International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 23s, 2025
https://www.theaspd.com/ijes.php

A Case Of Risperidone– Induced Angioedema: Bad "RISP" Onse

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Abstract

Background: *Risperidone is a second-generation antipsychotic widely used for schizophrenia and schizoaffective disorder. Although generally well tolerated, rare but potentially serious adverse effects such as angioedema have been reported.*

Case presentation: *We describe a 38-year-old male with paranoid schizophrenia who developed acute angioedema on day 9 of risperidone therapy. Laboratory evaluation excluded complement-mediated and hereditary etiologies. Risperidone was discontinued, cross-tapered to aripiprazole, and the patient received systemic corticosteroids and antihistamines, resulting in complete resolution within four days.*

Conclusion: *Clinicians should be aware of risperidone-induced angioedema, monitor inflammatory markers to aid diagnosis, and promptly discontinue the offending agent to prevent complications.*

INTRODUCTION

Risperidone is a benzisoxazole antipsychotic effective in treating schizophrenia and schizoaffective disorders. Common adverse effects include drowsiness, increased appetite, fatigue, insomnia, agitation, and anxiety[1]. Angioedema is a rare but potentially life-threatening hypersensitivity reaction characterized by localized subcutaneous or submucosal swelling. Although angioedema has been well documented with certain antipsychotics, reports implicating risperidone remain scarce[2,3]. Here, we report a case of risperidone-induced angioedema in a patient with paranoid schizophrenia and discuss the clinical approach to diagnosis and management.

MATERIALS AND METHODS

Study design and setting

This report describes a single-patient case study conducted at R.L. Jalappa Hospital, Sri Devaraj Urs Medical College, Kolar, India. The patient was managed on the inpatient psychiatry ward under the supervision of the Department of Psychiatry.

Patient selection and consent

A 38-year-old married male presenting with a 6-month history of persecutory delusions, auditory hallucinations, social withdrawal, poor self-care, and sleep disturbance was admitted and diagnosed with paranoid schizophrenia based on DSM-5 criteria. The patient provided written informed consent both for treatment and for publication of anonymized clinical details.

Treatment protocol

- **Antipsychotic therapy:** Risperidone was initiated at 2 mg once daily and titrated by 2 mg increments every 48 hours to reach 8 mg/day by day 7, per standard practice for acute psychosis management.
- **Onset of adverse reaction:** On day 9 of risperidone therapy, the patient developed painless swelling of the lips and periorbital regions without urticaria or respiratory distress.
- **Cross-tapering regimen:** Risperidone was discontinued immediately. Aripiprazole was introduced at 5 mg once daily, increasing to 15 mg/day over five days while risperidone was withdrawn.
- **Supportive management:**
  - **Corticosteroids:** Intravenous hydrocortisone 100 mg twice daily for 48 hours, followed by oral prednisolone 30 mg once daily, tapered over five days.
  - **Antihistamine:** Oral hydroxyzine 25 mg three times daily until complete resolution of edema.

Laboratory investigations

At onset of angioedema, the following tests were obtained to exclude alternative etiologies:

- **Inflammatory markers:** Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
- **Complement profile:** Serum C3 and C4 levels
- **C1 esterase inhibitor:** Antigenic and functional assays

Normal C3, C4, and C1 esterase inhibitor levels excluded hereditary or complement-mediated angioedema. Elevated ESR and CRP supported an acute inflammatory process.

Outcome assessment

Resolution of angioedema was monitored clinically every 12 hours. Complete disappearance of swelling was noted by day 4 post-intervention. Psychiatric symptom control and any recurrence of swelling were assessed at a four-week follow-up visit.

Ethical considerations

The case was reported in accordance with the CARE (CAse REport) guidelines. Institutional review board approval was not required for a single case report, but written informed consent for publication was obtained from the patient.

Case Presentation

A 38-year-old married male presented with a 6-month history of persecutory delusions, third-person auditory hallucinations, social withdrawal, poor self-care, and sleep disturbance. He was admitted to R.L. Jalappa Hospital, where psychiatric evaluation confirmed paranoid schizophrenia. Baseline systemic examination and investigations were unremarkable.

Treatment and onset of reaction: Risperidone was initiated at 2 mg/day and titrated to 8 mg/day over one week to control psychotic symptoms. On day 9, the patient developed sudden, painless swelling of the lips and periorbital regions without urticaria or respiratory compromise.

Investigations:

- **Inflammatory markers:** ESR and CRP were elevated, indicating an acute inflammatory response.
- **Complement studies:** Serum C3 and C4 levels were within normal limits.
- **C1 esterase inhibitor:** Functional and antigenic levels were normal, effectively excluding hereditary and complement-mediated angioedema.

Management: Risperidone was discontinued and cross-tapered with aripiprazole starting at 5 mg/day. The patient received intravenous hydrocortisone (100 mg twice daily) for the first 48 hours, then oral prednisolone (30 mg/day tapered over five days), alongside oral hydroxyzine (25 mg three times daily) for symptomatic relief. The angioedema resolved completely within four days, with no recurrence during a four-week follow-up. Psychotic symptoms remained well controlled on aripiprazole.

DISCUSSION

Angioedema related to risperidone is exceedingly rare. To our knowledge, only a handful of cases have been documented: Soumya et al. described a 15-year-old boy developing facial and pedal edema after risperidone dose escalation, which resolved following drug withdrawal and switch to haloperidol[2]; Talaei et al. reported a 38-year-old woman with mood disorder who developed angioedema on risperidone, resolving within four days of discontinuation and treatment with hydrocortisone and hydroxyzine[3].

The pathogenesis of risperidone-induced angioedema is unclear but may involve non-immunologic mast cell degranulation or idiosyncratic immune responses. Normal complement levels and absence of a family history make hereditary and bradykinin-mediated pathways unlikely. Elevated ESR and CRP in our patient point toward an inflammatory mechanism rather than isolated histamine release.

Prompt recognition is critical: airway compromise may ensue if swelling extends to the oropharynx. Clinicians should monitor for facial or mucosal swelling during the first two weeks of therapy, especially in patients with prior drug hypersensitivity. Measurement of inflammatory markers and complement studies can aid in distinguishing drug-induced angioedema from hereditary or acquired forms. Immediate discontinuation of risperidone, initiation of corticosteroids, and antihistamines typically lead to rapid symptom resolution.

CONCLUSION

Risperidone-induced angioedema, though rare, is a serious adverse effect necessitating high clinical suspicion. Early identification, withdrawal of the offending agent, and supportive therapy with corticosteroids and antihistamines result in favorable outcomes. Monitoring inflammatory markers can assist in differential diagnosis and management.

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