

# **A RARE REPORT TREATISE ON CLASSICAL HODGKIN LYMPHOMA-MIXED CELLULARITY STAGE 3B WITH VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY**

**Abstract:** We report a unique case of vincristine-induced peripheral neuropathy associated with acute pancreatitis in a 16-year-old male patient suffering from classical Hodgkin lymphoma with the primary symptom of bilateral cervical lymphadenopathy. However, upon diagnosis, this youngster was found to have cervical lymphoma, which differs from the other symptoms of the disease. Diagnosed in February 2023 with CHL, the patient was stratified based on the Ann Arbor staging of Hodgkin lymphoma guidelines by the European Network for Pediatric Hodgkin Lymphoma (EURONET-PHL). Laboratory and physical examination confirmed the clinical conditions of peripheral neuropathy and acute pancreatitis, which are adverse effects of chemotherapy, which were managed with IV Piperacillin Tazobactam (100 mg/kg) and opioid medications. Vincristine-induced neuropathy was treated with Morphine (10mg orally) and Gabapentin (300mg) was used to provide analgesia. His chemotherapy involved two cycles of an OEPA regimen, in accordance with guidelines for the treatment of CHL, and improved clinically. This case report is being offered to clinically enlighten people about the early diagnosis, treatment of CHL and adverse effects of the vincristine drug used in chemotherapy in pediatric patients.

Keywords: Hodgkin's Lymphoma, EURONET C1 Protocol, Peripheral Neuropathy, Acute Pancreatitis, OEPA Chemotherapy.

## **ABBREVIATIONS:**

CHL: Classical Hodgkin's Lymphoma

NSCHL: Nodular Sclerosis CHL

MCCHL : Mixed Cellularity CHL

LDCHK: lymphocyte-depleted CHL

LRCHL : lymphocyte-rich CHL

ASR - Age-Standardised Rate

ESR- Erythrocyte Sedimentation Rate .

VIPN -Vincristine Induced Peripheral Neuropathy.

EBV - Epstein-Barr virus

## INTRODUCTION:

Classical Hodgkin lymphoma is a lymphatic system cancer that affects 2-1 cases per 100,000 people annually in developed nations. <sup>1</sup> Unique clinical, morphologic, and epidemiologic characteristics comprise B cell-derived lymphoma, which is characterized by a distinctive immunophenotype and relatively few malignant cells in a non-neoplastic inflammatory background that involves cervical, axillary, mediastinal, and paraaortic lymph nodes. <sup>2</sup> Four distinct CHL subtypes have been identified based on histological characteristics, including nodular sclerosis CHL (NSCHL), mixed cellularity CHL (MCCHL), lymphocyte-depleted CHL (LDCHL), and lymphocyte-rich CHL (LRCHL). <sup>3</sup>

India has an age-standardized rate (ASR) of 0.4/100000 for Hodgkin lymphoma, compared to a global ASR range of 0.3/100000 for less developed nations and 0.6/100000 for developed nations. <sup>4</sup>

## 2. CASE PRESENTATION:

- A 16-year-old male patient with a known case of classical Hodgkin lymphoma was admitted to the hospital on 3<sup>rd</sup> March 2023 with complaints of severe abdomen pain and nausea with no fever on day 10 of OEPA chemotherapy.

During the **examination**, the patient was conscious, oriented, and febrile, and his vitals were stable. His pallor was soft with **diffuse tenderness, and his liver was palpable 2 cm below the RCM, BS+**. In the **local examination, multiple enlarged cervical lymph nodes** were present.

## PAST HISTORY:

The patient presented with swelling of the neck over the left side, which progressively increased in size and later developed swellings on both sides of the neck. A USG **abdomen done in another hospital showed bilateral cervical lymphadenopathy.**

## Diagnosis and staging:

- **Histopathological examination** of the excised lymph node was suggestive of Classical Hodgkin Lymphoma. IHC showed Reed-Stenberg cells, which were strongly positive for CD30, patchy positive for CD20, and negative for CD15.A

whole-body PET CT showed **hypermetabolic lymph nodes** on both sides of the diaphragm with hepatosplenomegaly.

