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Case Report

An Unusual Case of Bilateral Vocal Cord Paralysis Following Chemotherapy with Oxaliplatin

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Abstract

Chemotherapy-induced neuropathies, especially with platinum-based agents like oxaliplatin, are common, with Vocal Cord Paralysis (VCP) being a rare but severe complication. This case report describes an 83-year-old male with rectal adenocarcinoma who developed Bilateral Vocal Cord Paralysis (BVCP) after receiving CAPOX chemotherapy. The patient, who had recently undergone surgery and chemoradiotherapy, presented with difficulty swallowing and speaking. Over the following days, he developed airway obstruction and stridor, necessitating emergency intubation. Extensive investigations ruled out alternative causes, and the temporal association with oxaliplatin strongly suggested it as the culprit. Despite initial management, he required a tracheostomy after failed extubation attempts.

Oxalate, a metabolite of oxaliplatin, binds calcium through chelation, blocking calcium channels and altering neuronal signal transduction, which may contribute to laryngeal nerve dysfunction and VCP.

This case highlights the need for early recognition and prompt intervention in chemotherapy-induced VCP. Given the neurotoxic effects of oxaliplatin, VCP should be considered in patients with hoarseness or swallowing difficulties during chemotherapy.

Keywords: Vocal cord paralysis; Chemotherapy; Neuropathy; Oxaliplatin

Introduction

Chemotherapy-induced neuropathies are one of the most common side effects of cancer treatment. The incidence of neuropathy is highest for platinum-based chemotherapy agents such as cisplatin, carboplatin and oxaliplatin. Though there are several reports of mononeuropathy and polyneuropathy in these patients, the occurrence of Bilateral Vocal Cord Paralysis (BVCP) due to involvement of recurrent laryngeal nerve is rare. Here we report a case of BVCP requiring tracheostomy in a patient with rectal cancer treated with oxaliplatin.

Clinical Presentation and Course

An 83-year-old male was admitted to the Intensive Care Unit (ICU) post emergency intubation in the operating theatre for bilateral VCP of unclear origin causing airway obstruction.

Sixteen days prior to the admission to ICU, he had presented to the Emergency Department with high output (>3 litres/day) from colostomy and acute kidney injury. He was managed on the surgical ward with intravenous fluids, octreotide and loperamide. The stoma outputs remained persistently high, and he also started vomiting which required nasogastric tube insertion. Intravenous Total Parenteral Nutrition (TPN) was started to provide him with nutritional support. Gastroscopy performed on day 12 showed a normal oesophagus, bilious gastric fluid and duodenal erosions. Biopsies were taken from stomach and duodenum. Stomoscopy was normal. He was considered for reversal of colostomy.

Approximately 11 months prior to this admission he was diagnosed with locally advanced rectal adenocarcinoma located 8.5 cm from the anal verge. The rectal cancer was graded as T2N1 on pelvic MRI. There were no distant metastases on PET-CT after 4 months when he underwent loop colostomy.

He was then commenced on long course chemoradiotherapy (LC-CRT) for 8 weeks with capecitabine 1500mg BD on days of radiotherapy only. Capecitabine was ceased early due to high stoma output. Six weeks prior to the current admission he underwent low anterior resection. Three weeks following the surgery he began the first cycle of CAPOX chemotherapy (Oxaliplatin 200mg on day 1 and Capecitabine 1500mg twice daily). Capecitabine was ceased at the time of his admission to hospital again due to high stoma output.

A day after commencement of chemotherapy he started complaining of difficulty in swallowing and speaking. Flexible Nasal Endoscopy (FNE) performed 4 days later at the time of admission to the hospital revealed mildly inflamed larynx suggestive of mild laryngitis and reflux, normal epiglottis, left arytenoid hooding and inability to visualise left vocal cord. Repeat FNE on the following day showed left arytenoid hooding and left vocal cord paresis with slight flickering. The right vocal cord was moving well and compensating.

He developed stridor on day 21 of his recent chemotherapy. Repeat FNE showed no supraglottic oedema, significant pooling of secretions in pyriforms and vallecula and left arytenoid hooding making it difficult to assess the vocal cord mobility. The view was repeatedly getting obstructed with secretions as the patient was unable to swallow or clear effectively with cough. Epiglottis and arytenoid had decreased sensation with no cough reflex on stimulation.

Over the next 24 hours he continued to deteriorate with ongoing stridor and desaturations. FNE was repeated and revealed bilateral vocal cord palsy in paramedian position and narrowed airway. He underwent emergency intubation in the operating theatre by anaesthetists and was admitted to ICU.

The cause of BVCP remained unclear as no local structural abnormality was found. Therefore, neurologist's opinion was sought, and broad differential diagnoses were considered including vascular, variant of Guillain-Barre syndrome, vasculitis, infectious, inflammatory and nutritional. Magnetic Resonance Imaging (MRI) of Brain, base of skull and neck were all normal, and no central abnormalities were detected. The vasculitis screen (ANA, ENA, dsDNA, ANCA) was negative. The complement levels C3 and C4 were normal. The serum protein electrophoresis was normal, and the urine was negative for Bens Jones protein. Lupus Anticoagulant, Cardiolipin, Beta 2 Glycoprotein were not detected. The thyroid function test and serum levels of vitamin E, B6, copper and zinc were normal. The serology for hepatitis B, hepatitis C, human immunodeficiency virus and syphilis were negative. The serum angiotensin converting enzyme level was normal, thus ruling out sarcoidosis.

