

Paralytic Ileus as a Rare Complication of Vincristine Therapy: A Case Report

Keshavini Saravana Kumar, Prithiha Balaji, Leena Muppa*

Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, INDIA.

ABSTRACT

Paralytic ileus, a rare but serious complication of Vincristine therapy, is often underrecognized despite its potential to significantly impact patient outcomes. This case study describes a 68-year-old woman who had non-Hodgkin's lymphoma and developed paralytic ileus after receiving R-CHOP treatment for the first time. Severe distension, nausea, constipation, and stomach discomfort were the patient's initial complaints. Dilated bowel loops without a mechanical blockage were discovered by diagnostic imaging. Nasogastric decompression, bowel rest, intravenous fluids, and supportive drugs were all part of the conservative therapy. The patient's condition improved with meticulous therapy, including the administration of metoclopramide and electrolyte correction, despite early hypokalemia and gastrointestinal distress. After 10 days, the patient's belly circumference shrank, her bowel movements came back, and she was ultimately released in stable condition. This case underscores the need for awareness of VCR-induced paralytic ileus and highlights the importance of early diagnosis and supportive care, including the use of prokinetic medications like metoclopramide to manage gastrointestinal motility issues. Preventive measures, such as prophylactic stool softeners, should be considered for patients undergoing VCR-based chemotherapy to mitigate the risk of this complication.

Keywords: Paralytic ileus, Vincristine, Metoclopramide, Chemotherapy, Adverse Drug Reaction, Chemotherapy toxicity.

Correspondence:

Mrs. Leena Muppa

Assistant Professor, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, INDIA.
Email: leenamuppa220@gmail.com

Received: 12-04-2024;

Revised: 29-05-2024;

Accepted: 20-06-2024.

INTRODUCTION

Cancer is a disease resulted from aberrant cells proliferating out of control. Chemotherapy, sometimes known as "chemo," is a kind of cancer treatment in which chemicals are used to destroy cancer cells. Over the past few decades, chemotherapy and medicines have played a significant role in treating advanced-stage cancers when surgery and/or radiation therapy are not recommended for a variety of reasons. Despite its acknowledged negative consequences on the physical and mental well-being of patients, chemotherapy is still a widely used therapeutic option for cancer patients.¹ Following the initial cycle of chemotherapy, patients frequently reported mildly severe symptoms such as nausea or vomiting prior to treatment, ocular issues, and feeling down or depressed. Among the common symptoms that were reported to be of moderate severity were headaches, diarrhoea, and anxiety. Severe symptoms that were frequently reported included post-treatment nausea, post-treatment vomiting, constipation, pain, shortness of breath, temperature change, bleeding, skin,

hair, and mouth issues, changes in appetite, weight loss, weakness, unusual fatigue, and trouble sleeping.² For many cancer patients, GI side effects-such as nausea, vomiting, ulceration, bloating, constipation, and, most importantly, diarrhoea-are major obstacles that result in treatment delays, dosage reductions, and cessation.³ While certain chemotherapeutic treatments have been linked to a higher frequency of gastrointestinal side effects, reports have indicated that these side effects can occur in as many as 40% of patients receiving normal dosage chemotherapy and 60% to 100% of patients getting high-dose chemotherapy.⁴ The name "ileus" refers to an intestine that temporarily stops contracting, however, there isn't a universally recognized definition for it. When there is no mechanical obstruction, the intestinal tract paralyzes, this condition is known as paralytic ileus. Medications, severe metabolic issues, and intra-abdominal surgery are the major reasons. This toxicity is largely caused by a number of targeted therapy and anticancer medications. Similar to acute mechanical blockage, it can be fatal if left untreated for an extended period of time, therefore prompt diagnosis and treatment are crucial.⁵ Due Colic atony is brought on by an imbalance in autonomic bowel innervation. It is more likely to occur in people with trauma, electrolyte abnormalities, medications that affect gastrointestinal motility, and sepsis. The primary signs and symptoms of ileus are vomiting, constipation, trouble passing gas or stool, and stomach pain and distention.



