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DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS): A COMPREHENSIVE REVIEW

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ABSTRACT

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare but severe drug-induced hypersensitivity reaction with high morbidity and potential mortality if not promptly identified and managed. It is characterized by a triad of skin eruptions, systemic organ involvement, and hematologic abnormalities such as eosinophilia, DRESS syndrome presents a diagnostic challenge due to its variable presentation and delayed onset after drug exposure. This comprehensive literature review synthesizes findings on the epidemiology, pathogenesis, clinical manifestations, diagnostic criteria, and therapeutic strategies associated with DRESS syndrome. The review includes three pairs of basic pathophysiological pillars that underlie DRESS, a systemic illness, encompass: (1) inciting stimuli, including drugs; including anticonvulsants, antibiotics, antivirals, antidepressants etc. (2) genetic factors, such as ethnic predisposition with specific human leukocyte antigens (HLA); and CYP Polymorphisms (3) viral factors, or the reactivation of herpes virus family members, such as Epstein Barr Virus (EBV), cytomegalovirus (CMV), human herpes virus 6 (HHV-6), and HHV-7. Additionally, the literature highlights diagnostic tools like the RegiSCAR criteria and examines current management practices. Early detection and prompt suspension of the offending medicine are the most crucial measures to stop the disease from getting worse. This study focuses on corticosteroid use, alternative immunosuppressive therapies and the use of JAK inhibitors.

KEYWORDS: DRESS syndrome, RegiSCAR criteria, corticosteroid, JAK inhibitors.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS), also known as drug-induced hypersensitivity syndrome (DiHS), is a severe cutaneous adverse reaction (SCAR)[1] and a rare but severe, potentially fatal, idiosyncratic adverse drug reaction with cutaneous and systemic manifestations. It is distinguished by widespread skin involvement with mucocutaneous and multisystem involvement (exanthem), fever, lymphadenopathy, hematologic abnormalities (eosinophilia, mononucleosis-like atypical lymphocytes), viral reactivation, and significant multisystem involvement, which includes haematologic, hepatic, renal, pulmonary, cardiac, neurologic, gastrointestinal, and endocrine abnormalities.[4][5] The first reports of this syndrome date back to the 1950s under various names, such as "anticonvulsant hypersensitivity syndrome," "drug-induced hypersensitivity syndrome," "drug-induced delayed multiorgan hypersensitivity syndrome," or "drug-induced pseudo lymphoma," but it was Bocquet et al. who first reported it in 1996 as the "DRESS syndrome." Regretfully, DiHS/DRESS continues to be a highly morbid and sometimes lethal condition linked to immunological after-effects and chronic organ failure.[1] With an incidence ranging from 1/1000 to 1/10,000 depending on the responsible drug and an estimated mortality rate of 10%, the symptoms usually appear two weeks to three months after taking the causative drugs. This indicates a potentially fatal Type-IV T cell-mediated delayed drug hypersensitivity reaction.[3][6] However, cases with a quick onset (less than two weeks after the drug intake) have been documented often in children. The rash may begin locally, affecting the face, upper trunk, and upper extremities at first, but it may spread swiftly to cover more than 50% of the body's surface area. Bullae and vesicles may appear late in the course as a result of persistent dermal edema and inflammation. Purpuric lesions are less common, but they are linked to a higher severity. Pustular rashes are another uncommon rash morphology associated with the disease. In DRESS syndrome, mucosal involvement such as hypertrophy of tonsils, cheilitis, pharyngitis, and oral mucositis might occur; however, they are rare and only occur at one site.[2] The most prevalent comorbidities associated with DRESS are hypertension, diabetes, epilepsy, HIV, and hyperuricemia. Rather than being a result of an innate tendency to DRESS, these co-occurring diseases are probably connected to the offending medication.[8]

Diagnosis may be delayed due to the diverse clinical presentation, which takes into account similarities to viral or lymphoproliferative disorders. Early detection, though, might make it easier to begin the right course of treatment.[4]

EPIDEMIOLOGY

Incidence of DRESS varies according to the patient's immune system and kind of medicine, and many instances go undiagnosed or untreated. Over one occurrence is anticipated to occur in the general population for every 10,000 drug exposures. Additional information reveals a general population incidence of 10 cases per million and 0.9 cases per 100,000 individuals. This incidence varies from 2.18 to 40 per 100,000 inpatients among hospitalized patients. Black people and women have been found to have a higher incidence of DRESS. The mortality rate in DRESS can vary from 3.8% to 10%, even with the implementation of treatment.[7] The DRESS syndrome affects adults more frequently than children with a mean onset age of 40 to 60 years. There is a substantial correlation between DRESS and ethnic origin, since numerous studies have demonstrated that exposure to specific medicines can significantly increase the chance of particular human leukocyte antigen (HLA) alleles.

