



PRESENTATION OF GUILLAIN BARRE SYNDROME AS PARANEOPLASTIC SYNDROME IN CANCER PATIENT: A DIAGNOSTIC DILEMMA

Oncology

Dr. B. K. Shewalkar Professor And Head Of Department Of Radiotherapy And Oncology, Govt. State Cancer Institute, Maharashtra, India

Dr. Mahesh Rewadkar* Associate Professor, department Of Radiotherapy And Oncology, Govt. State Cancer Institute, Maharashtra, India *Corresponding Author

Dr. Roopa Balachandran Resident In Department Of Radiotherapy And Oncology, Govt. State Cancer Institute, Maharashtra, India

ABSTRACT

BACKGROUND: Paraneoplastic peripheral neuropathies may develop any time during the course of the neoplastic disease. These neuropathies are often masked by concurrent neurotoxicity from chemotherapy and other cancer therapies.

MATERIALS AND METHODS: Here, we report a case of a 40 year old female who was diagnosed as Guillain Barre Syndrome in a known case of triple negative breast cancer on second line chemotherapy. Patient presented with gait disturbances and slurred speech 2 weeks after receiving a 3rd cycle of second line nanosomal Docetaxel based chemotherapy. This case had a diagnostic dilemma. First we suspected brain metastasis, but MRI brain was normal. Nerve conduction study results led to suspicion of Docetaxel induced neurotoxicity. CSF cytology report showed raised protein levels and negative for malignant cells. Finally a diagnosis of paraneoplastic neuropathy or Acute Inflammatory Demyelinating Polyneuropathy (Guillain Barre syndrome i.e. GBS) was made. Patient was treated with intravenous immunoglobulin and other supportive measures. But Patient's condition deteriorated, and expired in ICU course.

CONCLUSION: GBS in cancer patients should be differentiated from chemotherapy induced toxicity & neuropathy, particularly as effective treatment is available for GBS like Paraneoplastic syndrome.

KEYWORDS

Paraneoplastic, Peripheral Neuropathy, Nanosomal Docetaxel, Guillain Barre Syndrome

INTRODUCTION

Paraneoplastic syndrome is the term used to refer to the disorders that accompany benign or malignant tumors but are not directly related to mass effects or invasion [1]. Paraneoplastic peripheral neuropathies may develop any time during the course of the neoplastic disease. These neuropathies are often masked by concurrent neurotoxicity from chemotherapy and other cancer therapies. In contrast, the neuropathies that develop in the early stages of cancer frequently show a rapid progression, sometimes with a relapsing and remitting course, and evidence of inflammatory infiltrates and axonal loss or demyelination in biopsy studies [2]. If demyelinating features predominate IVIg, plasma exchange, or glucocorticoids may improve symptoms. Occasionally anti-CV2/CRMP5 antibodies are present; detection of anti-Hu suggests concurrent dorsal root ganglionitis. Guillain-Barré syndrome and *brachial plexitis* have occasionally been reported in patients with lymphoma, but there is no clear evidence of a paraneoplastic association. Vasculitis of the nerve and muscle, Peripheral nerve hyperexcitability (neuromyotonia, or Isaacs' syndrome), Paraneoplastic autonomic neuropathy are some of the other paraneoplastic peripheral neuropathies [3].

CASE REPORT

Here, we report a case of a 40 year old female who was diagnosed as Guillain Barre Syndrome in a known case of triple negative breast cancer on second line chemotherapy.

Patient was non diabetic & non hypertensive, had initially completed 3 cycles of chemotherapy using Epirubicin, Cyclophosphamide and 5FU followed by 4 cycles of Paclitaxel and Carboplatin each cycle every 3 weekly then External Beam Radiation Therapy to Left Chest wall & Supraclavicular fossa to a total dose of 39 Gy in 13 fractions over 17 days as adjuvant to left Modified Radical Mastectomy. After adjuvant treatment patient was under regular follow-up on OPD basis. Then patient developed metastatic left axillary, infraclavicular, intramammary and intrathoracic lymphadenopathy confirmed clinically & using CECT Thorax scan with guided biopsy. Then we started patient on second line chemotherapy using single agent nanosomal Docetaxel lipid suspension.

