia (1.5 x 10^9 /L)
ALT= Alanine Aminotransferase HHV= human herpes virus

A complete blood count, peripheral blood smear, lactate dehydrogenase (LDH), ferritin, lipid profile, and clotting times are used to identify hematologic abnormalities. Liver function tests are performed to assess possible liver involvement. [5] Cardiac enzymes, an electrocardiogram, and a chest x-ray are used to assess cardiac and pulmonary involvement. Additional laboratory and imaging tests may be performed based on the clinical condition of the patient. [5] Identifying the causative drug can be challenging, as first-line ATDs are typically administered in combination therapy. [7] When DS-ATDs occur, experts typically suggest discontinuing the causative drug. In tuberculosis treatment, desensitization methods are also available for recovery from DS-ATDs. This approach has the potential to enhance cure rates, decrease costs, and reduce treatment duration. Consequently, patients may continue first-line therapy under the guidance of their primary care physician. Nonetheless, this methodology remains significantly underutilized.

Conversely, it is important to note that some patients, following multiple unsuccessful attempts to resume treatment, choose to discontinue their therapy. The rate of treatment abandonment solely attributable to skin reactions ranges from 4% to 10%. [3, 4]

Topical corticosteroids offer symptomatic relief; however, systemic steroids are typically required for effective management. Additional immunosuppressive therapies or concurrent administration of intravenous polyvalent immunoglobulin may also be considered. [4, 5] There are no universally accepted criteria for determining severity; however, it has been suggested that patients with transaminase levels five times above the upper limit of normal, along with pulmonary, renal, or cardiac involvement, may be classified as having severe clinical manifestations. In such cases, systemic steroids (dexamethasone, prednisone, or prednisolone) administered for eight weeks have been proposed as a management approach. [5] Desensitization protocols typically begin with the ATDs that are considered less likely to have caused DS. Moran et al. reported that rifampin and isoniazid were associated with over 68% of DS-ATDs cases, while Jin et al. identified rifampin (75.5%) and isoniazid (62.3%) as primary causes. In a literature review by Sharifzadeh et al. on antibacterial antibiotic-induced DS, 107 out of 254 cases involved ATDs. Rifampin was most frequently implicated, followed by isoniazid, ethambutol, and pyrazinamide; fluoroquinolones have also been reported in some cases. [7, 8] A retrospective cohort study conducted by Jung et al. involving 1,253 adult tuberculosis patients undergoing anti-tuberculosis (anti-TB) treatment reported a prevalence of DS of 1.2%. Alloucherry et al. conducted a case series (n=76) on DS associated with ATDs and reported that all drugs carried a risk of DS. Their findings indicated that rifampicin was most frequently identified, followed by isoniazid, ethambutol, and pyrazinamide. Rifampicin possesses a wider range of therapeutic indications, which may account for its higher number of reported suspected cases; nevertheless, allergy screening identifies isoniazid as being most strongly associated with DS. [9] According to the findings of Moran et al. it is recommended that desensitization begin with first-line drugs using the following sequence: pyrazinamide, subsequently ethambutol, then isoniazid, and lastly rifampicin. [6] Patients require management in the intensive care unit or specialized burn units, ensuring multidisciplinary and comprehensive care. Patients with DS typically experience improvement after discontinuing the offending drug and initiating systemic steroids. Fever often subsides within two days, the rash usually resolves in about 10 days, and liver function tests generally return to baseline after approximately 33 days. [5] Reintroducing or desensitizing anti-TB treatment in our country is challenging because the intensive phase relies on DoTBal (SILANES, Mexico), a tablet combining the four main first-line drugs, and the maintenance phase uses DoTBal-S (SILANES, Mexico), which contains only rifampicin and isoniazid. These fixed combinations limit access to individual drug formulations. Recently, dispersible tablets for children have been introduced, but they also come as multi-drug combinations for both treatment phases.

2. Case Presentation

We present a 16-year-old male with a family history of pulmonary tuberculosis (PTB)—his mother being affected at the time of admission—was evaluated in our medical unit. The patient received BCG vaccination at birth. His symptoms began on April 15, 2024, including productive cough, asthenia, hyporexia, and weight loss. He appeared at the Health Center on May 17, 2024, where PTB was diagnosed based on clinical and epidemiological findings(known exposure to maternal PTB, relevant clinical manifestations, and chest radiography consistent with active tuberculosis). Imaging revealed micronodular infiltrates in both lung bases and the right apical region, as well as linear opacity in the right upper lobe. (**Figure 1**).