PATHOGENESIS

DRESS is categorized as a delayed type IVb, and occasionally IVc, hypersensitivity reaction. It is believed that a complicated interplay involving genetic susceptibility, viral reactivation certain medications and vaccine exposure. It can include the liver, lungs, or both, and occasionally it can result in lesions from bacterial ulcers. It should be mentioned that DRESS caused by antibiotics is not as severe as DRESS caused by anticonvulsants or allopurinol.[9]

Three pairs of fundamental pathophysiological pillars support DRESS, a systemic disorder: (1) inciting stimuli, including drugs; (2) genetic factors, such as ethnic predisposition with specific human leukocyte antigens (HLA); and (3) viral factors, or the reactivation of herpes virus family members, such as Epstein Barr Virus (EBV), cytomegalovirus (CMV), human herpes virus 6 (HHV-6), and HHV-7.[13]

1. Drugs

The following medications are frequently linked to dress syndrome:

Anticonvulsants: It is commonly observed that phenytoin and phenobarbital provoke seizures. Within two to six weeks of exposure, phenytoin can cause DRESS syndrome, which manifests as fever, rash, and systemic symptoms.[23] It can also be brought on by lamotrigine, carbamazepine, and valproic acid. Levetiracetam is infrequently associated with acute renal damage and DRESS syndrome.[27] For the best possible outcome for the patient, the medication must be stopped as soon as possible.[25][26]

Sulphonamides: Sulfasalazine, a sulphonamide, can cause DRESS syndrome, which manifests as fever, rash, and eosinophilia. Typically occurring 2-4 weeks after exposure to sulfasalazine, this disorder can be difficult to diagnose because of overlapping signs with other illnesses.[46][47] DRESS syndrome has also been linked to dapsone. Severe morbidity and mortality may result from this hypersensitivity reaction. Usually, DRESS syndrome appears two to six weeks following the start of dapsone medication.[52]

Antibiotics: DRESS syndrome is associated with exposure to antibiotics, especially in children.[28][31][34][37] Examples of these antibiotics include cefotaxime and meropenem, ciprofloxacin, and azithromycin. Even in the absence of a beta-lactamase inhibitor or sulfasalazine allergy, amoxicillin can cause Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, underscoring the significance of early detection and treatment.[29] According to a review of the FDA Adverse Event Reporting System database, glycopeptide antibiotics such as vancomycin and linezolid are strongly linked DRESS syndrome.[30] Minocycline is also linked causing, a potentially fatal severe hypersensitivity reaction involving many organs, such as the kidney, lung, and liver.[32] Antibiotic-induced DRESS syndrome shows less eosinophilia, a quicker rate of recovery, and a weaker RegiScar score. They are associated with less severe renal impairment and a short latency period.[33] Cephalosporin antibiotics have the potential to cause severe endocrine problems such as hypophysitis and thyroiditis by inducing DRESS syndrome.[36] DRESS syndrome without eosinophilia is a severe drug reaction that can occur even in the absence of eosinophils and manifest as skin eruption, fever, and organ involvement.[35]

Antiviral medications: Antivirals which include acyclovir, ganciclovir, lopinavir, ribavirin, ritonavir, zidovudine, nevirapine, efavirenz, fever, rash, and eosinophilia have been associated to DRESS syndrome.[38, 39][43] It has been documented that telaprevir is a prevalent agent in antiviral-induced DRESS syndrome, which manifests as rash, fever, eosinophilia, and liver damage.[9][40] In particular, HHV-6 reactivation instances are associated with ganciclovir-related DRESS.[42]

First-line anti-tubercular medications that can cause DRESS syndrome include pyrazinamide, ethambutol, isoniazid, and rifampicin; patients with these medications have a range of clinical presentations.[53] Second line anti-tubercular drugs (ATDs) were associated with the development of DRESS syndrome in the reported case of multidrug resistant tuberculosis.[54]

Allopurinol: This medication has the potential to cause DRESS syndrome, which is defined by acute renal injury, kidney-limited necrotizing vasculitis, eosinophilia, cutaneous eruptions, and systemic

symptoms. These symptoms typically appear two to six weeks after the medication is started and carry a high risk of morbidity and death.[44, 45]

Antidepressants: DRESS syndrome has been caused by a number of mood stabilizers, including certain antidepressants.

