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Case Report Open Access

Acute Obstructive Hydrocephalus during Chemotherapy in T-Lymphoblastic Lymphoma

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Abstract

Acute obstructive hydrocephalus (AOH) represents a life-threatening event in which clinical presentation is often non-specific but may include severe headache, vomiting and lethargy. AOH often does not present in onco-haematology. yet, a significant number of case reports have described that patients with acute lymphoblastic leukemia (ALL) do possess such symptoms.

The present study reports on the first case of AOH, developed in a patient with lymphoblastic leukemia during induction chemotherapy period.

Keywords: Obstructive hydrocephalus; Lethargy; Lymphoblastic lymphoma

Case Descriptions

A 32 year old male was admitted to the Accident and Emergency (AE) department suffering from acute dyspnoea, left hand finger paraesthesia, diplopia, and right abdominal paralysis for the past five days. His past medical history was unremarkable. A chest and abdominal CT-scan showed a mediastinal mass (10x12 cm) with a left pleural effusion, compression of his left bronchus and splenomegaly (13 cm). A neck CT-scan revealed bilaterally enlarged laterocervicalis and supraclavear lymphoadenopathies. The Full Blood Count (FBC) revealed Hb 11.2 g/dL, WBC 7.20x10^9/L, PLT 102.00x10^9/L. Biochemistry and coagulative tests were within normal range. Due to the large size of the mediastinal mass with associated airways compression, the patient was immediately transferred to the Intensive Care Unit (ICU). The patient would be in danger due to standard chemotherapy CHOP schedule (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone). Although confirmation of T Lymphoblastic Lymphoma was lacking, biopsy of a supraclavicular lymph node confirmed an Acute Lymphoblastic Leukemia/ T-Lymphoblastic Lymphoma (ALL/LBL-T-cell) diagnosis. Cytogenetic showed a normal 46 XY male karyotype and bone marrow biopsy was negative. A lumbar puncture showed the central nervous system involvement with the presence of T- lymphoid blasts in the spinal fluid.

After six days of hospital admission, the patient's condition had improved and he was enrolled on to the Italian NILG ALL 10/07 chemotherapy protocol and was put on induction chemotherapy cycle C1 in four phases (vincristine 1.4 mg/m^2 on day 1, 8,15,22; idarubicin 12 mg/m^2 on day 1-2; dexamethasone 5 mg/m^2 BD on day 1-5 and 15-19; asparaginase Medac 3000 U/m^2 on day 8,10,14, 17,19). Intrathechal Chemotherapy (IT) with methotrexate 12.5 mg and cytarabine 75 mg was also given twice a week (5 doses in total). After the second IT, spinal fluid (CSF- F) was found to be negative for blasts. The patient became lethargic after 27 days although no neurological deficits were observed. Biochemistry studies, rammonemia and blood gas analysis were normal. However, a reduced antithrombin of 66.6%,with an elevated PT of 1.31 and a slightly elevated PTT of 1.1 was noted. Brain CT scan was reported as normal; however a cerebral magnetic resonance angiography strongly indicated the presence of bilateral hydrocephalus (Figure 1). A dry tap lumbar puncture was urgently performed and 40 ml of CSF- F was removed, following which the patient immediately responded and became fully alert. A neurosurgical intervention was attempted with the positioning of an Ommaya reservoir. The CSF- F remained positive for blast cells and spinal fluid microbiological testing including PCR-testing for enterovirus, adenovirus, CMV, EBV, JCV, HHV6 , herpes virus type-1, -2 and chickenpox virus were all negative, as was culture and staining for bacteria, fungi and mycobacterium tuberculosis and biochemical analysis.

The patient was started on high dose methotrexate and cytarabin (methotrexate 3.5 g/m^2 on day 1 plus cytarabine 2 g/m^2 twice a day on days 2-3) as previously described Ferreri AJ et al. [1] and continued on consolidation T-ALL protocol. He recovered slowly and completed the entire chemotherapy course with good clinical benefit. The right abdominal paralysis and the upper right limb paralysis were resolved with physiotherapy.

Discussion

Cyclophosphamide and Doxorubin have been reported to induce hydrocephalus [2]. In that case, the patient receive both drugs in the chemotherapy CHOP.