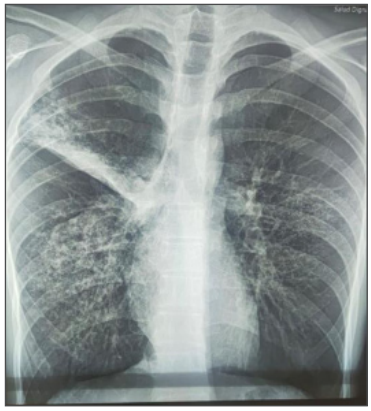

Figure 1. *Initial chest radiograph performed on May 17, 2024*

The patient started DoTBal treatment (rifampicin, isoniazid, pyrazinamide, ethambutol, SILANES, Mexico) on May 21, 2024. Eighteen days later, they developed a fever and received medication from a private physician: metamizole sodium with butylhyoscine, meclizine with pyridoxine, and chlorphenamine. Two hours after taking the medication, a generalized rash appeared. (**Figure 2**).

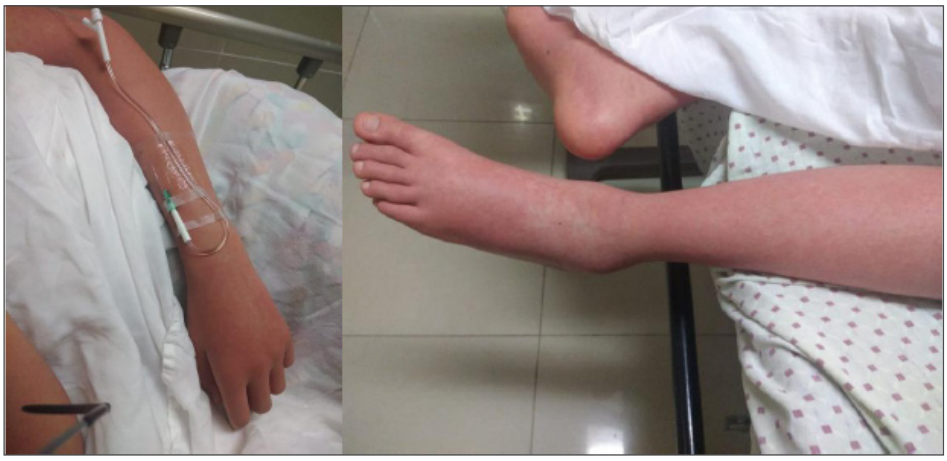

Figure 2. *A maculopapular rash is noted on the patient's upper and lower extremities.*

On June 11, 2024, the patient visited the Health Center and received prescriptions for dexamethasone and diphenhydramine over a three-day period. On June 16, 2024, he developed edema affecting both the upper and lower extremities (**Figure 3**). Subsequently, the patient consulted a private physician, who suspected an adverse drug reaction, discontinued the anti-TB therapy, and referred him to the hospital for further evaluation. The patient was admitted to the internal medicine service on June 21, 2024. Initial laboratory tests indicated abnormal liver function, with total bilirubin measured at 7.93 mg/dL, direct bilirubin at 6.53 mg/dL, aspartate aminotransferase (AST) at 1676 U/L, and alanine aminotransferase (ALT) at 2024 U/L. Physical examination showed icteric skin and sclera (**Figure 4**).

