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Guillain Barre Syndrome complicating lymphoblastic lymphoma

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ABSTRACT

Neurological complications are a rare feature of haematological malignancies. We here report a case of T-cell lymphoblastic lymphoma in a 15 year old girl complicated by Guillain BarreSyndrome (GBS). The GBS occurred after two cycles of chemotherapy. Diagnosis was done by electrodiagnostic studies which revealed AMAN subtype. The patient needed mechanical ventilation and was also treated with IvIg. Relevant literature pertaining to the association of the two conditions have also been discussed.

INTRODUCTION

Lymphoblastic lymphoma is an aggressive variety of non-Hodgkin's lymphoma found mainly in children and adolescents [1]. This type of malignancy is comparatively rare and hence its treatment protocol is not fully standardized. It has been treated successfully with the common chemotherapy of lymphoma (CHOP) orthe induction protocol of acute leukemia. The disease usually has mediastinal involvement at presentation[1]. This aggressive malignancy is often complicated by clinical conditions like tumour lysis syndrome and infections [2]. However, sometimes neurological complications may also occur which can thwart further management. We here describe such a rare neurological complication of lymphoblastic lymphoma.

THE CASE REPORT

A 15 year old girl presented to the emergency of our hospital with acute onset respiratory distress for two days and high grade fever for one week. She had no previous history of any significant medical or surgical condition. On examination, the girl was found to have severe pallor and a swollen face. The jugular venous pulse was engorged and non-pulsatile. Blood pressure was 90/60 mm of Hg and pulse was 120/minute. Her respiratory rate was 45/minute and oxygen saturation at presentation was 86% in room air. An emergency X ray revealeda mass in para-tracheal region. In view of these findings, a provisional diagnosis of superior vena caval obstruction was made. She was started on intravenous steroids and high flow oxygen. An emergency hemoglobin level was done and it came as 3.2 gm/dl. Hence, packed RBC transfusion was also given immediately.

After the patient was stabilized, further tests were done. Complete hemogram revealed hemoglobin of 6.8 gm/dl, total leukocyte count of 2000/µL (N: 80%; L: 12%) and platelet count of 80000/ µL. Urea/creatinine and liver function test were normal. C reactive protein was 108 mg/L (N<6). A CT scan of thorax was done which revealed a heterogeneous mass in superior mediastinum encasing the great vessels (figure 1). A trucut CT scan guided biopsy was done from the para-tracheal mass and the histopathology showed atypical monomorphic cells with high N: C ratio, pleomorphic nuclei and coarse chromatin (figure 2). Immunophenotyping was done which revealed the tumour to be CD10, CD99 and CD117 (c-kit) positive. CD3 and 43 were diffusely positive. Also, c-myc was patchy positive and CD20 was positive in some of the cells. CD34 and Tdt were negative. Thus, the final diagnosis was Tdt negative lymphoblastic lymphoma. A bone marrow biopsy was done (figure 3) which revealed replacement of normal marrow elements with mononuclear round cells. The CT scan also revealed bilateral pleural effusion and chink of pericardial effusion. An MRI scan of dorsal vertebrae was done and it showed small areas of signal changes in most of the dorsal vertebrae, compatible with neoplastic infiltration.

In view of the immunophenotype and the staging, the patient

was started on monthly R-CHOP chemotherapy regimen with a plan of radiotherapy in the future if needed. The first two chemotherapy doses were uneventful and the girl improved markedly. The para-tracheal tumour decreased in size and the respiratory distress was curtailed. Also, her blood counts improved and she did not need any more transfusion support.

However, one week after the second chemotherapy dose, the girl suddenly presented again to the ER with respiratory distress and generalized weakness. She was found to have flaccid paralysis of all four limbs with normal sensory system. The respiratory excursion was also weak and oxygen saturation was 72% in room air. All deep tendon reflexes were absent. The next day, a nerve conduction velocity study was done which revealed Guillain-Barre syndrome, AMAN subtype (figure 4). MRI scan of entire spinal cord did not reveal any new lesion. Meanwhile, the patient's oxygen saturation fell even further to 60%. Hence, she was put on mechanical ventilation and IvIg was infused at the rate of 400 mg/Kg/Day for five days, after consultation with the neurology department. After seven days, a CSF study was done which revealed a cell count of 6/μL (all lymphocytes) and protein of 280 mg/dl. No malignant cell was detected in the CSF. Gram stain and GeneXpert ® studies of CSF were also negative.After two weeks, the patient could be taken out of the ventilator. But just the next day, she developed high fever and crepitations in both lungs. An immediate blood culture revealed the presence of Klebsiella sp. She was put on high dose antibiotics in the form of meropenem and tigecycline. However, her condition deteriorated quickly and she passed away a couple of days later.

DISCUSSION

Guillain Barre Syndrome (GBS) is an acute demyelinating polyradiculo-neuropathy which can occur after an infection, vaccination or idiopathically. Rarely, this can complicate malignancies and lead to catastrophes like respiratory failure. The table below shows the data from some published reports of GBS in haematological malignancies.

