

# Numb Chin Syndrome as a presentation for Acute Myeloid Leukemia Relapse Post Hematopoietic Cell Transplant: Case Report and Review of Literature

Omar Banat<sup>1</sup>, Tamer Albataineh<sup>1</sup>, and Hasan Hashem<sup>1</sup>

<sup>1</sup>King Hussein Cancer Center

June 8, 2020

## Abstract

Numb chin syndrome (NCS) is defined as reduced or absent sensation in the chin and lower lip within the distribution of the mental or inferior alveolar nerves. Although commonly associated with local trauma, NCS can indicate an underlying malignancy or can be the presenting symptom of cancer recurrence. We describe the first pediatric patient with acute myeloid leukemia (AML) who presents with NCS as a sign of AML recurrence post allogeneic hematopoietic cell transplantation. We also review the current literature on acute leukemia and NCS.

## Abstract:

Numb chin syndrome (NCS) is defined as reduced or absent sensation in the chin and lower lip within the distribution of the mental or inferior alveolar nerves. Although commonly associated with local trauma, NCS can indicate an underlying malignancy or can be the presenting symptom of cancer recurrence. We describe the first pediatric patient with acute myeloid leukemia (AML) who presents with NCS as a sign of AML recurrence post allogeneic hematopoietic cell transplantation. We also review the current literature on acute leukemia and NCS.

## Introduction:

Numb chin syndrome (NCS) is defined as reduced or absent sensation in chin and lower lip within the distribution of mental or inferior alveolar nerves.<sup>1,2</sup> NCS can be unilateral or bilateral. The causes of NCS may be traumatic, dental, drug-induced, infectious, auto inflammatory, or neoplastic. The pathophysiologic mechanism of NCS involves compression or infiltration of mental or alveolar nerves. In patients with cancer, NCS may be preliminary symptom of malignancy, metastasis, or recurrence.<sup>3</sup>

Although numb chin syndrome (NCS) is most frequently seen in adults with both solid and hematologic malignancies,<sup>4,5</sup> it has rarely been described in children, of whom most had acute leukemia.<sup>6-8</sup> We present the first patient with acute myeloid leukemia (AML) who presents with NCS as a manifestation of relapse post allogeneic hematopoietic cell transplantation (HCT).

## CASE REPORT:

Our patient is a 6-year-old girl presented initially with facial palsy and blasts in her blood. She had bone marrow (BM) evaluation that showed acute myeloid leukemia (AML-M2). FISH showed t(8,21). Brain MRI showed multiple parenchymal lesions. She started chemotherapy and completed 5 cycles in January 2018 with no significant complications. Repeat brain MRI and BM evaluation at the end of therapy showed that she is in remission.

Six months later, she presented with low platelets count and blasts on blood film. BM evaluation was consistent with AML-M2 relapse. FISH was the same as original; t (8,21). She had no CNS disease at time of relapse (normal CSF analysis and brain MRI). Next generation sequencing (NGS) myeloid panel at relapse showed somatic mutations in both KIT and WT1. She was started on FLAG induction (fludarabine and high dose cytarabine). BM evaluation post FLAG showed non-remission with 8-10% blasts. She then received HAM protocol (Mitoxantrone and high dose cytarabine). BM re-evaluation was consistent again with non-remission (blasts 5-8%).

Due to non-remission status after 2 cycles of re-induction chemotherapy, she underwent sequential allogeneic HCT in October 2018. She underwent HCT using identical HLA-matched brother. Myeloablative conditioning regimen consisted of Cyclophosphamide and TBI 12 Gy with cytarabine and etoposide as cytoreductive regimen. Graft-versus-host-disease (GvHD) prophylaxis consisted of methotrexate and cyclosporine (CsA). At 1, 2, and 3 months post HCT, BM biopsy showed no morphologic evidence of acute leukemia. FISH x/y was 100% donor (male) cells. FISH was negative for t(8,21). Our patient course post HCT was complicated with CMV reactivation treated successfully with Ganciclovir.

Two months later (5 months post HCT), the patient presented with right-sided facial pain and numbness in her chin and lower lip. Brain abd neck MRI showed right-sided enhancement at the area of inferior alveolar nerve, suspicious for leukemic infiltration (Fig. 1). CT mandible showed small soft tissue density minimally eroding the right mandibular foramen. Accordingly, she was diagnosed with numb chin syndrome. Two weeks later, she presented with leukocytosis and blasts on blood film consistent with frank AML relapse.

#### DISCUSSION:

This case represents the first AML pediatric patient to present with NCS as an ominous sign of relapse post HCT.

NCS is a well-documented entity in adults to be associated with malignancy.<sup>4,5</sup> Though, it has received little attention in children because of its extreme rarity. NCS can be the presenting manifestation of a new malignancy, or recurrence.<sup>6,8,9</sup>

Review of literature revealed 8 cases of acute leukemia in children manifested with NCS either at diagnosis or at relapse.<sup>6,8-13</sup> All of 8 patients had either ALL or Burkitts leukemia but none had AML. Regarding AML, no children were reported to have AML and NCS. Review of literature revealed 5 cases of AML manifested with NCS at diagnosis and were all adults (Table 1).<sup>7,14-17</sup> Interestingly, it is important to highlight that 2 of the 5 patients with AML and NCS had t(8, 21).<sup>7,15</sup>

The pathophysiology of NCS underlying malignancy is not entirely clear but is believed to involve nerve compression or entrapment secondary to mandibular metastasis and/or direct nerve or nerve sheath infiltration, as biopsy was not obtained due to risk of bleeding. In the absence of trauma (mandibular bone injury) or dental injury, most common causes of NCS are related to metastatic malignancy.