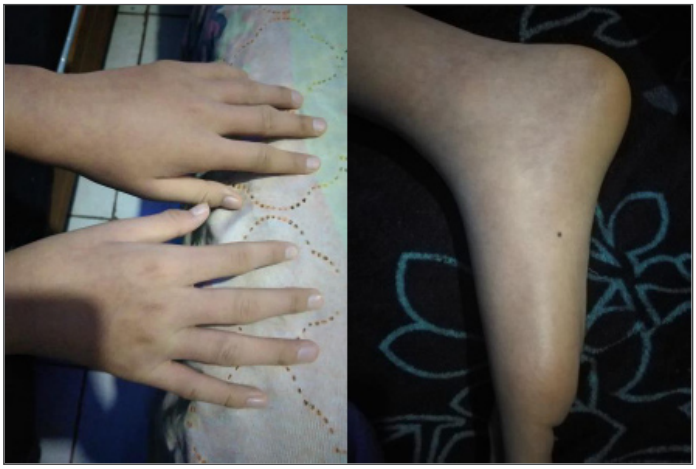

Figure 3. *Presence of edema affecting both upper and lower extremities.*

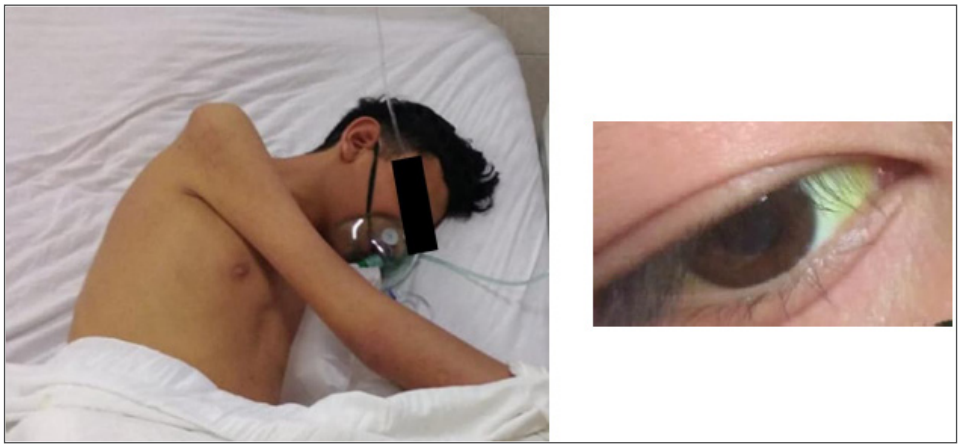

Figure 4. *The skin and sclera exhibit an icteric discoloration.*

Table 5 presents the timeline of liver function test (LFT) results recorded during the patient's hospitalization. The following diagnostics were established: a) acute liver failure associated with drug exposure (likely ATDs); b) mixed alkalosis; and c) West Haven I hepatic encephalopathy. On June 26, 2025, the patient was admitted to the intensive care unit and received treatment with Hepa-Merz, acetylcysteine, lactulose, metamizole, vitamin K, omeprazole, haloperidol, and magnesium sulfate. On June 28, 2024, grade II microcytic-hypochromic anemia and mild thrombocytopenia were documented. By July 3, 2024, while the patient remained in intensive care, he was noted to be asymptomatic, exhibiting no signs of hepatic encephalopathy, fever, or seizures. On July 4, 2024, the patient exhibited a generalized rash accompanied by pruritus and fever (up to 39.2°C). Evaluation by an infectious disease specialist resulted in prescription of an alternative anti-TB regimen consisting of amikacin, linezolid, and levofloxacin. On July 11, 2024, the patient was transferred from the intensive care unit to the internal medicine department. In view of favorable clinical progress, the patient was subsequently discharged on July 16, 2025. Final diagnoses included: (a) pulmonary tuberculosis; (b) hepatotoxicity secondary to DoTBal therapy; and (c) malnutrition.

The Jurisdictional Tuberculosis Program referred the patient to our medical unit on July 24, 2024, for initiation of individualized treatment due to a potential risk of toxicity associated with ATDs. On admission, the patient weighed 43 kg (<3rd percentile), was 165 cm tall (10th percentile), had a BMI of 15.8 kg/m² (<3rd percentile), temperature of 36.8°C, heart rate of 79 bpm, and respiratory rate of 19 breaths/min. Blood pressure (BP) was 123/72 and oxygen saturation (Sat O2) was 98%. The patient was admitted with the following diagnoses: a) pulmonary tuberculosis; b) drug-induced hepatotoxicity; and c) low body weight. Individualized treatment with ethambutol was initiated on July 24. Subsequently, pyrazinamide was introduced on July 27. Following this addition, the patient developed a pruritic skin rash and fever reaching 39.8 °C, prompting commencement of hydroxyzine therapy. Pyrazinamide was discontinued, while ethambutol treatment was maintained. On July 28, the patient's rash resolved, and by July 29, body temperature returned to normal. Rifampicin was initiated on July 29. On July 30, following the administration of rifampicin, the patient exhibited icteric staining of the sclerae. Laboratory tests conducted on July 31, 2024, showed a Complete Blood Count (CBC) with 10,390 leukocytes/µL, eosinophils at 4,300/µL (41.4%), and hemoglobin (Hb) of 10.10 g/dL. The complete metabolic panel (CMP) revealed urea at 101 mg/dL, urea nitrogen at 47.2 mg/dL, and creatinine at 1.49 mg/dL. Liver function tests indicated total bilirubin of 2.14 mg/dL, direct bilirubin of 1.51 mg/dL, indirect bilirubin of 0.63 mg/dL, Gamma Glutamyl Transferase (GGT) at 133 U/L, AST at 350 U/L, ALT at 1201 U/L, lactate dehydrogenase (LDH) at 341 U/L, and globulin at 5.45 g/dL. ATDs were discontinued once more. **Table 6** presents the timeline of laboratory results obtained during outpatient management.