This involves medications like:
Lamotrigine: Used as a mood stabilizer and primarily as an anticonvulsant.[51] As demonstrated by a patient who, after eight weeks of medication, developed a severe rash, fever, and haematological abnormalities.[55]

Carbamazepine: Frequently prescribed for bipolar disorder, this medication is a well-known cause of DRESS.[51] It usually happens two to six weeks after the start of treatment and is characterized by maculopapulous exanthema, fever, hepatitis, leucocytosis, and eosinophilia.[56][57]

2. Viral Factors
Although other human herpes viruses, such as HHV-7, cytomegalovirus (CMV), Epstein-Barr virus (EBV), and herpes simplex virus (HSV), have been described, human herpes virus-6 (HHV-6) has historically been most commonly linked to DRESS. Reactivation of the virus usually happens 2-4 weeks after the onset of symptoms and has been linked to more severe results, flare-ups, and a longer duration of the illness.[8]

Patients with signs of viral reactivation have a worse prognosis in terms of disease duration, relapses, constitutional symptoms, and organ involvement. Four avenues exist for viral reactivation to participate in the aetiology of DRESS:
1. Viruses can directly harm tissue and aggravate the early signs of DRESS.

2. The immune response may target them later in the disease's progression. Regarding this, corticosteroid treatment and/or immunosuppression to manage DRESS signs may result in a "immune-reconstitution like" state.

3. In the context of systemic inflammation, viral reactivation may be the epiphenomenon of a larger evolution of virus-hosting immune cells. T-lymphocytes and monocyte/macrophage lineage cells are among the immune system cells that latent human herpes viruses (HHVs) actually live in permanently. Therefore, instead of serving as a DRESS trigger event, viral reactivation and release may serve as an early indicator of stimulation of these cell reservoirs after drug-driven growth.

4. Viral misspecification of antigen-specific cells and molecular mimicry may be utilized to enhance anti-drug responses. Additionally, subjecting DRESS patients and healthy subjects to EBV-immortalized B-lymphocytes challenged with DRESS culprit drugs selectively induces increases in EBV production in DRESS subjects, suggesting a generalized dysfunction of tolerance and pathogen control in both arms of the immune response during DRESS.[14]

3. Genetic factors
Genetic variables influencing immune responses and drug metabolism may increase vulnerability to drug hypersensitivity reactions.[15]

HLA Associations: Certain HLA alleles influence the incidence of DRESS syndrome. Prospective HLA testing can help prevent severe reactions in sensitive individuals.[19] Certain HLA alleles, such as HLAB*58:01, have been linked to hypersensitivity reactions to medications like allopurinol.[18] HLA-A*32:01 is substantially related to vancomycin-induced DRESS syndrome, especially in people of European heritage.[21] HLA-B*53:01 has been linked to DRESS syndrome following raltegravir treatment, notably in African and Hispanic populations.[22] Abacavir, acyclovir, ganciclovir, lopinavir, nevirapine, ribavirin, ritonavir, and zidovudine have all been linked to DRESS syndrome, possibly through processes involving HLAB1502 and HLAB5801.[43]

CYP Polymorphisms: Drug-metabolizing enzyme genetic variants, specifically CYP2C9, might impact the metabolism of medications such as phenytoin, potentially resulting in toxic buildup and the development of DRESS syndrome.[20]

CLINICAL MANIFESTATION
After taking medication for two to six weeks, symptoms usually start to appear. Even within 24 hours, re-exposure to the same medication may result in symptoms. Months or even weeks may pass after the medicine is stopped before the symptoms go away. The most typical symptoms include malaise, pharyngitis, fever (38–40˚C), and cervical lymphadenopathy. In 75% of instances, a generalized exanthemata's morbilliform rash appears concurrently with or shortly after the fever. Exfoliative erythroderma, purpuric lesions or blisters, follicular or non-follicular pustules, and tense bullae brought on by dermal edema are a few examples of skin appearances. The face, upper trunk, and extremities are the areas that are usually affected. The most suggestive of DRESS lesions are those that cover more than 50% of the body's surface area and/or two of the following: facial edema, purpura or scaling, and infiltrating lesions.[9]