GBS is generally considered an autoimmune disease. However, its exact pathogenesis in cases of haematological malignancy is still unknown. There are still speculations as to whether this is a paraneoplastic phenomenon or a manifestation of immune dysregulation [5]. Some authors have found increased levels of IL-6 in the CSF of patients with GBS in lymphoma [7]. But no firm conclusion is still possible. Some authors have found direct infiltration of peripheral nerves by malignant cells [10]. But in most cases, indirect immunological phenomenon is responsible for the neurological deficit.

If the syndrome occurs after a particular chemotherapeutic drug, then that drug should probably be avoided, although a cause-effect relationship is difficult to establish [4]. Also, some authors have argued against such an approach because in that case, essential drugs like vincristine may be denied to the patient [8].

The diagnosis of GBS in malignancy is similar to normal GBS cases. However, the CSF should be examined carefully for the presence of malignant cells. As a previous case report shows, CNS Burkitt lymphoma was entirely diagnosed based on the

Table 1. : Table showing some case reports of GBS in haematological cancers

Year of publication	The type of malignancy	Timing of GBS with malignancy	Outcome	
			Malignancy	Neurology
2016 [3]	T-cell lymphoma	First presentation	Complete remission	Residual deficit
2015 [4]	Multiple myeloma	After bortezomib therapy	Treatment continued without offending drug	Recovery
2015 [5]	DLBCL	Post chemotherapy and radiotherapy	Death	
1994 [6]	CNS Burkitt's lymphoma	Initial presentation	Disease free at 2 years	Recovery
2006 [7]	Burkitt like lymphoma	During induction chemotherapy	Remission	Recovery
2013 [8]	ALL (2 cases)	During induction phase	Recovery for case-1 Death for case-2	
2012 [9]	DLBCL	Initial presentation	Remission	Recovery (this was a Miller-Fisher variant)

DLBCL: diffuse large B cell lymphoma; CNS: central nervous system

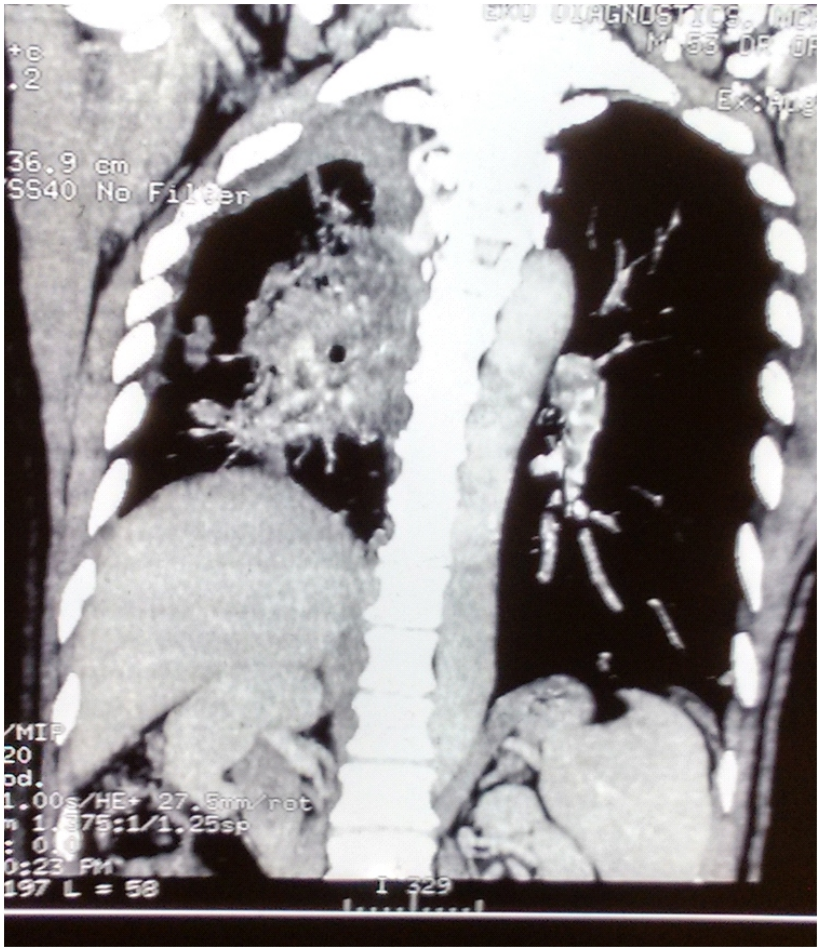


Fig 1. : CT scan of thorax showing right sided lung mass infiltrating superior mediastinal structures

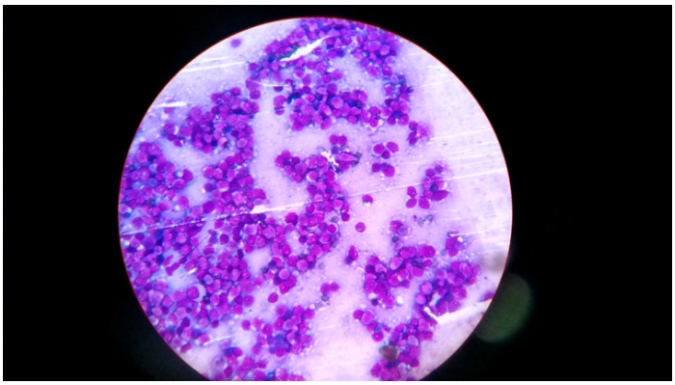


Fig 2. : Imprint smear of the mediastinal mass showing mononuclear round cells.