DOI: 10.5530/ijopp.17.4.65

Copyright Information :

Copyright Author (s) 2024 Distributed under Creative Commons CC-BY 4.0

Publishing Partner : EManuscript Tech. [www.emanuscript.in]

In the absence of a mechanical blockage, the diagnosis is made based on the patient's clinical presentation and X-ray evidence of significant colonic dilatation. This illness is not well known, and there is a lack of information regarding diagnosis and treatment. Timely identification and suitable patient therapy can potentially mitigate the notable morbidity and death associated with this rare ailment. Depending on what causes it, ileus might have different outcomes. The first course of treatment is conservative and includes nasogastric decompression, bowel rest, intravenous fluids, electrolyte imbalance correction, and stopping drugs that impair colonic motility.⁶

CASE REPORT

A 68-year-old female was admitted with chief complaints of severe abdominal pain, distension, frothy vomiting, nausea, dysphagia, heartburn, and obstipation. She is a known case of non-Hodgkin's Lymphoma- Right Parotid Gland. She had a total conservative parotidectomy a month ago. She was started with R-CHOP (cyclophosphamide, doxorubicin, Vincristine and prednisolone±rituximab), chemotherapy. Cycle 1 chemotherapy

was completed 6 days before she was admitted to the emergency. Baseline investigations were done and reported to have neutropenia (Table 1). X-ray showed dilated bowel loops and no air-fluid level. On examination bowel sounds were sluggish. Medical oncologist's opinion was obtained and was suggestive of chemotherapy-induced paralytic ileus. The Patient was kept on Nothing by mouth (NPO). Ryle's Tube (RT) was inserted and continuous RT drainage. Abdominal girth was monitored every 8 hr, it was 77cm. The patient was treated with aminoven infusion, filgrastim, IV fluids, antiemetics, prokinetics, Proton Pump Inhibitors (PPIs), and other supportive medications (Table 2). Medical oncologist reviewed the patient, serum electrolytes were monitored, and was found to have hypokalaemia for which KCl correction was given. The patient was started on oral sips of water and the patient C/o abdominal pain. Continuous RT drainage was done and was managed with analgesics. H/o mild pain was present. Medical Gastroenterology (MGE) opinion was obtained and suggested for Computed Tomography (CT) abdomen plain was done and reported as Gaseous distension of ascending, transverse colon and a few of the jejunal loops. The

Table 1: Lab Investigations.

Parameter	Day 1	Day 2	Day 3	Day 4	Day 5
Haemoglobin	11.4	11.0	10.0	10.4	10.1
Total cell count	1202	1142	3480	4580	23891
Packed cell volume	33	33	30	32	30
Platelet	112000	654000	57000	60400	129000
Blood Glucose	132	135	120	94	100
Sodium	133	129	130	131	127
Potassium	4.10	4.0	3.50	3.36	3.39
Blood Urea Nitrogen	26	-	-	24	27
Creatinine	0.45	-	-	0.35	0.33
Total bilirubin	1.04	-	-	-	-
Direct bilirubin	0.33	-	-	-	-
Aspartate aminotransferase	17.4	-	-	-	-
Alanine transaminase	18.6	-	-	-	-
Total Protein	6.0	-	-	-	-
Albumin	3.3	-	-	-	-
Globulin	2.7	-	-	-	-
Alkaline phosphatase	85	-	-	-	-
Gamma glutamyl transferase	24	-	-	-	-
Amylase	-	-	-	116	-
Lipase	-	-	-	44	-
Neutrophils	28.4	48.5	72.9	85.5	89.2
Lymphocytes	55.8	28.9	12.9	5.8	3.9
Monocytes	9.2	15.8	12.4	8.1	6.6
Eosinophils	5.8	6.1	0.9	0.3	0.1
Basophils	0.8	0.9	0.9	0.3	0.2

Table 2: Treatment.