In as many as 97% of cases, liver damage is the most prevalent visceral symptom of DRESS.[8] The primary cause of death linked to this illness, which affects 5% to 10% of cases, is full-blown hepatitis.[9]

From a moderate cough or dyspnea with nonspecific interstitial alterations on chest imaging to acute respiratory distress syndrome (ARDS) with potentially

fatal hypoxic respiratory failure, the pulmonary presentation of DRESS can take many different forms.[10]

When DRESS affects the kidneys, it can cause moderate acute kidney injury (AKI) or severe interstitial nephritis, which can occasionally lead to end-stage renal disease that is permanent. Renal impairment is most common in elderly individuals, allopurinol-associated DRESS, and those with pre-existing kidney disease.[8]

In certain DRESS syndrome instances, there have been reports of chronic enteropathy, pancreatitis, and intestinal symptoms such as diarrhea. There have been reports of some occurrences of colitis.

There may also be involvement of the cardiovascular system. Although myocarditis is rare (55%), it is linked to a high death rate. There may be tachycardia, arrhythmia, chest discomfort, nonspecific electrocardiography (ECG) abnormalities, and a drop in left ventricular ejection fraction.

Rarely can neurological involvement occur. There may be headaches, convulsions, coma, and motor impairment. Rarely reported are cases of HHV-6 reactivation and neurological symptoms including encephalitis and meningitis.

Since thyroid function abnormalities may be seen during DRESS syndrome, thyroid function monitoring is crucial. Additionally, spleen involvement has been documented in patients with DRESS syndrome, and it may possibly be linked to the development of diabetes and pancreatitis.[13]

Subsequently, hematologic involvement includes thrombocytopenia, atypical lymphocytosis (40%) hyper eosinophilia (90%), neutrophilia, and haemolytic anaemia. Long-term consequences of DRESS syndrome include autoimmune illnesses, such as Grave's disease and type 1 diabetes, which may appear months or years later.[9]

The peripheral nerve system may have polyneuritis and uveitis, while the musculoskeletal system may experience myositis and elevated creatine phosphokinase (CPK).[7]

The interval between drug exposure and the development of symptoms is longer than with other SCARs; reports have indicated both longer and shorter intervals. When the offending substance is re-exposed, symptoms may appear within hours or days. The medicine may also have an impact on lag time. As an illustration, compared to antibiotics or radiocontrast media, which have been demonstrated to have lag times of fewer than 14 days following exposure, antiepileptics and allopurinol typically have longer latency periods. More severe disease may be correlated with longer latency periods.[8]

DIAGNOSIS

Interviewing patients who arrive at an emergency department with symptoms and indicators of hypersensitivity if they have taken any medicine in the last six months is advised.[11]

Any time a patient presents with fever, skin eruptions, lymphadenopathy, and abnormal organ function tests after starting a new medicine within the last two to six weeks, DRESS should be investigated as a possible diagnosis. The three most prevalent characteristics in DRESS are fever, rash, and indications of liver injury. Since these findings may not all appear at the same time or in every instance, a high level of clinical suspicion is necessary to make the diagnosis.[2]

The most widely used methods for detecting DRESS in patients are the Collection of Biological Samples validation score and the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) to Drugs, both in clinical practice and in scholarly literature. Each suspected DRESS response can be categorized as no case, possible case, probable case, or definite case based on a number of factors, including fever, enlarged lymph nodes, eosinophilia, atypical lymphocytes, skin involvement, organ involvement, time to resolution, and assessment of other possible causes. One of the diagnostic criteria for DRESS is HHV-6 reactivation.

Recently, there has been interest in expanding the definition of the severity spectrum of DReSS. Simple MPE (maculopapular eruption), DReSS minor (also known as mini-DReSS, MPE/DReSS overlap, and systemic MPE), and DReSS or "DReSS major" are the divisions that some have suggested. DReSS major was defined as having a RegiSCAR score of ≥4 (DReSS minor as having a score of 1-3). those with DReSS major had higher liver enzyme increases, more facial edema, and needed longer immunosuppressive treatments than those with DReSS minor. Therefore, it is important to distinguish between DReSS major and minor, as either one is a more severe form of the disease, and facial edema can aid in this process.[8]

It is important to try to identify relevant agents (drug causation) in the weeks to months before the sickness starts.