Prior to Second line chemotherapy patient was neurologically asymptomatic. Then Patient presented with gait disturbances 2 weeks after receiving a 3rd cycle of second line nanosomal Docetaxel based chemotherapy. Symptoms were headache, vomiting, both lower limb

weakness to the extent of inability to stand & walk. Gradually she developed slurred speech & drooping of eyelids during ward course. On examination, patient had left eye enophthalmos, left sided ptosis, deviation of tongue to right side suggestive of glossopharyngeal nerve impairment and lower limb proximal muscle weakness to power of grade II.

Complete blood counts, Liver function test, Renal function test and Serum protein were within normal range. Serum potassium was 3.3 meq/L which was corrected in ward course. Vitamin B12, S.CPK, ADA, Free T3, Free T4, and Liver function test were done. Findings are given in Table 1. Endoscopy showed left vocal cord fixed in adductor position. We suspected brain metastasis hence we started treatment with steroids and mannitol. But subsequent MRI Brain with contrast was found to be normal. Cardiac CT, CT abdomen with pelvis and 2D echo were normal. CT chest revealed significant reduction in size of chest wall lesion and lymph nodes suggesting good response to chemotherapy. However patient's neurological symptoms clinically suggestive of intracranial disease spread but MRI being normal with no targeted lesion which led to diagnostic dilemma; hence to establish a etiology of neurological condition, Neurophysician opinion was taken who advised Nerve conduction study and CSF cytology.

Table-1

Vitamin B12	142 pmol/L
S.CPK	79.1 U/L
ADA	9.1 U/L
Free T3	2.02 pg/dl
Free T4	1.9 ng/dl
S. Bilirubin	1.22 mg/dl
Direct Bilirubin	0.45 mg/dl
Indirect Bilirubin	0.77 mg/dl

Nerve conduction velocity s/o Axonal Demyelinating sensory motor neuropathy. SNAP reduced in right sural nerve. F-waves normal in all nerves. CMAP reduced in left ulnar and bilateral peroneal nerves (Fig. 1, 2 & 3). As per neurophysician, it was a case of Polyneuritis cranialis with peripheral neuropathy. We suspected as nanosomal Docetaxel induced neurotoxicity, though it is uncommon with lipid suspension nanosomal Docetaxel. Intravenous Immunoglobulin, calcium, calcitriol, niacinamide and cyanocobalamin and other supportive treatment was started the same day. Patient developed

vomiting, headache and fever.

MRI brain with spine was normal (Fig. 4 & 5). Inbetween Csf cytology report showed suspicious malignant cells. With suspicion of leptomeningeal involvement by prevailing malignant condition of triple negative breast cancer, empirical intrathecal inj. methotrexate, hydrocortisone and cytarabine single dose was given. While giving intrathecal injection, a second CSF sample was sent for examination. This CSF cytology showed negative for malignant cells, 1-2 pus cells/hpf and raised protein (120 mg%). Neurologist second opinion bedside was taken. To our surprise it was then diagnosed as paraneoplastic neuropathy or Acute Inflammatory Demyelinating Polyneuropathy (Guillain Barre syndrome i.e. GBS) and restarted on IV Immunoglobulin.

The relevant points suggesting GBS were signs of demyelination on nerve conduction study. Raised LFT levels (seen in one third of GBS patients). Elevated CSF Protein levels with normal cell counts. But Patient's condition deteriorated, developed respiratory muscle paralysis, went into respiratory failure, was intubated for ventilator and shifted to Intensive Care Unit. She later developed septic shock and multiorgan dysfunction and patient expired in ICU course.