- A bilateral bone marrow biopsy showed no evidence of infiltration.

Table 1 :Result of pathological examination

PARAMETERS	OBSERVED VALUES	REFERENCES
Haemoglobin	9.7	11.2-14.5 g/dl
Packed Cell Volume	29	40-50 %
Total WBC Count	3770	4000-11000 cells/mm <sup>3</sup>
RBC Count	3.7	4.5-5.5 mill/mm <sup>3</sup>
Platelet	170000	150000-450000 cells/mm <sup>3</sup>
Neutrophils	79.8	40-80%
Lymphocytes	17.0	20-40 %
Eosinophils	0.0	1-6 %
Sodium	133	135-145 mmol/L
Potassium	4.30	3.4-4.7 mmol/L
Total/ HDL cholesterol	4.4	<3.5 mg/dl
Total Protein	7.4	6.0-8.0 g/dL
Albumin	4.5	2.8-5.4g/dl
Globulin	2.9	2.0-3.5g/dl
Osmolality serum	235	275 to 295 mOsm/kg
Osmolality Urine	13	50 to 1,200 mmol/kg
Spot Urine for Sodium	111	135.9 to 167.6 mEq
Serum AMYLASE	279	40 to 140 U/L
Serum LIPASE	297	0 to 160 U/L

## ACUTE PANCREATITIS:

He developed abdominal pain with loose stools on Day 2 of his chemotherapy and experienced elevated amylase and lipase levels. So he has kept NPO once again and started IV fluids. He began receiving IV piperacillin and tazobactam (100 mg/kg). Opioids administered intravenously were used to manage the pain, i.e., a FENTANYL infusion at a dose of 30 mg/kg/min. He began receiving it orally.

## NEUROLOGICAL ISSUES:

- He began experiencing a strong headache and intermittent blurred vision on day 13 or later. A clinical examination revealed sinus pain. A normal study was revealed by a usual CT brain. His headaches were sporadic, and he felt shock-like feelings all over his face and arms. The brain was subjected to an MRI, with mediocre results. The neuropathy caused by vincristine was taken into consideration. For analgesia, gabapentin (300 mg) was administered in addition to morphine (10 mg) orally. He grew less polyuric over time.

## TREATMENT

The European Network-Paediatric Hodgkin Lymphoma Study Group (EuroNet-PHL) developed the standard protocol for the first-line therapy of Hodgkin lymphoma in children. The patient's stratification was determined by the Ann Arbor staging system for Hodgkin lymphoma. The patient's weight was found to be 60 kg and his body surface area (BSA) was calculated as  $1.7\text{m}^2$

### Medications before Chemotherapy:

- Inj ONDANSETRON 8 mg IV started before 30 minutes of chemotherapy.
- Inj METOCLOPRAMIDE 7.5mg in 20 ml Normal Saline IV over 20 minutes.
- Inj FOSAPREPITANT 150 mg in 50 ml Normal Saline IV over 30 min
- Inj PANTOPRAZOLE 40 mg IV once a day.

## CHEMOTHERAPY - OEPA:

The patient was treated with an OEPA regimen of chemotherapy which followed medications under the EURONET - C1 Protocol.

**Table 2 : OEPA regimen of chemotherapy**

DRUG NAME	DOSE / BSA	DOSE ADMINISTERED	DAYS GIVEN
VINCRIStINE	1.5-2 mg/m <sup>2</sup> /dose	2mg IV in 100ml NS	DAY 1,8 & 15
DOXORUBICIN	60-90 mg/m <sup>2</sup>	68mg IV in 100 ml NS	DAY 1 & DAY 15
ETOPOSIDE	100mg/m <sup>2</sup> /day	215 mg IV in 500 ml NS	DAY 1 - DAY 5

PREDNISOLONE	0.1-2 mg/kg	20 mg PO TDS	DAY 1 - DAY 15
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- TAB. PREDNISOLONE(0.1-2 mg/kg/day) 20mg orally from DAY 1 TO DAY 15, two tablets in the morning and afternoon, and one tablet at night.
- Because of poor general condition, day 15 chemotherapy with Inj Vincristine and Inj doxorubicin was postponed and given on Day +17 when his clinical condition was better and blood counts started improving. His general condition improved. He tolerated the treatment well. Hence being discharged on March 15, 2023, with a duration of 12 days of treatment in a hemodynamically stable condition.