Diagnosing the culprit drug(s)

Patch tests

Patch testing and recording the history of drug use are part of the assessment process to determine whether substance or drugs are at fault. Patch testing can, in fact, be quite useful in determining which medications caused DRESS. Intradermal tests (IDTs) or prick tests are the next diagnostic step after patch tests come back negative.

Intradermal tests

Both rapid and delayed medication hypersensitivity reactions can be detected with intradermal testing. These

tests were formerly thought to be contraindicated in SCARs (DRESS, AGEP, SJS/TEN) because, although extremely seldom, serious and even deadly reactions have occurred despite the low dosages used. Only medications that are available in commercially produced sterile parenteral formulations are used for IDTs. Similar to patch testing, the method and interpretation of IDTs should not be carried out until six months following the regression of DRESS. IDT has mostly been employed in SCARs where hypersensitivity has been linked to anti-infective medications that are frequently marketed as sterile preparations and for which it is crucial to determine their safety. In general, IDTs are more sensitive than patch tests, and this seems to be especially true for DRESS linked to antibiotics. A negative delayed IDT, like the patch test, does not, however, rule out a drug's involvement in a cutaneous adverse event.

Prick tests

Skin prick tests with commercial medications read 24 hours later have shown some positive results in DRESS, AGEP, and maculopapular eruptions in delayed cutaneous adverse drug reactions (CADRs). However, little is known about the safety, specificity, sensitivity, drug concentration, test procedure, and prick testing in CADRs. However, because skin prick tests might be safer than IDTs, they are frequently suggested before IDTs. Additionally, if a sterile injectable form of the offending drug—which is required for IDTs—is not available, skin prick tests can be conducted.

In vitro tests

The enzyme-linked immunosorbent spot assay (ELISPOT) and the lymphocyte transformation test (LTT) are examples of in vitro assays.

1. The enzyme-linked immunosorbent spot assay (ELISPOT): The diagnostic routine does not include this method or ELISPOT, which detects drug-specific T cells or identifies the culprit drug via drug-specific interleukin 4, interferon γ, or granulizing production. These methods are not commonly available and need specialized knowledge. According to reports, the IFNY-ELISpot sensitivity ranges from 42% for abacavir to 64% for allopurinol/oxpurinol.[12], [13]

2. The lymphocyte transformation test (LTT): The LTT can assist in identifying the substance or drugs that are causing the problem and is frequently positive in DRESS. Positive LTT reactions, however, are not possible during the acute phase of DRESS and can only be acquired 4–8 weeks following remission.

A negative lymphocyte transformation test does not rule out a drug hypersensitivity reaction, therefore while LTT may be useful in identifying the questionable drug, its sensitivity is limited (38). According to reports, LTT is most helpful during the DRESS recovery period. Its sensitivity and specificity during this phase were 73% and 82%, respectively. In contrast, during the acute phase, the sensitivity and specificity were 40% and 30%, respectively. Thus, five to eight weeks following the start of skin eruption is the ideal window for LTT. LTT, however, is mainly recommended for determining if anticonvulsants are the medicine causing DRESS.[13]

Drug provocation tests

Drug provocation tests are generally contraindicated in patients with DRESS and other SCARs due to the risk of recurrence of the hypersensitivity reaction; however, in cases where other diagnostic procedures, such as in-vivo skin testing and in-vitro laboratory tests, do not yield definitive results, drug provocation tests may be conducted when there is a compelling need for testing (e.g., treatment is necessary and there are no safe and effective treatment alternatives) and the benefit of the provocation is far greater than the risk. Provocation tests are often limited to specific specialized facilities where patients are carefully chosen and supplies, equipment, and skilled staff are available to handle severe reactions.[12]

Lab investigation test

Following the onset of a morbilliform rash, a full blood count with differential should be ordered in order to detect eosinophilia or other hematologic abnormalities.

Concurrently, tests of renal and hepatic function are useful in identifying systemic involvement. A urinalysis to check for active urinary sediment (white cells, white cell casts, eosinophils, and fresh blood and/or protein findings) is advised if there is an acute kidney damage.

If DRESS-related myocarditis is suspected, an echocardiography and cardiac enzymes may be done. Based on the patient's medical history and physical examination, additional organ-directed assessments can be carried out.

In DRESS, the thyroid can also be impacted, particularly as a late-onset autoimmune sequelae. Thyroid tests are challenging to interpret acutely due to their overlap with ill euthyroid syndrome, particularly in the hospital environment.

