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CASE REPORT

Subdural hemorrhage – a serious complication post-intrathecal chemotherapy. A case report and review of literature

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Key Clinical Message

We need to have a high index of suspicion for subdural hemorrhage (SDH) post-lumbar puncture in hematological patients given their increased risk and the significant morbidity and mortality associated with SDHs.

Keywords

Intrathecal chemotherapy, lumbar puncture, post-lumbar puncture headache, subdural hemorrhage.

Introduction

Subdural hemorrhage (SDH) is a rare but known serious complication of lumbar punctures (LP), resulting in significant morbidity and mortality [1, 2]. The mechanism of SDH formation post-LP is postulated to be due to intracranial hypotension from cerebrospinal fluid (CSF) leakage from the LP site. This causes traction on bridging subdural veins with subsequent hemorrhage [1]. The risk of SDH is increased in patients undergoing intensive chemotherapy for hematological conditions, due to the prolonged periods of profound thrombocytopenia and treatment regimens comprising multiple intrathecal injections. In fact, postmortem studies on bone marrow transplant (BMT) patients have shown an incidence of SDH of 6.66% [3] and 5% in leukemia patients undergoing BMT in ante mortem studies [4]. A literature review revealed 50 cases of SDH post-LP in patients undergoing chemotherapy for hematological conditions [4–10]. Of these 50, 34 (68%) were bilateral, which is in keeping with the proposed mechanism of SDH formation through intracranial hypotension, implicating the LP as being causative. A summary of these cases is provided in Table 1.

Report of a Case

We report a case of bilateral SDH in a 73-year-old man with T-cell acute lymphoblastic leukemia who received multiple intrathecal methotrexate (IT MTX) injections as part of his induction chemotherapy (Phase II UK-ALL protocol). He received IT MTX injections on Day 1, 8, and 15. Lumbar puncture on D8 was noted to be a difficult procedure with multiple passes. Post-LP headache was first reported on D9, initially intermittent then becoming a mild persistent occipital headache. On D13, he reported mild altered sensation in bilateral feet and in his right 5th finger, without any other neurological signs or symptoms. The headache resolved on D14 and he received D15 IT MTX. Of note, platelet count on D15 was 26×10^9/L, below the standard practice threshold of 50×10^9/L for LPs. This low platelet count was not replaced due to an oversight by the treating team. This procedure was straightforward with a single clean pass, without any immediate complications. The platelet count was more than 50×10^9/L on all earlier LPs (D1 and D8). On D19 the headache returned without any new neurological signs or symptoms. On D22 computed

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Table 1. Summary of published cases of post-LP SDH cases in patients undergoing chemotherapy for hematological conditions.

Study	Case numbers	Patient characteristics	Findings/outcomes
Pomeranz et al. [4]	13 of 471 BMT patients	All leukemia patients Age range 9–46 years All had diagnostic LP +/− IT chemo 5 of 13 SDH patients had post-LP headache	All diagnosed on CT (2 had initial normal CT) 9 bilateral SDH 7 required surgical drainage No long term morbidity/mortality
Jourdan et al. [5]	5 of 86 AML patients	Age range 33–60 years All had LP; 4 had IT chemo All had post-LP headache	All diagnosed on CT 1–15 days post-LP 2 bilateral SDH 1 required drainage No long term morbidity/mortality
Hentsche et al. [6]	3 of 272 BMT patients	All CML patients Age range 34–49 years All received IT MTX All had post-LP headache	All diagnosed on CT 22–29 days post-LP All bilateral and requiring drainage No long-term morbidity/mortality
Colosimo et al. [7]	17 of 657 BMT patients	Age range 25–61 years 16 had IT MTX, 1 had antecedent minor head trauma. 13 had post-LP headache	13 diagnosed on CT, 4 diagnosed on MRI Diagnosed 6–248 days post-LP 11 bilateral SDH 4 requiring drainage No mortality. 1 with residual neurological deficit
Kannan et al. [8]	Case series of 2 SDH in BMT patients	1 with T-cell lymphoma; 1 AML Age range 33–46 years Both had IT MTX Both had post-LP headache	Both had initially normal CT (18–34 days post-LP), then later diagnosed on repeat CT (31–38 days post-LP) Both bilateral and requiring drainage. No morbidity/mortality from SDH
Openshaw et al. [9]	17 of 4812 BMT patients	Age range 15–65 years 8 had LP (7 had IT chemo), 3 had post-LP headache Of the 9 without LPs, 2 had antecedent head trauma 54% of SDH patients had LP, higher than average of all BMT patients (21%)	Of the 8 who had LPs: SDH was diagnosed 5 – 112 days post-LP 5 hematomas (2 bilateral), 3 hygromas (all bilateral); 2 required drainage No morbidity/mortality from SDH Of the 9 without LP: All 9 hematomas, 4 requiring drainage. 2 fatal
Patel et al. [10]	3 of 10 patients receiving imatinib + systemic and IT chemo	All Philadelphia chromosome positive ALL Age range 35–47 years All received IT chemo 2 had post-LP headache	2 diagnosed on CT, 1 on MRI Diagnosed 3 days to >3 months post-LP 2 bilateral 2 received surgical drainage, 1 was not fit for surgery and subsequently died