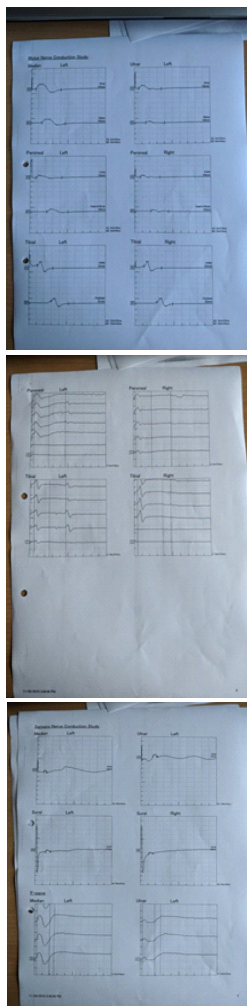


Fig 1, 2 & 3 Nerve conduction study

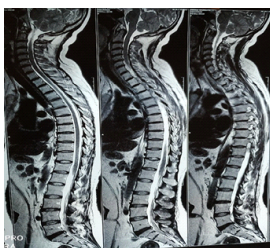


Fig. 4 MRI Spine with contrast

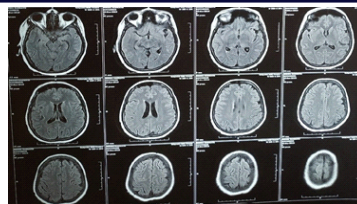


Fig. 5 MRI BRAIN with Contrast

DISCUSSION

Guillain-Barré syndrome (GBS) is an autoimmune disorder that is thought to be a postinfectious polyneuropathy, involving mainly motor but also sensory and sometimes autonomic nerves. Acute inflammatory demyelinating polyneuropathy, chronic inflammatory demyelinating polyneuropathy, Miller-Fisher syndrome are some of the variants of GBS[4]. The first symptoms of Guillain-Barré syndrome are numbness, tingling, and pain, followed by weakness of the legs and arms, weakness of muscles of face, eye muscles. Patient can develop weakness of the breathing muscles leading to respiratory failure. 20% may experience severe blood-pressure fluctuations and irregularities in the heart beat.

The causative agents are Campylobacter jejuni bacteria, cytomegalovirus, Epstein-Barr virus, varicella zoster virus, Mycoplasma pneumoniae, dengue virus, Zika virus and hepatitis E virus. Some cases may be triggered by influenza vaccine. The underlying mechanism involves an autoimmune disorder in which the body's immune system mistakenly attacks the peripheral nerves and damages their myelin insulation. Characteristic CSF findings in Guillain-Barré syndrome are an elevated protein level, and fewer than 10 white blood cells per cubic millimeter of fluid ("albuminocytological dissociation"). Nerve conduction study reveals demyelinating polyneuropathy.

Docetaxel is a semisynthetic taxane. It binds to microtubule enhances tubulin polymerisation. Metabolised in liver. The main adverse effects are myelosuppression, hypersensitivity reaction, fluid retention, maculopapular skin rash, alopecia, mucositis and diarrhea. Peripheral neuropathy is less commonly observed with docetaxel than paclitaxel[5].

Nanosomal docetaxel lipid suspension (NDLS) [DoceAqualip] is a novel formulation of docetaxel approved in India for the treatment of breast cancer, hormone-refractory prostate cancer, locally advanced squamous cell carcinoma of the head and neck, non-small cell lung cancer and advanced gastric adenocarcinoma. The lipid-based delivery system of NDLS eliminates the need for polysorbate 80 and ethanol, which are contained in the conventional docetaxel formulation and are associated with hypersensitivity reactions and infusion-related toxicities. Because of the diminished potential for NDLS to cause hypersensitivity reactions compared with conventional docetaxel, corticosteroid premedication is not required with NDLS[6]. Guillain Barre syndrome as paraneoplastic syndrome has been reported in patient with stage IV Peripheral T-cell Lymphoma-NOS who presented with severe infection and progressive flaccid quadriplegia following chemotherapy[7].

Out of 7 cases of GBS reported in patients with lung cancer, in 6 cases, GBS develop at the initial point of presentation[8-14]. A GBS case was reported in small cell lung cancer in which GBS developed after patient received 6 cycles of cisplatin, doxorubicin and cyclophosphamide and palliative brain radiation[14].

A case of GBS has been reported in colorectal cancer[15].

Here in our case, The GBS syndrome was idiopathic in onset and not related to nanosomal docetaxel based chemotherapy. The presentation was vague, hence diagnosis was difficult and hence delayed.

CONCLUSION

Patients with cancer are immunocompromised hence, vulnerable to infection and can have problems with the immune system. As illustrated by this report, paraneoplastic GBS is very rare but life-threatening Paraneoplastic Syndrome. GBS in cancer patients should be differentiated from chemotherapy induced toxicity & neuropathy, particularly as effective treatment is available for GBS like Paraneoplastic syndrome.

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