DISCUSSION: The name "Hodgkin's disease," which was well-known for many years and represented the cellular heritage of Hodgkin/Reed-Sternberg (HRS) cells and uncertainties about whether they were reactive or malignant, was studied by Thomas Hodgkin from the Guy's Hospital in London (Hodgkin, 1832).<sup>3</sup> Approximately 80% of patients present with painless adenopathy, most commonly involving the supraclavicular or cervical area. 15% to 25% of teenagers and young adults with Hodgkin lymphoma in affluent nations have positive EBV tumor cells. Developing countries have a high frequency of mixed-cellularity histology in children with Hodgkin lymphoma.<sup>5</sup> However, upon diagnosis, this youngster was found to have cervical lymphoma (bilateral cervical lymphadenopathy). **Histopathological examination** of the excised lymph node was suggestive of classical Hodgkin lymphoma. IHC showed Reed-Stenberg cells, which were strongly positive for CD30, patchy positive for CD20, and negative for CD15. The **hallmark of Hodgkin lymphoma** is the HRS cell and its variants. The eosinophilia in mixed-cellularity Hodgkin lymphoma may be caused by interleukin-5.<sup>5</sup> Differentiating this subtype from non-Hodgkin lymphoma can be challenging. FROM THE CASE DETAILS, THE HISTOLOGY REPORT CORRELATES WITH THE HISTOLOGY FEATURES OF THE TYPE OF CHL and hence is diagnosed as CLASSICAL HODGKIN LYMPHOMA—MIXED CELLULARITY STAGE 3B.

According to the guidelines of the European Network for Pediatric Hodgkin Lymphoma (EURONET-PHL), the patient was treated, and the protocol followed was EURONET-PHL-C1. **The patient was categorized as part of the third therapy group (TG3) since the disease had progressed to stage III B.** One limitation of vincristine treatment is the development of peripheral sensory neuropathy. Pediatric patients are more difficult to identify and track for vincristine-induced peripheral neuropathy (VIPN), a side effect that can lower their long-term quality of life.<sup>6</sup> In this case, the child developed periodic headaches, and he felt shock-like sensations all over his face and arms. An MRI of the brain produced mediocre results. **The neuropathy caused by vincristine was taken into consideration. This adverse event was reported to PVPI and got the worldwide unique ID IN-IPC-300785105.** Gabapentin (300 mg) was administered orally in addition to morphine (10 mg) to give analgesia. The  $\beta$ -tubulin subunit of microtubules, which are essential parts of nerve fibre axons, is the target of the vincas (and taxanes), as these drugs induce axonopathy, which presents as a gradually progressing axonal sensory neuropathy, because vincas have an affinity for both mitotic spindles and axonal microtubules, especially when vincristine is used.<sup>6</sup> **In 2016, Erika Mora et al. reported vincristine-induced neuropathy in paediatric**

**patients as supporting literature for this case report.** Acute pancreatitis can result from several medications such as tetracyclines, steroids, and antibiotics which are used in paediatric oncology. However, the diagnosis of AP caused by drugs is frequently inaccurate and primarily grounded in clinical suspicion.<sup>7</sup> In this child, corticosteroids such as prednisolone were suspected for causing ACUTE PANCREATITIS

CONCLUSION: Hodgkin lymphoma (HL) is a malignant tumour originating from B lymphocytes that is characterised by the presence of giant multinucleated Reed-Sternberg (RS) cells. As HL is curable, therapies aimed at reducing the long-term morbidity of these patients are becoming more essential. Remember that patients taking vinca alkaloid medicines may experience shock-like sensory symptoms, which should be properly examined as they could indicate peripheral neuropathy (VIPN). Acute pancreatitis and peripheral neuropathy are a couple of adverse reactions that need to be treated appropriately right away since they can progress. We would like to bring attention to this potential and document this association in paediatric patients receiving chemotherapy.

#### ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

#### CONSENT

As per international standards, parental written consent has been collected and preserved by the author(s).

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