Brand name	Generic name	Dose	ROA	Frequency	Duration										
					1	2	3	4	5	6	7	9	10	11	
Inj. para	Paracetamol	1 g	IV	1-1-1	/	/	/	/	/	/	/	/	/	/	/
Inj. pan	Pantoprazole	40 g	IV	1-0-1	/	/	/	/	/	/	/	/	/	/	/
Pc enema	Sodium phosphate	0.65% 100 mL	PR	0-1-0	/										
Inj. cyclopam	Dicyclomine hydrochloride	10 mg	IV	1-0-0	/	/	/	/							
Inj. Aminoven	Essential amino acids	20%	IV	Over4 hr		/	/	/	/	/	/				
Inj. Kcl	Potassium chloride	40mEq in NS	IV	Over 4 hr				/	/	/					
Inj. perinorm	Metoclopramide hcl	10 mg	IM	1-1-1		/	/	/							
Inj. emeset	Ondansetron	4 mg	IV	1-0-1	/	/	/	/	/	/	/				
Inj. Neukine	Filgrastim	300 mcg	SC	0-1-0		/									
T. Zolfresh	Zolpidem	5 mg	RT	0-0-1				/	/	/	/	/	/	/	/
Syp. Sucrafil o	Sucralfate& oxetacaine	10 mL	PO	1-1-1				/	/	/	/	/	/	/	/
T. pan	Pantoprazole	40 mg	PO	1-0-1											/
T. para	Paracetamol	650 mg	PO	1-1-1											/

descending colon appears collapsed. No evidence of a transition point is seen at present. MGE reviewed the patient. Clear liquids were started. The patient still C/o abdominal pain hence analgesics were given. Clear liquids were started and the patient tolerated them well. On examination, bowel sounds were auscultated. Hence escalated to full liquids and then to a semisolid diet. The patient tolerated well and abdominal girth was found to be 84 cm. The patient was symptomatically better and passed dark stools. The patient recovered and was discharged after 10 days.

DISCUSSION

The rare condition known as paralytic ileus is linked to autonomic neuropathy or infections brought on by chemotherapy medications like vinblastine and Vincristine (VCR), as well as opioids that slow down bowel movements.⁶ VCR is an anticancer medication of the vinca alkaloid class that inhibits microtubule assembly. Vinca alkaloids have different toxicity profiles; among them, the most neurotoxic drug is VCR (VCR > vinblastine > vinorelbine > vinflunine).⁷ Constipation, paralytic ileus, and peripheral neuropathy are some of the symptoms of VCR-induced neurotoxicity. Fewer publications discuss adult ALL patients than there are case reports on VCR-induced paralytic ileus in juvenile Acute Lymphoblastic Leukemia (ALL) patients.⁸ VCR-based treatments, including cyclophosphamide, doxorubicin, VCR, and prednisolone (CHOP)±Rituximab (R-CHOP), Rituximab (R-CVP) with VCR and prednisolone (CVP) additionally VCR, pirarubicin, prednisolone, and cyclophosphamide Rituximab (R-THP-COP) and (THP-COP)