Various options for managing this life life-threatening condition were considered such as cordotomy, vocal cord lateralisation and surgical tracheostomy. The first two options were ruled out due to increased risk of aspiration from pooling of secretions, possibility of rebound stridor and airway distress. On day seven of intubation, the patient was taken back to the operating theatre and had a trial of extubation. Repeat FNE showed flickering of right vocal cord and immobile left vocal cord. There was only minimal glottic gap. He was reintubated and surgical tracheostomy was performed.

He was discharged to the surgical ward on day 10 of ICU admission. Subsequently he was assessed by speech pathologist and the Videofluroscopic Swallow Study (VFSS) showed small volume aspiration during swallow on thin fluids. Therefore, percutaneous endoscopic gastrotomy (PEG) tube was inserted to facilitate feeding. He was discharged home after spending four months in the hospital. At his last follow up, eight months after the initial presentation, he still had persistent BVCP.

His other past medical history included malignant neoplasm of urinary bladder (high grade invasive urothelial carcinoma, sarcomatoid variant), three years prior to the admission and was treated with intravesical BCG vaccine. Subsequent cystoscopies were normal. Three years prior to the admission, he was diagnosed with ischemic heart disease for which he underwent percutaneous intervention to left anterior descending artery.

His routine medications included amlodipine, valsartan, aspirin, atorvastatin, furosemide, calcium carbonate, Ural powder, cholecalciferol, esomeprazole, loperamide, mirtazapine, nebivolol, ondansetron, paracetamol and silver sulfadiazine topical cream.

Discussion

Our patient had BVCP shortly after the administration of oxaliplatin. There was no local structural abnormality and MRI of brain, skull base and neck were all normal. All other causes such as infection, inflammation and vasculitis were ruled out. The neurological assessment was normal except for frailty. In the absence of any other explanation for BVCP and its temporal association with the administration of oxaliplatin, we believe that BVCP was due to oxaliplatin.

Vocal Cord Paralysis (VCP) is a rare but life-threatening complication of chemotherapy. It has been described with vinca alkaloids (such as vincristine and vinblastine) and platinum-based agents, also known as platins [1,2]. The platins belong to a large class of synthetic anti- cancer drugs. Their main antineoplastic action is triggered by DNA- cross- linking inhibiting cancer cell DNA synthesis and repair [3]. Platinum-based drugs are enlisted on the WHO Model List of Essential Medicines [4] and are used in the treatment of a variety of tumours from lung, ovaries, bladder, testes and colorectal cancers. Neurotoxicity is their main dose-limiting side effect and affects a large number of platin-treated patients, with neuropathy incidence rate ranging from 70% to 100% of all treated patients [5].

Most cases of chemotherapy induced VCP were bilateral. In unilateral VCP, only involvement of the left cord has been reported, which is activated by the longer recurrent laryngeal nerve [1,6].

Only three cases of VCP due to oxaliplatin have been described so far in the literature. In these cases, VCP appeared immediately after the first administration of oxaliplatin and was rapidly reversible. The allergy workup ruled out the hypersensitivity reaction in all these cases [7].

A single case of cisplatin induced VCP has been reported [2]. In this case, the patient developed bilateral VCP 48 hours after the 6th course of cisplatin and required endotracheal intubation. VCP following administration of carboplatin in combination with paclitaxel has also been described [8].

Most cases of VCP secondary to chemotherapy agents occur after several courses and resolve with cessation of chemotherapy within a few months. The pathogenesis of VCP induced by these drugs remains unclear and in vinca alkaloids is probably related to cumulative damage to the laryngeal nerve.

Studies suggest that the neurotoxic effects of oxaliplatin are triggered by drug accumulation in the dorsal root ganglia, causing neuronal dysfunction and apoptosis, thus leading to long-term, often, irreversible changes in the peripheral nervous system [9,10]. Oxaliplatin disrupts cell membrane ion channels and causes nerve hyperexcitability which results in acute peripheral neuropathy [11]. The oxaliplatin-induced VCP could be related to the direct effect of oxaliplatin on laryngeal nerve excitability. An oxalate released during oxaliplatin metabolism binds to calcium through chelation and blocks the calcium channels. This results in altered neuronal signal transduction [5,9].

A transient post intravenous infusion neurotoxic effects have also been observed, which manifests as jaw tightening, eye pain, leg cramps, pseudolaryngospasm, and cold hypersensitivity. These symptoms usually occur 30–60 min post infusion and resolve within a couple of days [12].

We believe this is the first reported case from Australia and only the fourth described so far in the literature. VCP should be considered in patients treated with chemotherapy who present with hoarseness and swallowing difficulties, and it should be promptly investigated. To confirm the diagnosis of VCP and establish the degree of upper airway compromise, an immediate ENT evaluation with FNE is necessary.

Author contributions

BMJ: Writing original draft, review and editing, SA, DP, JM: review and editing, KD: conceptualisation, literature review, review and editing, validation, supervision

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