Case Study

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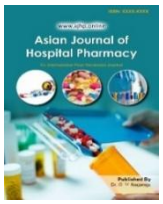

CASE STUDY ON CARBAMAZEPINE INDUCED DRUG RASHES AND ITCHING OVER FACE AND BODY

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Abstract

Background: A 19-year-old female with a history of epilepsy presented with a 3-day history of itching, rashes over her face, and intermittent fever. The patient had recently been started on Carbamazepine 200 mg for seizure management. The temporal relationship between the initiation of Carbamazepine and the onset of symptoms raised the possibility of a drug-induced hypersensitivity reaction.

Case Presentation: The patient reported pruritic, erythematous maculopapular rashes localized to the face, without mucosal involvement. The rashes progressively worsened over 3 days, along with intermittent fever. No previous history of similar rashes was reported. The neurological exam showed no signs of active seizures, and the patient appeared generally well, aside from the discomfort from the itching.

Differential Diagnosis: The primary differential diagnoses included a drug-induced eruption (likely due to Carbamazepine), viral exanthema, allergic reactions, seborrheic dermatitis, and systemic lupus erythematosus (SLE). The absence of mucosal involvement and systemic symptoms made SLE and viral rashes less likely.

Investigations: Relevant investigations included a complete blood count (CBC), liver function tests (LFTs), serum electrolytes, and an eosinophil count. A skin biopsy or dermatology consultation was considered if the diagnosis remained uncertain.

Management: The management plan involved discontinuing Carbamazepine and switching to an alternative anticonvulsant. Symptomatic treatment was provided with antihistamines for itching and topical corticosteroids for inflammation. Antipyretics were prescribed to manage fever, and close monitoring was recommended for potential progression to more severe reactions, such as Stevens-Johnson syndrome.

Conclusion: This case highlights the importance of recognizing drug-induced hypersensitivity reactions, particularly in patients with epilepsy starting new medications. Carbamazepine-induced rashes are common, and early recognition with prompt discontinuation of the drug can prevent severe complications. The patient's symptoms were effectively managed with symptomatic treatment, and follow-up will ensure ongoing seizure control with an alternative anticonvulsant.

Keywords: Carbamazepine, Drug-induced hypersensitivity, Rashes, Epilepsy, Seizure management, Stevens-Johnson syndrome.

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Introduction to Carbamazepine 200 mg

Carbamazepine is an anticonvulsant (antiepileptic) and mood-stabilizing drug primarily used in the treatment of various neurological and psychiatric conditions. It is most commonly prescribed for the management of epilepsy, particularly in patients with partial seizures, generalized tonic-clonic seizures, and mixed seizure types. Carbamazepine is also employed in the treatment of **trigeminal neuralgia** (a type of facial nerve pain), **bipolar disorder**, and certain **neuropsychiatric conditions**.

Mechanism of Action

Carbamazepine works by stabilizing the hyper-excitable electrical activity in the brain. It achieves this by:

- **Blocking voltage-gated sodium channels:** Carbamazepine inhibits the repetitive firing of neurons by blocking sodium channels, which reduces the

propagation of abnormal electrical impulses. This action is particularly beneficial in controlling seizures.

- **Modulating neurotransmitter release:** The drug may also influence the release of neurotransmitters such as glutamate and serotonin, contributing to its mood-stabilizing effects.

Indications

Carbamazepine is primarily used for the following conditions:

1. **Epilepsy:**
   - It is effective in controlling partial seizures (simple and complex) and generalized tonic-clonic seizures.
   - It is also used as an adjunct in treating mixed seizure disorders.
2. **Trigeminal Neuralgia:**
   - Carbamazepine is considered the drug of choice for the treatment of trigeminal neuralgia due to its ability to stabilize nerve electrical activity and reduce pain.
3. **Bipolar Disorder:**
   - Used as a mood stabilizer in treating acute manic or mixed episodes in patients with bipolar disorder.
4. **Other Uses:**
   - Occasionally used in neuropathic pain and certain psychiatric disorders.