are often used to treat non-Hodgkin's lymphoma. Its usage is restricted by neurotoxicity, but it has beneficial efficacy and none of the typical anticancer drug's myelotoxicity or emetic effects. Peripheral neuropathy, which is mostly sensory in nature, and decreased intestinal motility leading to constipation are prominent symptoms of neurotoxicity.⁹ The exact process causing this disruption is uncertain, despite the fact that myenteric plexus injury is the most common explanation. In a study conducted in the year 2017, constipation was observed in 34.6% of patients receiving CHOP for non-Hodgkin's lymphoma.¹⁰ Variants in CYP3A5, the VCR metabolizer, that result in decreased expression of CYP3A5, have been repeatedly identified as a risk factor for VIN. It is noteworthy that different ethnic groups have different frequencies of CYP3A5 variations; as a result, Caucasians have a greater reported prevalence of VIN than African Americans.¹¹ Up till now, supportive therapies including metoclopramide, sinalide, and prostaglandin F2 have been used to treat VCR-induced ileus.¹²⁻¹⁴ As a prokinetic drug, metoclopramide inhibits postsynaptic and presynaptic D2 receptors, stimulates 5-HT3 receptors, and releases acetylcholine to increase gastrointestinal motility. Metoclopramide is frequently prescribed to individuals receiving chemotherapy to address the symptoms of vomiting, gastroparesis, and gastroesophageal reflux disease.¹⁵ After intestinal blockage was ruled out, the patient received intravenous infusions of metoclopramide 10 mg three times a day, as metoclopramide is contraindicated in cases of gastrointestinal obstruction. Although VCR-induced neurotoxicity has been shown to be surprisingly reversible, some individuals may continue to have neurotoxicity for some time.¹⁶

CONCLUSION

In order to prevent gastrointestinal motility issues, it should be remembered that all patients receiving VCR-based chemotherapy should be administered prophylactic stool softeners. In our case, the patient recovered from paralytic ileus with metoclopramide, there is currently no standard protocol for managing ileus due to VCR. With the help of the evidence available, we know that prokinetic medications such as metoclopramide are viable alternatives for treating ileus when intestinal obstruction has been ruled out.

ACKNOWLEDGEMENT

We are greatly indebted to our highly respected and beloved, Mrs. Leena Muppa, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy for her benevolent and ever-helping arms which provided us with all the essential facilities in bringing out this paper. We would like to thank our beloved parents for trusting and supporting us. Above all, we would like to give thanks and praise to the almighty God for his grace and blessing throughout the entire work.

CONSENT TO PARTICIPATE

The patient has been informed about the publishing and assured that the information will only be used for scientific and research purposes and identity of the patient will not be disclosed. Oral consent was obtained.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

GI: Gastro Intestinal; **R-CHOP:** Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone ± Rituximab; **NPO:** Nil Per Os (Nothing by mouth); **RT:** Ryle's Tube; **PPI:** Proton Pump Inhibitor; **MGE:** Medical Gastroenterology; **CT:** Computed Tomography; **C/o:** Complaints of; **H/o:** History of; **VCR:** Vincristine; **ALL:** Acute Lymphoblastic Leukemia; **CVP:** Cyclophosphamide, Vincristine, Prednisolone; **THP-CHOP:** Prednisolone, Pirarubicin, Cyclophosphamide, Vincristine; **CYP:** Cytochrome P.

SUMMARY

A rare condition called paralytic ileus halts the intestine's contractions, leading to symptoms of nausea, vomiting, and diarrhea. This condition can result from medications, extreme

metabolic disorders, and major abdominal surgeries. Timely diagnosis and treatment are vital for cancer patients to survive. The treatment involves nasogastric decompression, bowel rest, intravenous fluids, correction of electrolyte imbalance, prokinetic agents and discontinuation of drugs causing colonic stasis.

A 68-year-old woman with right parotid gland non-Hodgkin's lymphoma experienced severe abdominal symptoms including pain, distension, vomiting, nausea, dysphagia, heartburn, and obstipation. The patient's paralytic ileus was caused by chemotherapy and could be attributed to autonomic neuropathy from vinblastine and VCR. Non-Hodgkin's lymphoma is treated with VCR-based regimens like R-CHOP, but their use is limited due to neurotoxicity. These therapies, including metoclopramide, sinalide, and prostaglandin F₂, have been utilized to address VCR-induced ileus. VCR-induced neurotoxicity is usually reversible in most cases but can persist in some individuals.