tomography (CT) imaging revealed bilateral subacute frontoparietal hematomas measuring 10 mm on the left, and 8 mm on the right, with associated local mass effect. Neurosurgical consult was obtained and the decision made for conservative management, based on his stable clinical status and the subdural hematoma size that was not greater than 10 mm with no midline shift. His platelet count was replaced to above 50×10^9/L and no further LPs were performed. Serial imaging showed no progression of the subdural hematomas and the patient remains well 11 months post-SDH with no residual symptoms. The oversight of performing an LP without recognizing his severe thrombocytopenia was noted in an internal incident report as part of our risk reduction program. Suggestions to reduce the risk of future similar incidents include emphasizing checking platelet count on the lumbar puncture protocol and a reminder via internal memo to medical staff regarding this risk.

Discussion

Pomeranz et al. [4] and Kannan et al. [8] both report patients with initially normal imaging (CT) up to 34 days post-LP that are later diagnosed with SDH up to 38 days post-LP, suggesting that SDH could occur weeks after LP. This is in keeping with the presumed mechanism of ongoing CSF leak post-LP causing SDH formation over a period of time, suggesting that the platelet count post-LP

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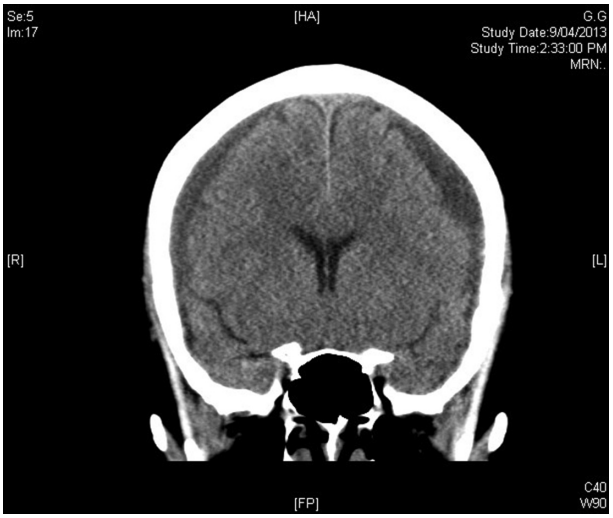

Figure 1. Brain CT revealing bilateral subacute frontoparietal subdural hematomas, measuring 10mm on the left and 8mm on the right, with associated local sulcal effacement.

is as important as the platelet count during the LP itself. This is particularly relevant to our case as the thrombocytopenia on the D15 LP would otherwise be assumed to be the sole cause of the SDH. Furthermore, the patient reported post-LP headache and neurological symptoms prior to the D15 LP, suggesting the SDH may have already occurred. Unfortunately, while prolonged thrombocytopenia and coagulopathies are known risk factors [7], the long period of potential SDH formation makes it impractical to attempt to maintain a threshold platelet count over this period.

In stratifying risk of SDH post-LP, presence of headache is one of the most important factors. Colosimo et al. [7] reported that out of 19 patients with headache post-LP, 14 had SDH (73.7%), compared with three of 175 (1.7%) patients without headache. Furthermore, 33 of 50 (66%) of published post-LP SDH cases reported post-LP headache. Another possible risk factor is IT MTX, which appears to increase risk compared to diagnostic LP [6, 7], though it is difficult to compare with other intrathecal chemotherapy due to low case numbers.

Our case illustrates the importance of having a high index of suspicion for SDH in this patient group. Importantly, suspicion must remain high even if normal brain imaging is performed days-to-weeks post-LP. The most important risk factor is post-LP headache [7], with the majority of patients (73%) presenting with this. While post-LP headache is common [2], features that should arouse suspicion include persisting or worsening headache post-LP and neurological symptoms.

Conflict of Interest

None declared.

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