DS was diagnosed based on clinical data, RegiSCAR and Boquet criteria: a rash three weeks after ATDs, leukocytosis, eosinophilia >1,500/L, organ involvement, fever >38°C, suspected drug reaction, and hospitalization. On August 5, 2024, prednisone and omeprazole were started, and hydroxyzine was stopped.On August 20, laboratory tests were reported as being within normal ranges. A gradual reduction of prednisone was started, and ATDs were reintroduced at low doses with daily increases until full dosages were reached in the following sequence: ethambutol, isoniazid, pyrazinamide, and rifampicin. No adverse effects were noted after the administration of ethambutol. However, upon the reintroduction of isoniazid and pyrazinamide, the patient developed a skin rash and fever reaching 40°C. ATDs were discontinued again, and additional laboratory tests were ordered. The patient remains on prednisone, hydroxyzine, paracetamol, and omeprazole. Laboratory tests from August 28 showed an increased leukocyte count with eosinophils measured at 1200/µL and persistently elevated liver enzymes (refer to **Table 6**). Laboratory tests from September 4, 2024, showed all results were normal except for an elevated ALT of 216 U/L; the patient remained asymptomatic. Due to side effects from isoniazid and pyrazinamide, both drugs were stopped. On September 12, 2024, rifampicin, ethambutol, and levofloxacin were reintroduced at low doses, with daily increases in the order: ethambutol, rifampicin, then levofloxacin. Hydroxyzine was re-prescribed, and a progressive reduction of prednisone was implemented. On September 20, 2024, the patient began a full ATDs regimen at standard therapeutic doses with no reported adverse events. Prednisone was gradually tapered and discontinued on September 26, 2024. Hydroxyzine therapy ended on October 17, 2024. The patient received monthly medical evaluations and ongoing treatment for nine months, ending on June 16, 2025, with no adverse events noted during

that period. All sputum smears and cultures obtained during the patient's treatment at our institution were negative. As part of our responsibilities, we conducted a contact investigation, which revealed active pulmonary tuberculosis in the patient's brother and latent tuberculosis infection in the father; both were successfully treated at our medical unit. The patient's mother also completed her treatment at her own medical facility.

Table 5. *Liver function tests during the patient's hospitalization.*

DATE	TOTAL BILIRUBIN (mg/dL)	DIRECT BILIRUBIN (mg/dL)	AST (U/L)	ALT (U/L)
06/21/2024	7.93	6.53	1676	2024
06/22/2024	9.83	7.90	860	1421
06/24/2024	15.35	11.32	362	1111
06/25/2024	20.58	15.76	307	1098
06/26/2024	22.12	17.91	172	882
06/27/2024	15.42	11.41	142	553
06/28/2024	10.76	7.59	105	420
06/30/2024	8.05	5.89	145	358
07/01/2024	6.71	5.11	119	267
07/03/2024	9.65	8.16	181	281
07/04/2024	9.72	8.23	363	385
07/05/2024	10.22	8.74	520	556
07/06/2024	8.45	7.08	285	452
07/07/2024	6.67	5.73	174	357
07/08/2024	6.04	5.15	131	285
07/09/2024	5.39	4.61	108	252
07/10/2024	4.47	3.68	79	216
07/11/2024	3.57	2.90	63	183
07/12/2024	3.36	2.58	57	155
07/15/2024	2.27	2.26	47	95

Table 6. *Laboratory tests during the patient's outpatient treatment.*

DATE	TOTAL BILIRUBIN (mg/dL)	DIRECT BILIRUBIN (mg/dL)	AST (U/L)	ALT (U/L)	LEUKOCYTES (/µl)	EOSINOPHILES (/µl)
07/31/2024	2.14	1.51	350	1201	10,390	4,300
08/14/2024	1	0.4	21	48	11,200	11.2
08/28/2024	1.4	0.4	540	470	14,050	1200
09/04/2024	0.5	0.1	42	216	10.930	770
09/18/2024	1.3	0.4	85	146	12,900	1,210
10/10/2024	0.7	0.1	44	19	6,340	1,660
11/06/2024	-	-	27	19	4.080	1,070
12/12/2024	-	-	25	18	5,100	360
01/08/2025	-	-	24	16	4,000	330
02/05/2025	-	-	27	16	3,500	220
03/04/2025	-	-	21	14	5.100	350
04/09/2025	-	-	26	18	5,000	240
05/06/2025	-	-	23	18	5,200	360
06/04/2025	-	-	23	13	4,800	200
07/09/2025	-	-	22	12	5.000	220