REFERENCES

- Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, *et al.* Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. *Genes Dis.* 2023;10(4): 1367-401. doi:10.1016/j.gendis.2022.02.007
- Rohilla K, Batra A, Kalyani C. Incidence and severity of self-reported chemotherapy side-effects in patients with hematolymphoid malignancies: A cross-sectional study. *Cancer Res Stat Treat.* 2020;3(4):736. doi: 10.4103/CRST.CRST_87_20
- Escalante J, McQuade RM, Stojanovska V, Nurgali K. Impact of chemotherapy on gastrointestinal functions and the enteric nervous system. *Maturitas.* 2017;105:23-9. doi: 10.1016/j.maturitas.2017.04.021.
- Gupta K, Walton R, Kataria SP. Chemotherapy-induced nausea and vomiting: Pathogenesis, recommendations, and new trends. *Cancer Treat Res Commun.* 2021;26(100278):100278. doi: 10.1016/j.ctarc.2020.100278
- Roy R, Sarkar S. Paralytic ileus- A rare but serious side-effect of oral capecitabine. *Int J AnatRadiol Surg.* 2022; doi: 10.7860/IJARS/2022/56456.2843
- Carraro F, Rivetti E, Romano E, Fagioli F. Two cases of paralytic ileus in onco-hematologic patients. *Pediatr Rep.* 2012;4(1):3. doi: 10.4081/pr.2012.e3
- Li GZ, Hu YH, Li DY, Zhang Y, Guo HL, Li YM, Chen F, Xu J. Vincristine-induced peripheral neuropathy: A mini-review. *Neurotoxicology.* 2020;81:161-71. doi: 10.1016/j.neuro.2020.10.004.
- Yasu T, Ohno N, Kawamata T, Kurokawa Y. VCR-induced paralytic ileus during induction therapy of treatment protocols for acute lymphoblastic leukemia in adult patients. 2016;54:471-3. doi: 10.5414/CP202584.
- Legha SS. Vincristine neurotoxicity: Pathophysiology and management. *Med Toxicol.* 1986;1(6):421-7. doi: 10.007/BF03259853
- Hayashi H, Suzuki A, Ohata K, Ishihara M, Kubota Y, Kobayashi R, *et al.* Control of constipation in patients receiving CHOP or CHOP-like chemotherapy regimens for non-hodgkin's lymphoma. *Jst.go.jp.* doi: 10.1248/bpb.b16-01001.
- Madsen ML, Due H, Ejsskjær N, Jensen P, Madsen J, Dybbæk K. Aspects of vincristine-induced neuropathy in hematologic malignancies: a systematic review. *Cancer ChemotherPharmacol.* 2019;84(3):471-85. doi: 10.1007/s00280-019-03884-5
- Jackson DV Jr, Wu WC, Spurr CL. Treatment of vincristine-induced ileus with sincalide, a cholecystokinin analog. *Cancer ChemotherPharmacol.* 1982;8(1):83-5. doi:10.1007/BF00292876
- Ikehara O. Vincristine-induced paralytic ileus: role of fiberoptic colonoscopy and prostaglandin F₂ alpha. *Am J Gastroenterol.* 1992;87(2):207-10. PMID: 1734699.
- Garewal HS, Dalton WS. Metoclopramide in VCR-induced ileus. *Cancer Treat Rep.* 1985;69:1309-11. PMID: 3867404
- Lee A, Kuo B. Metoclopramide in the treatment of diabetic gastroparesis. *Expert Rev EndocrinolMetab.* 2010;5:653-62. doi: 10.1586/eem.10.41
- Park SB, Goldstein D, Krishnan AV, *et al.* Chemotherapy-induced peripheral neurotoxicity: a critical analysis. *CA Cancer J Clin.* 2013;63:419-37. doi: 10.3322/caa.c.21204

Cite this article: Kumar KS, Balaji P, Muppa L. Paralytic Ileus as a Rare Complication of Vincristine Therapy-A Case Report. *Indian J Pharmacy Practice.* 2024;17(4):396-9.