Case report

A RAREREPORTTREATISE 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. Most CHL patients initially appear to have lymphadenopathy. However, upon diagnosis, this youngster was found to have cervical lymphoma, which differs from the other symptoms of the disease. Of juvenile malignancies, 6% are Hodgkin lymphomas. Diagnosed in February 2023 with classical Hodgkin lymphoma, the patient was categorized based on the Ann Arbor staging of Hodgkin lymphoma guidelines, which are set out by the European Network for Pediatric Hodgkin Lymphoma (EURONET-PHL). The patient was categorized as part of the third therapy group (TG3) since the disease had progressed to stage III A . Laboratory and physical examination confirmed the clinical conditions of acute pancreatitis and peripheral neuropathy as adverse effects of chemotherapy, which was 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 treatment.

Keywords: Hodgkin's lymphoma, EURONET C1 Protocol, peripheral neuropathy, acute pancreatitis, febrile neutropenia, OEPA chemotherapy.

ABBREVIATIONS:

CHL - Classical Hodgkins 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

IPS - International Prognostic Scores IPS-7 and IPS-3

NLR - Neutrophil-Lymphocyte Ratio (NLR),

LMR- lymphocyte monocyte ratio (LMR),

PLR-platelet lymphocyte ratio (PLR)

SII- systemic immune-inflammation index (SII),

PET CT - Positron Emission Tomography and Computed Tomography

EBV - Epstein-Barr virus

OEPA - Vincristine, Etoposide, Prednisolone, Doxorubicin

OPPA- Vincristine, Adriamycin, Procarbazine,

COPP - Cyclophosphamide, Oncovin, Procarbazine and Prednisone

COPDAC - Cyclophosphamide, Vincristine, Prednisolone, Dacarbazine

ABVE-PC - Adriamycin, Bleomycin, Vincristine, Etoposide, Prednisone and Cyclophosphamide.

BEACOPP - Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, Procarbazine, Prednisolone.

ABVD - Adriamycin, Bleomycin, Vinblastine, Dacarbazine

1. INTRODUCTION:

Classical Hodgkin lymphoma is a lymphatic system cancer that affects 2-1 cases per 100,000 people annually in developed nations. [1]

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 nonneoplastic inflammatory background .

It Involves cervical > axillary, mediastinal, and paraaortic lymph nodes.

Bimodal age distribution with peaks between the ages of 15 and 35 and 50 and 70 [2]

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). [3]

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. Ann Arbor Staging of lymphomas categorizes it into four different stages based on the involvement of lymph nodes, organs that gain damage, and symptoms present.[4]

2. CASE PRESENTATION:

A 16-year-old male patient with a known case of classical Hodgkin lymphoma came to the hospital with complaints of severe abdomen pain and nausea with no fever. He was admitted for a chemotherapy routine that includes OEPA chemotherapy, which contains a combination of vincristine sulfate, etoposide phosphate, doxorubicin hydrochloride, and the steroid hormone prednisone. His pallor was found to be soft with diffuse tenderness. In the local examination, multiple enlarged cervical lymph nodes were present.

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 previously showed 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.

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

His ailments included the following,

- 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 (DNS and NS). He began receiving IV Piperacillin 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 oral feeds.

POLYURIA/NEUROLOGICAL ISSUES:

His severe headache and sporadic vision blurring started on day 13 or later. Sinus discomfort was detected during a clinical examination. The ophthalmological examination performed at the bedside was normal. A typical CT-brain result showed a normal study. Polyuria set in. The blood sugar level was normal. Fluid replacement was done. His sensory sensations across his face and limbs resembled shock, and he experienced intermittent headaches. An MRI of the brain was performed, and the results were average. Consideration was given to

vincristine-induced neuropathy. Along with morphine (10mg orally), gabapentin (300mg) was used to provide analgesia. He gradually became less polyuric.

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 1.7m^2

Medications before Chemotherapy:

- Inj ONDANSETRON 8mg 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.