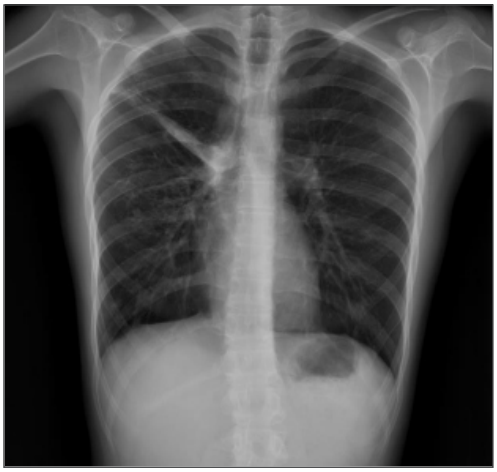

Figure 5. *Thoracic radiography performed at the end of treatment on June 11, 2025*

3. Discussion

In the hospitals of our country, the management of adolescent patients presents certain challenges. Most pediatric hospitals only accept patients under 15 years of age, while it is uncommon for adolescents to be treated by physicians who typically care for adults. This gap can complicate appropriate and timely care for this age group. Our patient was treated in a general hospital by specialists in internal medicine and adult intensive care, under the diagnosis of hepatotoxicity due to ATDs. The possibility of a diagnosis of DS was not initially considered, likely due to the diagnostic complexity of this condition and the limited number of cases reported in the pediatric literature. This highlights the challenges in recognizing DS in adolescent patients, particularly outside pediatric-focused settings.The diagnosis of DS was established in our medical unit, based on the clinical data described in the preceding paragraphs. As reported in the medical literature, our patient developed the first signs and symptoms suggestive of DS 18 days after initiating anti-TB treatment. These symptoms were primarily characterized by fever, rash, eosinophilia, edema, and internal organ involvement. As described in the literature, the skin rash in our patient was a generalized maculopapular eruption. In addition, there was clear evidence of liver and kidney involvement. The patient presented with severe hepatotoxicity, with liver enzyme levels exceedingly more than 10 times the upper limit of normal, as detailed in **Table 6**. According to the literature, up to 95% of DS cases associated with ATDs are caused by first-line group, with up to 48.1% involving two or more drugs from this group, scenario that occurred in our patient. Although rifampin is the most frequently reported ATD associated with DS, in our case, isoniazid and pyrazinamide were identified as causative agents.

The therapeutic regimen consisting of rifampicin, ethambutol, and levofloxacin was selected in accordance with current guidelines for the management of patients exhibiting polyresistance to isoniazid and pyrazinamide. [10] The patient's anti-TB treatment was carried out using video directly observed therapy (VDOT). It is important to note that, after presenting skin reactions, between 4% and 10% of patients discontinue treatment. Fortunately, this did not occur in our case; the patient not only continued with the anti-TB regimen but also achieved 100% adherence to VDOT over the 9-month treatment period. The patient was hospitalized for 25 days, 15 of which were spent in intensive care. He received steroid therapy for 9 weeks, which gradually tapered until discontinuation. Although clinical and laboratory findings were sufficient to establish a definitive diagnosis of DRESS syndrome, it would have been valuable to expand the investigation by assessing additional parameters, such as IgE levels, as well as potential genetic predispositions, including histocompatibility antigens, particularly human leukocyte antigens (HLA).

4. Conclusions

Early diagnosis and timely initiation of effective treatment improve patient prognosis and reduce the mortality associated with this disease. Similarly, the prompt reintroduction of ATDs not only mitigates the serious public health challenges posed by both DRESS syndrome and tuberculosis but also decreases the risk of developing resistance to ATDs.

Patient Consent Statement.

The authors certify that they have obtained informed consent from the patient's parents. In the consent form, the parents authorized the use of the patient's images and other clinical information for publication in this article. They understand that the patient's name and initials will not be disclosed and that all reasonable efforts will be made to protect the patient's identity.

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