Case Report

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Purpuric rashes: A case report on rare adverse effect of Donepezil

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Abstract

Donepezil is a reversible acetylcholinesterase inhibitor approved for use in mild to severe Alzheimer's Disease. There have been a few cases of cutaneous adverse effect related to donepezil. The first documented case report of purpuric rash attributed to Donepezil was by Brian et al. in 1998. We present a case of purpuric rashes and periorbital swelling in a patient on donepezil. The symptoms resolved gradually after the discontinuation of Donepezil.

Keywords: Donepezil; Alzheimer's Disease; Purpuric Rash; Swelling; Older People; Acetylcholinesterase.

Introduction

Donepezil is a reversible acetylcholinesterase inhibitor approved by the Food and Drug Administration for use in mild to severe Alzheimer's Disease (AD) [1, 2]. It works by inactivating the enzyme acetylcholinesterase (AchE) and increasing acethylcholine(Ach) levels in the brain [3]. It has also been shown to reduce the emergence of neuropsychiatric symptoms (NPS) such as psychosis (hallucinations and delusions) and other behavioral changes associated with cholinergic deficiency in approximately 60 – 90% of AD patients [4]. The well known side effects of Donepezil are bradycardia, falls, vomiting, syncope, convulsion and death [5]. However, the incidence of rash as an adverse effect (AE) is rare. We present a case of a patient with mixed dementia found to have purpuric rashes and periorbital swelling after initiation of Donepezil.

Case Description

A 75-year-old woman with Mixed Dementia presented with skin itchiness and rashes. She was started on Donepezil at a dose of 2.5mg once daily 6 weeks prior. For her other comorbids of diabetes mellitus, hypertension, and dyslipidemia, she was on Metoprolol 50mg twice daily, Metformin 1g twice daily, Gemfibrozil 300mg once daily, Perindopril 4mg once daily and S/C Mixtard 20IU twice daily. She had smoked around 2 – 3 cigarettes per day previously but quit 10 years ago. She does not consume alcohol. On examination, patient

***Figure 1:** Purpuric rashes with donepezil treatment.*

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S.N	Headings	Prior to hospitalization	Index hospitalization
1.	Presentation	Periorbital swelling and rashes over face and right upper limb	Day 2: Swelling and rashes improved. Still having rashes over face and right upper limb.
2.	Treatment	Severe allergic reaction	Donepezil discontinued. Patient received IV hydrocortisone 100mg three times daily for 2 days and discharged with prednisolone 30mg once daily and loratadine 10mg once daily for 5 days. After 17 days, patient fully recovered and started with memantine 5mg once daily for a month.

was comfortable and not in distress. She was a febrile and her vital signs were normal. There were erythematous petechial and purpuric rashes over her face and right upper limb (Figure 1). Additionally, there was also periorbital swellings bilaterally. As the working diagnosis was allergic reaction due to Donepezil, the medication was discontinued. Intravenous Hydrocortisone 100mg three times daily, Chlorpheniramine 4mg three times daily were given while maintaining her other medications. Her blood investigations were unremarkable except for a slightly raised AST level (56u/L). She was discharged after 3 days of admission with Predisolone 30mg once daily for 5 days. Her rashes were improving and the periorbital swellings completely resolved on discharge. She was reviewed 17 days later in the outpatient clinic, in which her rashes have completely resolved as well. She was then started on Memantine for the treatment of her Mixed Dementia.

Discussion

Purpuric rashes and periorbital swelling presenting as adverse effects of AchE inhibitors are rare. The most commonly reported AE with Donepezil in Chinese AD patients are dizziness, gastrointestinal (nausea, vomiting, diarrhoea, and constipation), insomnia, and bradycardia [6, 2]. To our knowledge, this is the second incident of cutaneous AE reported in older patients. Brial et al in 1998 reported a case of purpuric rash in a 82-year-old woman treated with this [7]. Another case of drug-induced lupus erythymatosous (DILE) has also been reported [8]. Although in the earlier case, the patient was restarted on Donepezil with subsequent reappearance of rash 16 days later, our patient was not rechallenged due to the severity of her presentation that warranted hospitalization. Given the temporal relationship between the initiation of treatment and the onset of the rash, and the resolution of the patient's symptoms after discontinuation, the likely culprit for our patient's presentation is likely Donepezil.

Conclusions

Due to physiological changes associated with ageing, the pharmacokinetics and pharmacodynamics of a drug may be affected in older patients leading to increased frequency of common AE and occurrence of uncommon AE. Drug-drug interactions as well as drug-disease interactions are also more common in the older patient due to the presence of co-morbid medical conditions [9,10]. This case report highlights an uncommon AE in a commonly used drug, suggesting the importance of educating the patient and their care giver when initiating any treatment.

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