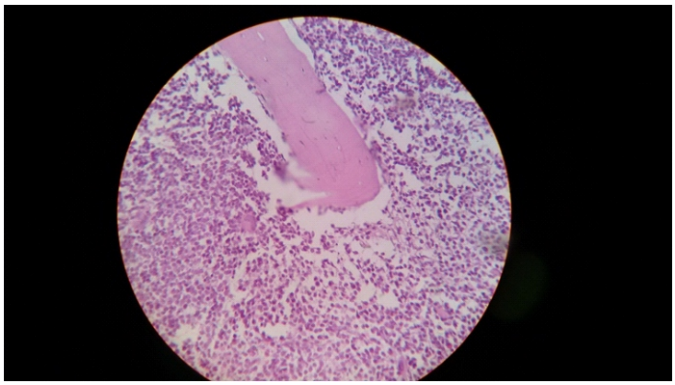


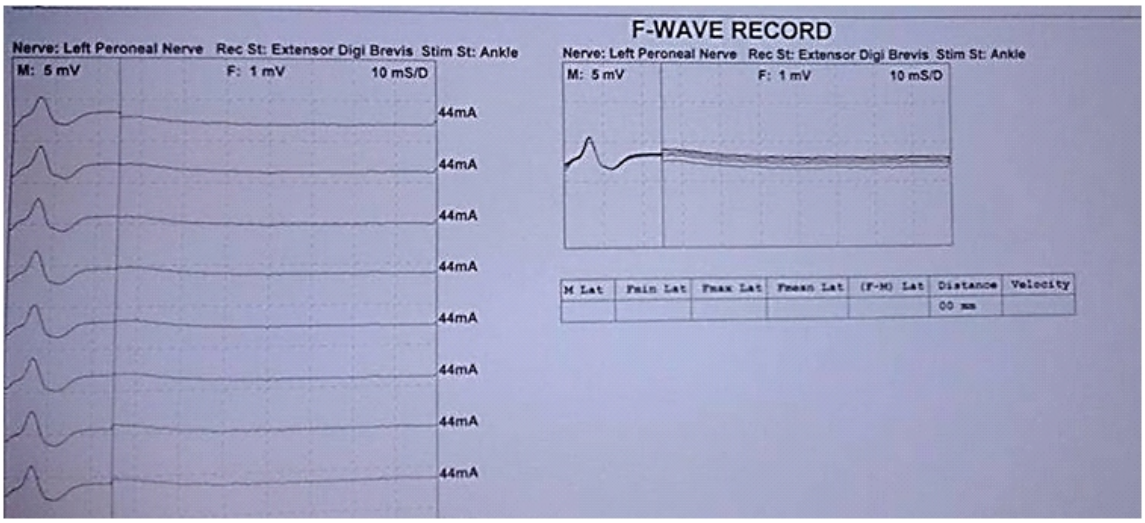
Fig 3. : Bone marrow biopsy specimen showing replacement of normal marrow elements with lymphocytes

study of CSF in a GBS patient [6]. However, sometimes, thrombocytopenia may be a contraindication to CSF study in GBS in these cases [8]. Then, electrodiagnostic studies become the mainstay of diagnosis.

Although most reported cases of GBS in haematological malignancy presented with the classical ascending paralysis variant, there are still some cases of atypical presentations like Miller-Fisher syndrome [11]. Thus, any neurological syndrome in these cancers should be investigated further. Another caveat in this respect is therapeutic misadventure. There has been reports of inadvertent intrathecal administration of vincristine in ALL giving rise to GBS like features [12]. Thus, in case of an acute onset neuropathy in a malignancy, all previously used drugs and their mode of administration should be reviewed again.

As the table above shows, the outcome of GBS in haematological malignancy varies. While some patients have been reported to recover fully, some others have expired with multiorgan failure, like our patient [5]. Most reported case reports depict the use of IvIg therapy or plasmapheresis paripassu with the chemotherapy for the underlying malignancy [3, 4].

Fig 4. : NCV study of the patient after onset of quadriparesis showing absent F waves



There has been very few reports of GBS in haematological malignancy from India. We report this case to make clinicians aware of this rare association.

CONCLUSION

Haematological malignancies may be compounded by neurological disorders. Such manifestations require separate, aggressive management.

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