Dosage and Administration

Carbamazepine is typically started at a low dose and gradually increased to avoid potential side effects. The standard oral dose for an adult is **200 mg twice a day**, but this can vary depending on the condition being treated, the patient's response, and tolerance to the drug. The dose may be titrated upwards based on clinical needs, often to **400 mg-1200 mg per day** in divided doses. However, individualization of therapy is crucial to ensure efficacy while minimizing side effects.

Pharmacokinetics

- **Absorption:** Carbamazepine is well-absorbed from the gastrointestinal tract, with peak plasma levels occurring within 4-12 hours after oral administration.
- **Metabolism:** It is extensively metabolized by the liver via **cytochrome P450 enzymes**, mainly CYP3A4, into an active metabolite, **carbamazepine-10,11-epoxide,** which also contributes to its therapeutic effects.
- **Half-life:** The elimination half-life of carbamazepine is approximately **12-17 hours,** but this can be prolonged with chronic use due to auto-induction of liver enzymes, which leads to increased metabolism over time.

Side Effects

Carbamazepine is generally well tolerated but can cause various side effects, some of which are dose-dependent or related to individual sensitivity:

1. **Common side effects:**
   - Dizziness
   - Drowsiness
   - Nausea and vomiting
   - Ataxia (lack of coordination)
   - Diplopia (double vision)
2. **Serious adverse reactions:**
   - **Hematologic:** Carbamazepine can cause **leukopenia** (low white blood cell count), **thrombocytopenia** (low platelet count), and **aplastic anemia** (bone marrow failure).
   - **Dermatologic:** Drug-induced rashes, ranging from mild exanthems to severe reactions like **Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN),** can occur. Patients of Asian descent are at a higher risk, particularly if they carry the **HLA-B*1502 allele.**
   - **Hepatic:** Liver enzyme abnormalities and **hepatotoxicity** may also occur, necessitating regular liver function monitoring.
3. **Central Nervous System:** Sedation, confusion, and cognitive impairment may occur, especially with high doses.
4. **Endocrine:** Long-term use may affect thyroid function and lead to **hyponatremia** (low sodium levels), particularly in elderly patients.

Drug Interactions

Carbamazepine is known to interact with several other medications, mainly due to its influence on the **cytochrome P450 enzyme system**. It can decrease the effectiveness of other drugs, particularly oral contraceptives, and can increase the metabolism of medications such as:

- **Warfarin** (blood thinner)
- **Theophylline** (for asthma)
- **Corticosteroids**
- **Antidepressants**

Monitoring and Safety

Because carbamazepine can cause serious side effects, particularly in the first few weeks of treatment, regular monitoring is necessary:

- **Complete blood count (CBC)** to monitor for hematologic abnormalities (e.g., leukopenia, thrombocytopenia).
- **Liver function tests** to detect potential hepatotoxicity.
- **Serum sodium levels** to prevent and detect hyponatremia.
- **Electrolyte levels** and renal function tests as needed, especially in high-risk individuals.

Patient Profile

- **Age:** 19 years old
- **Gender:** Female
- **Presenting Complaints:**
  - Itching over the face
  - Rashes since the last 3 days
  - On and off fever for the last 3 days
  - Erosion positive in oral cavity, lips, diffuse erythema over body

Past Medical History

- **Epilepsy:** The patient has a known history of epilepsy.
- **Medications**
  - Carbamazepine 200 mg (administered 3 days ago).

Present Illness

- The patient reports the onset of itching and rashes over her face for the past 3 days, which started acutely and have progressively worsened.
- The rashes have a pruritic (itchy) component, with varying intensity of the itching.
- She also mentions intermittent fever during the same time frame.
- The patient denies any history of similar skin rashes in the past.

