Case Report

Chronic Myeloid Leukemia with an Unusual Paraneoplastic Syndrome

Namita Sharma1, Harsh Dua1, Deepak Rosha2

Abstract
We report a 34 year old man who developed bilateral ptosis and predominantly respiratory, truncal and bulbar weakness, and a high titer of anti acetylcholine receptor antibodies along with a diagnosis of Philadelphia chromosome positive Chronic Myeloid Leukemia (CML). The temporal relationship suggests a possible association.

Introduction
CML is one of a group of diseases called the myeloproliferative disorders. It is a clonal disorder where the leukemic cells of more than 95% of patients have a distinctive cytogenetic abnormality, the Philadelphia chromosome. Paraneoplastic syndromes are clinical syndromes involving non-metastatic systemic effects that accompany malignant disease. In a broad sense, these are collections of symptoms that result from substances produced by the tumor, and they occur remotely from the tumor itself. Paraneoplastic syndromes may be the first or most prominent manifestation. Neurologic paraneoplastic syndromes are estimated to occur in fewer than 1% of patients with cancer. Myasthenia gravis is an autoimmune disorder of peripheral nerves in which antibodies form against acetylcholine postsynaptic receptors at the myoneural junction. It occurs as a paraneoplastic syndrome most commonly with thymomas. There have been only rare documentations of an association with CML.

Case Report
A 34 years old gentleman, non smoker, attended our emergency with gradually increasing breathlessness, fatigue and progressive drooping of eyelids with double vision since one month. On investigation he had been found to have a high TLC and he came to IAH for further management. On examination, he had bilateral ptosis along with anemia and hepato-splenomegaly. He was dyspnoeic but not cyanotic and was afebrile. Investigations showed leucocytosis (233x10^9/L) and the peripheral smear was suggestive of CML. Serum biochemistry was normal but serum uric acid was 14 mg%. Chest X-ray was normal. Bone marrow was Philadelphia Chromosome positive and bcr/abl assay (RT-PCR) on peripheral blood was also positive (98%). He was diagnosed as a case of CML in chronic phase and was started on hydration, allopurinol and hydroxyurea. Despite a good response in leucocytosis, he continued to be breathless and soon required non-invasive ventilation (BiPaP). He had developed weakness of neck and shoulder muscles which increased with repeated efforts along with bulbar weakness causing dysphagia. ABG, Chest X-ray, CT head and orbits were normal but CT chest showed a small area of consolidation in right lower lung. He was started on IV antibiotics but remained dyspnoeic despite an improvement in the chest X-ray. He was given a Neostigmine challenge test (in the absence of Edrophonium) and had a dramatic improvement in his breathing, ptosis and muscle weakness. Anti acetylcholine receptor antibodies were strongly positive (28.2 nmol/L) by radioimmunoassay. Repetitive nerve stimulation study was suggestive of a decremental post synaptic defect at the neuromuscular junction. Pyridostigmine, steroids and intravenous Immunoglobulin were added to his medications and his neurological weakness improved. His hematological parameters also continued to improve. Unfortunately, our patient took a turn for the worse. He developed fever and became progressively drowsy – ABG showed CO2 narcosis. He was placed on mechanical ventilation and all support care was continued. He remained unconscious, developed multi organ failure and passed away.

Discussion
Paraneoplastic syndromes are rare disorders triggered by an altered immune system response to a neoplasm. They are defined as clinical syndromes involving nonmetastatic systemic effects that accompany malignant disease. The pathophysiology of paraneoplastic syndromes is complex and intriguing. When a tumor arises, the body may produce antibodies to fight it by binding to and destroying tumor cells. Unfortunately, in some cases, these antibodies cross-react with normal tissues and destroy them, which may result in a paraneoplastic disorder. For example, antibodies or T cells directed against the tumor may mistakenly attack normal nerve cells. Treatment varies with the type and location of the paraneoplastic syndrome. When possible the cancer is treated first, followed by efforts to decrease the autoimmune response. This is based on immunosuppression, by intravenous immunoglobulin, steroids or other immunosuppressive drugs or plasma exchange. This treatment ideally helps patients with clearly identified antibodies in their serum.

Paraneoplastic phenomenon in CML is rare. There have been a few case reports of the development of CML in patients with preexisting Myasthenia gravis following thymectomy or long-term treatment with 6-Mercaptopurine1,2 – suggesting secondary or therapy-related CML. There is a single case report of a patient who was diagnosed simultaneously with CML and Ocular Myasthenia gravis.3 And there is one case report of a patient with CML who developed myasthenic symptoms when treatment with Busulphan was stopped.4

Any patient with a malignancy who develops a neuromuscular syndrome should be investigated for the

1Apollo Cancer Institute, 2Department of Pulmonary Medicine, Indraprastha Apollo Hospital, New Delhi
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The presence of paraneoplastic syndromes like Myasthenia gravis. The associated syndrome can be as or more sinister than the primary malignancy. Early recognition may lead to clues about the underlying condition and thus avoid diagnostic errors and permit earlier diagnosis and faster treatment.

References