- Inj VINCRISTINE (1.5-2 mg/m^2/dose) 2 mg intravenously in Normal Saline as slow push on DAYS 1,8 and 15.
- InjDOXORUBICIN (60 mg-90 mg/m^2)68 mg intravenously in 100ml Normal Saline on DAY 1 and DAY 15.
- Inj ETOPOSIDE (100mg/m^2/day)215 mg intravenously in 500ml Normal Saline over 2 hours from DAY 1 TO 5.
- 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.

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). Hodgkin lymphoma (HL) is a malignant tumor originating from B lymphocytes that is characterized by the presence of giant multinucleated Reed-Sternberg (RS) cells. 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. Approximately 80% of patients

present with painless adenopathy, most commonly involving the supraclavicular or cervical area. In developed countries, 15% to 25% of teenagers and young people with Hodgkin lymphoma are EBV tumor cell positive. 17–19] The majority of these cases (around 80%) are EBV-positive. Developing countries have a high frequency of mixed-cellularity histology in children with Hodgkin lymphoma. Most CHL patients initially appear to have lymphadenopathy. However, upon diagnosis, this youngster was found to have cervical lymphoma (bilateral cervical lymphadenopathy), which differs from the other symptoms of the disease. The eosinophilia in mixed-cellularity Hodgkin lymphoma may be caused by interleukin-5. Differentiating this subtype from non-Hodgkin lymphoma can be challenging. From these factors, the diagnosis is confirmed 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. TG3 refers to stages IIB and IIIA with E-lesions, or stages IIIB or IV. A blood evaluation should include a complete blood count, erythrocyte sedimentation rate (ESR), liver function, renal function, bone profile, and testing for hepatitis B/C and HIV.. Long-term observations of people treated for HL as children have shown the risk of long-term sequelae, including gonadotoxicity, cardiovascular issues, thyroid dysfunctions, and secondary cancers.The patient was treated with an OEPA regimen of chemotherapy, which includes the following medications as per the standard guidelines for CLASSICAL HODGKIN LYMPHOMA—MIXED CELLULARITY STAGE 3B.The chemotherapeutic drug vincristine is an essential component of regimens for a range of malignancies, including several common tumors in children. 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. In this case, the child developed periodic headaches, and he felt shock-like sensations all over his face and arms. The brain was subjected to an MRI, with average results. The neuropathy caused by vincristine was taken into consideration. Gabapentin (300 mg) was administered orally in addition to morphine (10 mg) to give analgesia. The β-tubulin subunit of microtubules, which are essential parts of nerve fiber 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. In 2016, Erika Mora et al. reported vincristine-induced neuropathy in pediatric patients as supporting literature for this case report. Acute pancreatitis can result from a number of medications, including those used for pediatric oncology. However, the diagnosis of AP caused by drugs is frequently inaccurate and primarily grounded in clinical suspicion. In the field of pediatric oncology, tetracyclines, and steroids are antibiotics. Asparaginase, trimethoprim/sulfamethoxazole, and mercaptopurine are linked to AP brought on by drugs. In this child, corticosteroids such as prednisolone were suspected.

CONCLUSION:

As Hodgkin lymphoma is recoverable, greater importance is being placed on treatments that minimize these patients' long-term morbidity. It should be kept in mind that any shock-like sensory symptoms in a patient who intakes vinca alkaloid drugs should be closely diagnosed as they may be a symptom of peripheral neuropathy. While this drug is characterized by an overall safe profile and proves to be very efficient in treating refractory Hodgkin's disease, peripheral neuropathy, and acute pancreatitis are severe adverse reactions that require immediate, adequate treatment and may lead to further complications. We wish to highlight such a possibility and report such an association in pediatric patients during chemotherapy.

CONSENT

As per International Standard or university standard written ethical approval has been collected and preserved by the author (s)

ETHICAL APPROVAL

As per International Standard or university standard written ethical approval has been collected and preserved by the author (s)

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