Recent Medication History

- The patient was started on Carbamazepine 200 mg three days ago as part of her ongoing management of epilepsy.
- No changes in the dosage or medication regimen prior to the development of the symptoms.

Physical Examination

- **General Appearance:** The patient appears slightly uncomfortable due to itching.
- **Vital Signs:**
  - Temperature: 37.8°C (on and off fever).
  - Blood Pressure: 120/80 mmHg
  - Pulse: 90 beats per minute (regular)
  - Respiratory Rate: 16 breaths per minute
- **Skin Examination:**
  - The patient has erythematous (red) maculopapular rashes over the face, predominantly on the cheeks, and extending slightly to the neck.
  - No mucosal involvement (e.g., mouth, eyes).
  - No vesicles, blisters, or crusting observed.
- **Neurological Examination:**
  - Clear sensorium; no signs of active seizure.
  - No focal neurological deficits noted.

Differential Diagnosis

1. **Drug Eruption (Carbamazepine-induced Rash):**
   - **Clinical reasoning:** The recent onset of a rash after the initiation of Carbamazepine suggests the possibility of a drug-induced hypersensitivity reaction. Carbamazepine is known to cause rashes, ranging from mild exanthems to severe reactions like Steven-Johnson Syndrome (though the absence of mucosal involvement makes the latter less likely).
   - **Rash characteristics:** Maculopapular and pruritic, beginning on the face, may be consistent with a drug rash.
2. **Viral Exanthema (Viral Rash)**
   - **Clinical reasoning:** The intermittent fever and rash could also suggest a viral etiology, such as measles, rubella, or roseola. However, viral exanthems are less likely to be localized to the face and generally have a more widespread pattern.
3. **Allergic Reaction**
   - **Clinical reasoning:** The rash and itching could be the result of an allergic reaction to a new product (e.g., skincare, makeup) or food; however, the temporal association with carbamazepine makes this less likely.
4. **Seborrheic Dermatitis or Acneiform Rash**
   - **Clinical reasoning:** These conditions can sometimes present with facial rashes and itching, but the acute onset with fever makes these less likely.
5. **Systemic Lupus Erythematosus (SLE)**
   - **Clinical reasoning:** The butterfly-shaped rash across the cheeks could suggest SLE, but there are no other signs such as joint pain, photosensitivity, or systemic symptoms that would be typical for lupus.

Investigations

1. **Complete Blood Count (CBC):** To check for signs of infection or systemic inflammation.
2. **Liver Function Tests (LFTs):** To assess for hepatic toxicity, which can be a complication of Carbamazepine.
3. **Serum Electrolytes:** To monitor for any electrolyte imbalance.
4. **Skin Biopsy:** If the rash progresses and the cause remains unclear, a skin biopsy may be performed to confirm the diagnosis.
5. **Eosinophil Count:** This may be elevated in drug-induced hypersensitivity reactions.
6. **Serology for Viral Exanthems:** If a viral infection is suspected, tests for common viral causes (measles, rubella, etc.) can be conducted.

Management Plan

1. **Discontinuation of Carbamazepine:** Given the temporal relationship between the initiation of Carbamazepine and the onset of the rash, it is important to discontinue the drug to prevent further hypersensitivity reactions. An alternative anticonvulsant may need to be considered.
2. **Symptomatic Treatment for Rash**
   - **Antihistamines:** To relieve itching and prevent further histamine-related symptoms.
   - **Topical corticosteroids:** A mild to moderate corticosteroid cream (e.g., hydrocortisone 1%) to manage the inflammation of the rash.
3. **Antipyretics:** For fever management (e.g., acetaminophen).
4. **Referral to Dermatology:** If the rash does not resolve with the withdrawal of Carbamazepine or if the diagnosis remains uncertain, a dermatology consultation and possibly a skin biopsy may be needed.
5. **Monitoring:** The patient should be closely monitored for signs of worsening systemic involvement, especially in cases of severe drug reactions (e.g., Stevens-Johnson syndrome).
6. **Consider Alternate Antiepileptic Medication:** If the Carbamazepine-induced rash is confirmed, a new

antiepileptic drug regimen (e.g., levetiracetam, lamotrigine) may be initiated.

