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RESEARCH ARTICLE

CARBAMAZEPINE INDUCED DRESS SYNDROME : A CASE REPORT

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Abstract

The Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) presents clinically as an extensive mucocutaneous rash, accompanied by fever, lymphadenopathy, hepatitis and hematological abnormalities with eosinophilia & atypical lymphocytes. It may cause damage to several organs, especially to the kidneys, heart, lungs and pancreas. The mortality rate is approximately 10% and the rate of incidence of dress syndrome ranges from 1 in 1,000 to 1 in 10,000 drug exposures. There are around 50 culprit drugs which can induce dress syndrome. Among these, Carbamazepine and Allopurinol are the most commonly observed drugs that induce this syndrome. In this case report, we discussed regarding a 56 years old female patient who was diagnosed with Carbamazepine induced Dress Syndrome. The clinical manifestations of this disease are quite similar to many disease conditions which might lead to misconception. Along with the prevailing manifestations, it is essential to correlate the past medical & medication history and laboratory findings to make an accurate diagnosis. A multidisciplinary approach must be required for early cessation of the suspected drug and initiation of the symptomatic therapy in order to provide a better supportive care to the patient in the clinical scenario. This prevents the further complications thus paving a way for the improvement of the quality of life in the patients.

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Introduction:-

The Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) presents clinically as an extensive mucocutaneous rash, accompanied by fever, lymphadenopathy, hepatitis and hematological abnormalities with eosinophilia & atypical lymphocytes. It may cause damage to several organs, especially to the kidneys, heart, lungs and pancreas. The mortality rate is approximately 10% and the rate of incidence of dress syndrome ranges from 1 in 1,000 to 1 in 10,000 drug exposures.¹⁻⁴ Adults are more prone to dress syndrome when compared to children. There are around 50 culprit drugs which can induce dress syndrome. Among these, Carbamazepine and Allopurinol are the most commonly observed drugs that induce this syndrome.⁵ Carbamazepine is a chemical derivative obtained from iminostilbene that belongs to the class of tricyclic antidepressants. It was synthesized by Walter Schindler in the year 1953. In 1962, Carbamazepine was the first marketed drug in Europe to treat trigeminal neuralgia and a few years later it was approved as an antiepileptic drug.⁶ Now a days, Carbamazepine is indicated for conditions like partial seizures, generalized tonic-clonic seizures, mixed seizure patterns and for the treatment of trigeminal &

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glossopharyngeal neuralgia. In some instances, the Carbamazepine induced adverse drug reaction might affect hepatic, hematopoietic & cardiovascular systems and the cutaneous reactions that occur due to this drug might have various clinical manifestations which may differ in their severity. The diagnosis of this disease usually gets delayed due to the clinical manifestations such as fever and rash which are quite similar to broad spectrum of conditions like rheumatic, allergic and infectious diseases. The differential diagnosis of DRESS syndrome involves toxic epidermal necrosis, Stevens Johnson syndrome, hypereosinophilic syndrome, neoplastic diseases, autoimmune diseases and connective tissue diseases.⁷⁻¹¹

Case Description:

A 56 years old female patient visited the dermatology outpatient department with the chief complaints of facial puffiness, swelling of eyelids, hoarseness of voice and difficulty in taking food. Patient developed radiating pain on the left upper limb which was diagnosed one month back as post herpetic neuralgia and treated with Carbamazepine 200mg/day by a physician. After that she developed intense pruritis and burning sensation over palms, abdomen and inner thighs. Next day, she was observed with scaly and erythematous rash initially over palms & soles and gradually appeared on the entire body.

On clinical examination, maculopapular rash was seen over trunk, extremities along with swelling of face, eyelids & fingers along with edema of the ear lobe. Scaling & fissuring were observed over both palms and excoriations were also observed on both the palms along with the involvement of left upper limb & abdomen. Mucosa was normal. The patient was advised for an admission in the hospital.

On the day of admission, patient's physical examination was remarkable with the following observations that include temperature: 98.1° F, pulse rate: 96 beats per minute, blood pressure: 110/70 mm Hg and respiratory rate: 28 breaths per min.