AOH is a life-threatening condition. Yet, if treated immediately by diversion (e.g. lumbar puncture) it can be cured. For this reason prompt recognition is imperative. Intra-ventricular bleeding also may lead to AOH. After lumbar puncture, cerebrospinal fluid should be

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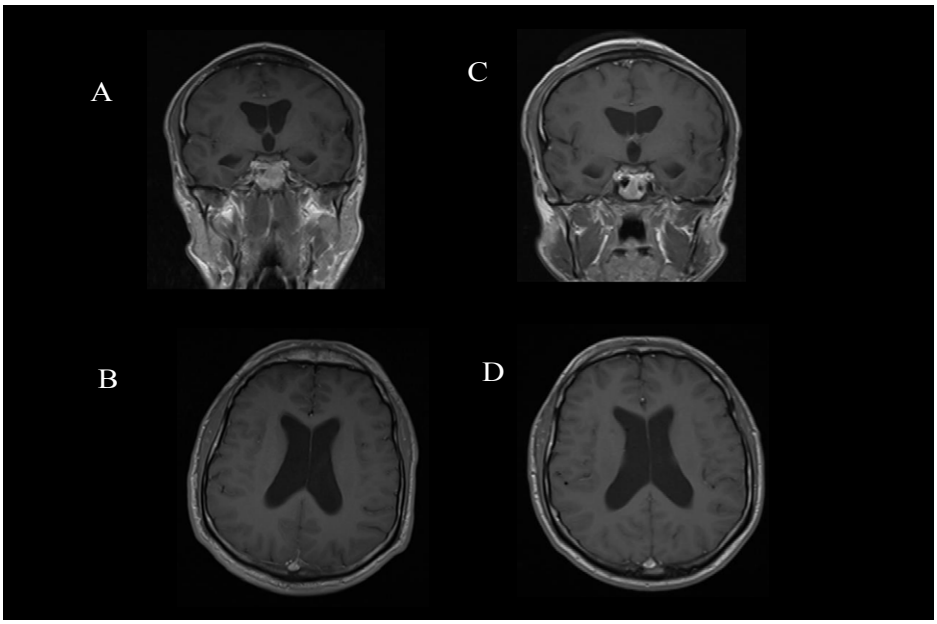

Figure 1: A-D. MRI-scan before (A,B) and after (C,D) lumbar puncture for hydrocephalus treatment. Only a partial decrease in the ventricle size is seen after procedure (C,D) compared to before (A,B). In this patient the compliance of the CSF compartment is decreased which indirectly, at least in this case, has facilitated the removal of liquor and prompt hydrocephalus correction.

tested for evidence of intracranial hemorrhage.

Studies on large animals like primates, Milhorat TH and past studies show that lethargy is the most reliable and common symptom of hydrocephalus [3]. This was also the case with the patient presented here. Other symptoms include headache and vomiting, however these are often non-specific symptoms and in children may be interpreted as signs of gastro-enteritis, which could lead to misdiagnosis and delayed recognition of AOH.

The majority of AOH cases occurr in association with hematological malignancies and in the cases infiltrations of choroid plexus, aqueducts are common [4,5]. Involvement of central nervous system (CNS) may account for up to 7% of cases; however CNS symptoms are reported in 4% of cases only [6]. The present clinical case concerns lymphoblastic lymphoma alone. However, according to the WHO, lymphoblastic lymphoma simply reflects leukemic bone marrow infiltration < 25% and/or the presence of a mass lesion. In the context of AOH, the difference is probably irrelevant.

Usually the majority of cases worsen due to the presence of hyper-leukocytosis blasts that correlate with the risk of CNS infiltration and CNS haemorrhage [7]. However, a higher incidence of AOH is not reported in the case illustrated here and the WBC was not increased without any blasts present in the peripheral blood.

CNS side effects are another major concern with the use of asparaginase and all associated treatment [8,9]. However, to the best of our knowledge, AOH has never been reported before in association with asparaginase. Previous studies have also showed that Cyclophosphamide [2] in mice and Doxorubin in humans [10] may induce hydrocephalus. Both these drugs were used even in the present case and therefore these possibilities should also be taken into account.

Although the authors are unable to explain why AOH occurred in this case, they would like to suggest the possibility of marginated leukemic cells within the CNS occluding CSF passages. In this respect, De Reuck J and other studies have already shown on post-mortem that leukemic cells may infiltrate the arachnoidal villi and dural sinuses [11]. Switching to a high dose of chemotherapy treatment with cytarabine and methotrexate may have cleared any obstructive blasts within the aqueducts causing AOH.

In conclusion, clinicians should be aware of the possibility of developing AOH in all lymphoblastic lymphoma cases in the presence a very high WBC and CSF involvement. The symptom of lethargy should alert clinicians to immediately rule out the presence of AOH. If diagnosed, CSF diversion should be performed as a matter of urgency. In the event of death, brain post-mortem studies should be considered to clarify AOH aetiology and CNS chemotherapy efficacy.

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