Prognosis

- The prognosis largely depends on the nature and resolution of the rash and the response to discontinuation of the offending drug (Carbamazepine).
- If the rash is indeed drug-induced, it should resolve upon discontinuation of the drug, with no long-term sequelae if managed appropriately.

Follow-Up

- The patient should be scheduled for follow-up in 1-2 weeks to monitor the resolution of symptoms and to evaluate the effectiveness of the management plan. A follow-up assessment for seizure control with the new anticonvulsant (if applicable) will also be necessary.

Conclusion

This 19-year-old female's presentation with itching, rashes, and fever in association with the recent use of Carbamazepine strongly suggests a drug-induced hypersensitivity reaction. The management involves discontinuing Carbamazepine and symptomatic treatment of the rash and fever. Monitoring for potential systemic involvement is essential, and follow-up will ensure the resolution of symptoms and seizure management.

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Conflict of Interest

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Informed Consent

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Ethical Statement

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Author Contribution

All authors are contributed equally.

References

1. Bala, M., &Vora, V. (2016). Drug-induced exanthems. Indian Journal of Dermatology, 61(2), 143-151.
2. Chung, W. H., & Hung, S. I. (2010). The genetics of drug-induced hypersensitivity reactions. Current Opinion in Allergy and Clinical Immunology, 10(4), 327-332.
3. Kehoe, E., & Haw, C. (2020). Carbamazepine: A review of its clinical pharmacology and adverse drug reactions. Therapeutic Advances in Drug Safety, 11, 2042098619870984.
4. Köhler, S., &Möller, H. J. (2009). Adverse drug reactions in epileptic patients: A focus on carbamazepine. Pharmacology & Therapeutics, 123(3), 356-365.
5. Schwartz, R. A. (2006). Dermatologic manifestations of systemic lupus erythematosus. The American Journal of Clinical Dermatology, 7(5), 269-281.
6. Cohen, A. L., & Krishnan, S. (2017). Drug-induced rashes and the management of anticonvulsant-related reactions. Seminars in Neurology, 37(5), 472-481.
7. Jang, H. H., & Kim, Y. K. (2014). Drug-induced hypersensitivity syndrome and carbamazepine: A review. Journal of Clinical Neurology, 10(1), 3-9.
8. Cifuentes, S., &Auzary, C. (2011). A review of the treatment of carbamazepine-induced hypersensitivity syndrome. Journal of Clinical Pharmacology, 51(3), 297-304.
9. Swinson, C., &Molyneux, G. (2016). Differential diagnosis of drug rashes in the context of epilepsy. Epilepsia, 57(4), 584-593.
10. Naga Subrahmanyam S, Vijaya Lakshmi DT, Naga Raju GV, Pavan Kumar GV, Gayathri G, Carbamazepine Induced Drug Rash with Eosinophilia and Systemic Symptoms, Journal of Drug Delivery and Therapeutics. 2019; 9(1-s):367-368 DOI: **http://dx.doi.org/10.22270/jddt.v9i1-s.2330**
11. Naga Subrahmanyam S et al., Int. J. Res. Pharm. Sci., 11(1), 173-175
12. S.nagasubrahmanyam et.al., carbamazepine induced drug rash with eosinophilia and systemic symptoms, journal of drug delivery and therapeutics, vol 9 no 1-s(2019):367-368. DOI: **http://dx.doi.org/10.22270/jddt.v9i1-s.2330**
13. S.nagasubrahmanyam et.al., cefotaxime induced macular rashes, Saudi journal of medicalandpharmaceuticalsciences,vol-4,iss-9(sept,2018):1032-1034. doi:10.21276/sjmps.2018.4.9.7