CASE REPORT

Clinical Presentation of Inadvertent Intrathecal Vincristine Masquerading Guillain–Barre Syndrome

Agni Sekhar Saha¹ · Md. Fekarul Islam² · Sukanta Bhattacharya² · Prabhas Prasun Giri²

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Abstract Vincristine, a potent chemotherapeutic agent, is highly neurotoxic. If given intrathecally by accident it is almost always fatal. We are reporting a 6 year old girl with acute lymphoblastic leukaemia in complete remission, who was given inadvertent intrathecal Vincristine instead of Methotrexate. She developed gradually progressive quadriplegia and respiratory paralysis requiring prolonged mechanical ventilation, initially mimicking Guillain–Barre Syndrome, both clinically and electro-physiologically. She also developed progressive encephalopathy. The clinical deterioration subsequently plateaued without any significant improvement and after more than 5 months, she finally expired.

Keywords ALL · Intrathecal vincristine · GB syndrome

Introduction

Prescribing error or procedural error resulting in wrong route drug administration, especially when handling chemotherapeutic agents, can be fatal. Despite its boxed label warning, there have been a number of cases in which Vincristine was inadvertently administered intrathecally (IT) rather than intravenously (IV) with devastating consequences [1]. Our proband is a girl with acute lymphoblastic leukaemia (ALL) in remission. She became the

victim of this procedural error and died after surviving 5 months on ventilator.

Case Report

A 6 year old girl was diagnosed with ALL (L1), 1 year ago. She went into complete remission and was on maintenance therapy with IT Methotrexate, IV Vincristine and oral 6-Mercaptopurine. She had IT therapy 2 days before the current illness. She started complaining of pain in the injection site followed by pain in the lower limbs few hours after IT therapy and then started developing fever, vomiting and weakness of both lower limbs. She subsequently developed gradually progressive encephalopathy, quadriplegia and respiratory paralysis for which she was intubated and put on mechanical ventilation. She was shifted to our hospital on the 2nd week of illness. At this stage, her Glasgow coma scale (GCS) was 6/15. Pupils were sluggishly reacting. Bilateral ptosis was present. Deep tendon reflexes were absent. Power was 0/5 in all limbs along with severe hypotonia. Heart rate was 150/min, blood pressure was 170/92 mm of Hg. Autonomic instability in the form of intermittent hypertension, tachycardia and excessive sweating was evident.

Presence of sepsis, dyselectrolytemia and myositis were excluded by routine blood examinations. Nerve conduction velocity (NCV) revealed sensory-motor polyneuropathy. Cerebrospinal fluid (CSF) revealed albumino-cytological dissociation. Magnetic resonance imaging (MRI) of brain and spine was normal. A presumptive diagnosis of acute inflammatory demyelinating polyneuropathy or Guillain–Barre (GB) syndrome was made and intravenous immunoglobulin (IVIG) in a dose of 2 g/kg over 5 days was given but there was no improvement and

✉ Agni Sekhar Saha
agnisekhar@hotmail.com

¹ Fortis Hospital, 30/H Mahendra Roy Lane, Kolkata, West Bengal 700046, India

² Institute of Child Health, Kolkata, India

encephalopathy progressed further contrasting a classical GB syndrome. At that time, we came to know that, actually Vincristine was inadvertently given through IT instead of IV route.

Tracheostomy was done and ventilation continued for more than 4 months. But there was no improvement in either encephalopathy or muscle power. Efforts to wean from the ventilator consistently failed in keeping with the muscle weakness.

MRI brain was repeated after 2 months which showed diffuse brain atrophy with small signal abnormalities in bilateral white matter and subcortical cerebellar regions (Fig. 1) and EEG showed evidence of significant cortical dysfunction and mild left sided focal epileptiform discharges.

In view of the non-progress, she was transferred back to a hospital in her home town and ultimately expired there after few days.

Discussion

ALL is the commonest leukaemia in pediatric population. Maintenance therapy involves IT Methotrexate along with IV Vincristine. Accidental IT Vincristine administration instead of IT Methotrexate is a clinical risk issue with devastating consequences and had been reported many times [1]. Even when used in its proper doses, clinical or

sub-clinical neurotoxicities with Vincristine are very common. In a recent study, as many as 50 % of Indian children were found to have features of neurotoxicity after receiving standard dose of Vincristine [2]. Central nervous system (CNS) toxicity do not occur as Vincristine cannot cross the blood brain barrier. When given IT, Vincristine cause intense, central, progressive, ascending myelo-encephalopathy leading to rapid sensory and motor dysfunction, usually followed by encephalopathy, coma and death [1, 3, 4]. The first sign is characterized by leg weakness, leg pain and loss of the tendo-calcaneus reflex [3]. Autonomic dysfunction may follow. Symptoms of meningitis such as stiffness in the neck and high fevers may also occur. Ultimately, generalized inflammation and dysfunction of the CNS lead to respiratory failure and death. Autopsy findings include grossly edematous and congested brain and spinal cord tissue with axonal degeneration and myelin loss of the spinal nerves [1, 3, 4].

The first reported case of IT administration of Vincristine occurred in the United States in 1968 in a 23-month-old girl with ALL, who ultimately died. Qweider et al. [4] reported a 32 year old patient with Burkitt lymphoma. Immediately after the incidence, CSF aspiration was done and external ventricular and lumbar drains were placed for CSF irrigation, combined with IT administration of FFP and IV antineurotoxic therapy involving Pyridoxine, Folic acid and Glutamic acid. The patient survived 18 months post event but remained wheel chair bound. The Research on Adverse Drug Events and Reports (RADAR) project of Northwestern University conducted a review of literature published from 1968 to 2006 and found 55 cases worldwide, of which 32 were published. Of those 32 cases, 27 (84 %) died [1].

There are few isolated case reports of salvage therapy after IT Vincristine, none of which are standardised. So, we must concentrate on prevention. Measures like mini-bag infusion, using separate order sheets, separate packaging and transport of IT drugs, not giving IT and IV therapy on same day, cross checking of drugs have been tried [1, 5].

In our case, the initial clinical features of rapidly progressing ascending paralysis with areflexia, CSF albuminocytological dissociation and NCV were suggestive of GB syndrome. However, non-responsiveness to IVIG, unexplained encephalopathy, no improvement of muscle power even after 4 months and history of IT Vincristine suggested otherwise. Without any immediate and aggressive intervention, clinical course of our case was a bit slow and she managed to survive for almost 5 months in a persistent vegetative state. As per our knowledge, it is the only reported case from India and the uniqueness of this case is that initially it behaved like a GB syndrome and survived up to 5 months.

Fig. 1 MRI 2 months after the incidence showing diffuse brain atrophy with some bilateral white matter signal changes

Compliance with Ethical Standards

Conflict of interest Agni Sekhar Saha, Md. Fekarul Islam, Sukanta Bhattacharya, Prabhas Prasun Giri has no conflict of interest to declare.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from the family of the individual patient included in the study.

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