Investigations:

The abnormal laboratory investigations are hemoglobin: 9.3 g/dl (↓), white blood cells: 3,100 cells/cumm (↓), neutrophils: 31% (↓), eosinophils: 26% (↑), erythrocyte sedimentation rate: 35/hr (↑), aspartate aminotransferase: 153 IU/L (↑), alanine aminotransferase: 300 IU/L (↑), alkaline phosphatase: 282 IU/L (↑), total proteins: 5.8 g/dl (↓) and albumin: 3.3 g/ dl (↓). Grade-I fatty liver was observed on abdominal ultrasonography.

Diagnosis:

Based on the clinical examination, laboratory findings, past medical and medication history, the patient was diagnosed with DRESS syndrome which was induced by Carbamazepine. Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) score was used to assess the disease severity and the patient was observed with a definite ADR (score: 6).

Treatment:

The patient was advised to stop Carbamazepine and the treatment for DRESS syndrome was initiated. The dermatologist advised Methylprednisolone 500mg IV OD for 4 days, Pheneramine maleate 45.5mg/2ml IM BD for 12 days, Pantoprazole 40mg IV OD for 12 days, Azithromycin 500mg PO OD for 5 days, Betamethasone lotion and olesoft cream (Olive oil 2%W/V + Sodium lactate 2.5%W/V + Sodium pyrrolidone carboxylic acid 2.5%W/V). From day 5 onwards, the dose of the drug Methylprednisolone was tapered gradually.

Outcome and Follow Up:

A significant improvement of the laboratory findings was observed on day 4, the levels of aspartate aminotransferase (54 IU/L), alanine aminotransferase (181 IU/L) & alkaline phosphatase (243 IU/L) were decreased and the levels of the total proteins (6.1 gm/dl) was increased and remained stable. The patient was relieved from edema on day 6, the erythematous rashes were decreased on day 9. By considering the above prognosis, the patient was discharged on day 12 and advised to come for review after 2 weeks.

Discussion:-

In dress syndrome, the patients experience characteristic features such as rash, fever & lymphadenopathy along with abnormalities in organs (kidney, lungs, heart & pancreas) and organ systems (hematological, hepatic systems). The diagnosis can be made based on the RegiSCAR (Registry of Severe Cutaneous Adverse Reaction) scoring system developed by European Registry. It consists of 8 parameters that include acute rash, fever above 38°C,

lymphadenopathy at two sites, involvement of at least one internal organ, abnormalities in lymphocytes & eosinophil count, resolution ≥ 15 days and negative results in atleast 3 serological tests.^{1, 12} To meet the definition of DRESS syndrome, the patient must have any 5 of the above 8 parameters. In this case, the patient was observed to meet the definition of RegiSCAR with the precipitating symptoms like erythematous rash, fever, facial edema, swelling of ear lobe, eyelid & fingers. Along with the above characteristic features, abnormalities in liver with increased serum transaminase levels and haematological abnormalities with increased eosinophilic count (26%), erythrocyte sedimentation rate (26%) were observed. Thus, based on the clinical manifestations, laboratory data and history of recent usage of the drug Carbamazepine, the dermatologist diagnosed the patient with Carbamazepine induced DRESS syndrome. Immediate withdrawal of the suspected drug is the basic step in the treatment of DRESS syndrome.¹³⁻¹⁵ Supportive and symptomatic treatments are indicated. Systemic corticosteroids have been considered as the treatment of choice if the patient is observed with internal organ involvement.¹⁶ In this case, Methylprednisolone was prescribed to the patient and other supportive care was provided.

Conclusion:-

Dress syndrome is a rare, potentially life threatening adverse drug reaction in the clinical setting. The clinical manifestations of this disease are quite similar to many disease conditions which might lead to misconception. Along with the prevailing manifestations, it is essential to correlate the past medical & medication history and laboratory findings to make an accurate diagnosis. A multidisciplinary approach must be required for early cessation of the suspected drug and initiation of the symptomatic therapy in order to provide a better supportive care to the patient in the clinical scenario. This prevents the further complications thus paving a way for the improvement of the quality of life in the patients.

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