Since reactivation can be observed in patients with DRESS and may be a sign of the severity of the disease, PCR studies for viral replication, such as testing for human herpes virus-6, human herpes virus-7, Epstein Barr virus, and cytomegalovirus, can be conducted. However, these tests are costly, and it is unclear how the results affect management because it is still up for debate whether viral reactivation is a causative or epiphenomenon.

In regards to skin biopsy, patients with DRESS may have nonspecific histologic alterations in the epidermis and dermis. A skin biopsy is currently not required for diagnosis and is mostly useful for ruling out other pathologic skin processes.[2]

MANAGEMENT OR TREATMENT

The most important steps to prevent the evolution of the condition are early detection and swift suspension of the offending medication.[4]

Identification and discontinuation of the causative drug

It might be difficult to identify the causal agent in DRESS, particularly in patients taking several drugs. Looking for a temporal relationship alone might not be enough to distinguish between several probable drugs because the latency between the first drug exposure and the development of DRESS clinical signs can vary greatly.[16]

Hospitalization and Supportive treatment

With the option of comprehensive clinical and analytical follow-up every 48 hours, hospitalization is advised for all patients, with the exception of mild cases.[17] To monitor potential delayed systemic involvement and response to treatment, all patients should be admitted to the hospital, at least during the initial phase. A peripheral blood smear, liver enzymes and liver function tests, kidney function with creatinine and urea, electrolytes, pancreatic enzymes including lipase and amylase, viral serology for HHV-6, and a complete blood cell count with a differential should all be part of the initial evaluation. Depending on the history, physical examination, and differential diagnosis, additional virus testing and laboratory work-up may be performed as clinically warranted. It is also essential to provide supportive care that includes close monitoring, electrolyte and hydration replacement, hemodynamic support, and proper skin care.[8] The intensity of the manifestations determines the management. To stabilize the patient, supportive care ought to be administered. A warm, humid atmosphere and careful skin care with warm baths, wet bandages, and emollients are further precautions.[17]

Corticosteroids and other immunosuppressive agents

Systemic steroids are presently the most effective treatment for DRESS syndrome. Recent research indicates that steroid-sparing immunosuppressives, including cyclosporine and mycophenolate, may be utilized to treat immune-mediated disorders. To control the disease acutely, cyclosporine in particular may be administered. Traditionally, steroid treatments have lasted between four and six weeks, with the length of treatment being customized based on test abnormalities and skin normalcy as the immunosuppression is tapered down.[2] A slower taper or the use of steroid-sparing medications are advised if a recurrence happens during steroid tapering. Topical corticosteroids, emollients, and antihistamines can be utilized if the systemic involvement is low. They recommend systemic corticosteroids equal to 1 mg/kg/day of prednisone and multidisciplinary examination for severe involvement (transaminase levels $\geq$ 5 times normal, renal involvement, pneumonia, hemophagocytosis, or cardiac involvement). They advise systemic steroids with intravenous immunoglobulin (IVIG) at a dose of 2 g/kg over five days for life-threatening symptoms such as respiratory failure, severe hepatitis, encephalitis, bone marrow failure, and renal failure.[8] Based on observational data, topical corticosteroids were preferable in patients with less severe organ involvement. However, the majority of doctors also support the use of steroids even in these situations, citing the fact that DRESS syndrome relapses frequently follow steroid tapering.

JAK inhibitors

In addition to conventional immunosuppressive treatments, JAK inhibitors may be a useful therapy option for DRESS syndrome, especially in instances that are resistant to them.[48] JAK inhibitors may lessen the severe symptoms of DRESS by targeting the JAK-STAT signalling system, which is linked to a number of inflammatory reactions.[49] Patients with DRESS have an active JAK-STAT signalling pathway. The syndrome's abnormal immunological response is a result of this activation. By inhibiting this mechanism, tofacitinib, a specific JAK 1/3 inhibitor, lowers inflammation and immunological dysregulation linked to DRESS.[50]

CONCLUSION

In conclusion, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome remains a significant clinical challenge due to its complex presentation, delayed onset, and potential for life-threatening complications. In order to reduce morbidity and mortality, this thorough study emphasizes the importance of early detection, timely drug withdrawal, and cautious management. Corticosteroids remain the primary treatment for DRESS syndrome, while alternative immunosuppressive therapies, ZAK inhibitors, offer hope for patients with refractory or severe cases. Enhanced awareness, timely intervention, and multidisciplinary collaboration will be pivotal in addressing the complexities of DRESS syndrome in clinical practice.

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