Numbness of chin and Lower lip may be regarded as a trivial sign. However, in a patient with cancer, it often has an ominous meaning. This report indicates that oral manifestation can be extremely important in the early recognition of acute leukemia. When a patient with leukemia has NCS, symptoms should be considered a potentially ominous sign of acute leukemia recurrence. This report may hopefully increase awareness of physicians to the importance of prompt recognition of NCS, as early detection of malignancy permits timely treatment.

In conclusion, this is the first description of NCS in the setting of AML in a child post HCT. Although NCS remains a rare diagnosis especially in children, it usually indicates an advanced disease, and is commonly associated with grim prognosis. This report highlights the importance of early detection and recognition of an imminent relapse when patients with acute leukemia presents with NCS. Further research is needed to study the link between NCS and specific cytogenetic abnormalities.

Conflict of interest statement: nothing to declare.

ACKNOWLEDGMENTS: None.

#### REFERENCES:

1. Calverley JR, Mohnac AM. Syndrome of the Numb Chin. *Arch Intern Med* . 1963;112(6):819–821.
2. Aggarwal A, M Pai K. Orofacial Manifestations of Leukemic Children on Treatment:A Descriptive Study.*Int J Clin Pediatr Dent* .2018;11(3):193–198.
3. Baskaran RK, Krishnamoorthy, Smith M. Numb chin syndrome - A reflection of systemic malignancy. *World J Surg Oncol* . 2006;4.
4. Sasaki M, Yamazaki H, Aoki T, Ota Y, Sekiya R, Kaneko A. Bilateral numb chin syndrome leading to a diagnosis of Burkitt's cell acute lymphocytic leukemia: A case report and literature review. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology* . 2011;111(3).
5. Kuklok KB, Burton RG, Wilhelm ML. Numb chin syndrome leading to a diagnosis of acute lymphoblastic leukemia: Report of a case. *J Oral Maxillofac Surg* . 1997;55(12):1483–1485.
6. Kraigher-Krainer E, Lackner H, Sovinz P, Schwinger W, Benesch M, Urban C. Numb chin syndrome as initial manifestation in a child with acute lymphoblastic leukemia. *Pediatr Blood Cancer* . 2008;51(3):426–8.
7. Babikir MM, Mohamed SF, Nashwan AJ, et al. Acute myeloid leukemia presenting with numb chin syndrome: A case report and review of literature. *Am J Case Rep* . 2020;21.
8. Seixas DV, Lobo AL, Farinha NJ, et al. Burkitt leukemia with numb chin syndrome and cavernous sinus involvement. *Eur J Paediatr Neurol* . 2006;10(3):145–147.
9. Maeda K, Taniguchi JI, Matsui K. Two Cases of Numb Chin Syndrome Diagnosed as Malignant Disease. *Oxford Med case reports* . 2018;2018(12).
10. Bernstein ML, Schwartz S. Mandibular relapse in acute leukemia: Report of a case. *J Pediatr Hematol Oncol* . 1986;8(3):240–244.
11. Hiraki A, Nakamura S, Abe K, et al. Numb chin syndrome as an initial symptom of acute lymphocytic leukemia: Report of three cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* . 1997;83(5):555–561.
12. Mantadakis E, Katragkou A, Papadaki E, et al. Spinal cord compression in an adolescent with relapsed B-precursor acute lymphoblastic leukemia and mental neuropathy. *Int J Hematol* . 2008;88(3):294–298.
13. Pansy J, Lackner H, Benesch M, Urban C. Numb chin syndrome in acute lymphoblastic leukemia. *Indian Pediatr* . 2011;48(6):481–3.
14. Ohno T, Yasuda Y, Furukawa H. Acute monoblastic leukemia (M5a) presenting numb chin syndrome. *Am J Hematol* . 1994;45(4):352–352.
15. Jenkins RW, McDonald K, Greenberg CS. Numb chin syndrome in acute myeloid leukemia. *Am J Med Sci* . 2012;344(3):237–240.
16. Liapis K, Apostolidis I, Karmiris T, Harhalakis N. Numb chin syndrome as the initial manifestation of acute megakaryoblastic leukemia. *Leuk Lymphoma* . 2010;51(12):2310–2311.
17. Quintela A, Sujobert P, Tigaud I, et al. Bone Marrow Necrosis in Newly Diagnosed Acute Leukemia: Two Case Reports and Review of the Literature. *Oncol Ther* . 2017;5(1):111–118.

Legends:

**Figure 1:** Initial MRI, Axial T1 post contrast (A) and T2 STIR (B) show contrast enhancing soft tissue thickening in the right mandibular canal involving the right inferior alveolar nerve with surrounding osseous infiltration/invasion. Follow-up MRI after 2 weeks, Axial T1 post contrast (C) and T2 STIR (D) show significant progression in the size of the previous contrast-enhancing lesion with new invasion/extension to

the right pterygoid muscles. ADC map (E) and DWI (F) show diffusion restriction indicating high cellular tumor. Side to side comparison of coronal T2 STIR of initial MRI (G) and 2 weeks follow-up (H) show significant tumor progression and new right pterygoid muscles invasion/extension.

### Hosted file

TABLE 1 NCS 6.7.2020.docx available at <https://authorea.com/users/331003/articles/457744-numb-chin-syndrome-as-a-presentation-for-acute-myeloid-leukemia-relapse-post-hematopoietic-cell-transplant-case-report-and-review-of-literature>

