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Acute Myeloid Leukemia Presenting with Numb Chin Syndrome: A Case Report and Review of Literature

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Patient: Male, 30-year-old
Final Diagnosis: Acute myeloid leukemia
Symptoms: Jaw numbness and pain
Medication: —
Clinical Procedure: None
Specialty: Hematology

Objective: Rare co-existence of disease or pathology

Background: Numb chin syndrome is a rare and under diagnosed neuropathy of the inferior alveolar branch of the trigeminal nerve usually causing a lower lip and chin anesthesia or paresthesia. The syndrome is commonly associated with broad-spectrum malignant and non-malignant conditions.

Case Report: Here we report a case of a 30-year-old male who presented with numb chin syndrome in the form of jaw pain, paresthesia, and hypoesthesia of the mental area as the presenting symptoms of acute of myeloid leukemia with t(8;21) treated with (3+7) protocol (3 days anthracycline+7 days cytarabine). The pain and paresthesia improved but hypoesthesia persisted.

Conclusions: Acute myeloid leukemia is one of the most serious causes of numb chin syndrome which should not be overlooked.

MeSH Keywords: Chin • Leukemia, Myeloid, Acute • Paresthesia

Units: Hemoglobin gm/dL (normal range: 13.0–17.0 mg/dL); platelet 10³ μL (normal range: 150–400×10³/μL); WBC 10³/μL (normal range: 4.0–10×10³/μL)

Abbreviations: AML – acute myeloid leukemia; MNN – mental nerve neuropathy; NCS – numb chin syndrome

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/920117>



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Background

Numb chin syndrome (NCS), also known as mental nerve neuropathy and earlier named hypoesthesia of the chin, is a rare and under diagnosed neuropathy of the inferior alveolar branch of the trigeminal nerve usually causing a lower lip and chin anesthesia or paresthesia [1,2]. The syndrome is commonly associated with broad-spectrum malignant and non-malignant conditions such as trauma, infection, neurologic, or odontogenic cause [3–5]. This syndrome is most often a sign of malignancy presentation, progression, or relapse [6–8].

The association of NCS with both solid tumors and hematologic malignancies has been estimated to be up to 30% to 50% of patients at presentation [1,4,9]. However, no extensive prospective studies were done to confirm these percentages.

The association between acute of myeloid leukemia and NCS has been described, but only a few cases have been reported in the literature (see discussion). In this case, we highlight this association to draw the attention to acute myeloid leukemia as an important differential to look for in patients with such presentation and to invite further researches in describing cytogenetic abnormalities linked to NCS.

Case Report

We report a case of 30-year-old Indian male with no significant past medical history. The patient presented initially to a health center with severe jaw pain which was present for 4 days along with decreased sensation over the entire lower jaw. He also had an on-and-off fever, malaise, and 4 kg unintentional weight loss during the preceding 1 month. There was no preceding trauma, recent skin or mucosal eruptions, or hepatitis vaccination. At the time of assessment, he looked pale and there was obvious swelling over the submandibular area bilaterally and he had restricted opening of the mouth due to pain. Neurologically, pain, touch, and temperature sensations were reduced over the mental area; however, vibration sensation and motor function were spared. Other parts of the nervous system were intact as well as the rest of other systems.

Laboratory results revealed hemoglobin of 3.6 mg/dL (normal range: 13.0–17.0 mg/dL), platelet of $12 \times 10^3 \mu\text{L}$ (normal range: $150\text{--}400 \times 10^3/\mu\text{L}$), WBC of $6.3 \times 10^3/\mu\text{L}$ (normal range: $4.0\text{--}10 \times 10^3/\mu\text{L}$). Based on the picture of bicytopenia, peripheral smear was sent and it showed marked neutropenia with left shift, dysplastic features, and 47% circulating blasts with some Auer rods, a picture highly suggestive of acute myeloid leukemia, and that was confirmed by flow cytometry of bone marrow aspirate with the presence of 52% abnormal precursors. Chromosome analysis revealed 45, X,-Y with t(8;21)



Figure 1. X-ray of skull anteroposterior view shows subtle heterogeneity of bone marrow of both mandibles with no definite focal osseous lesions.

(q22;q22); RUNX1-RUNX1T1. Infectious causes like Epstein Barr virus and human immune virus (HIV) were ruled out; of note, herpes serology was not done. Antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, and rheumatoid factor were all negative.

A magnetic resonance imaging (MRI) of the head was performed, to further explore the reason of his neurological deficit, and showed subtle heterogeneous marrow signal of the bone marrow with no focal destructive bony lesions or soft tissue masses, with a possibility of underlying infiltrative process. There was also near total opacification of the left mastoid air cells suggestive of left mastoiditis, otherwise no definite focal brain parenchymal abnormality seen; all ventricles looked normal with no midline shift or deformity. The submandibular glands were normal as well. No destructive bony lesion was seen (Figures 1, 2).

After the first induction cycle with (3+7) protocol (3 days anthracycline + 7 days cytarabine), the patient had a resolution of jaw pain and swelling. Paresthesia over the left half of the mental area resolved, however, decreased sensation and paresthesia persist over the right half of the mental area even after the second induction cycle. X-ray of the skull done 7 weeks after diagnosis showed the heterogeneous texture of the mandible.

He received a total of 2 cycles of induction and 3 cycles of consolidation, as per hospital protocol, and the end of therapy bone marrow examination revealed 4% blasts. He traveled back to his home country.

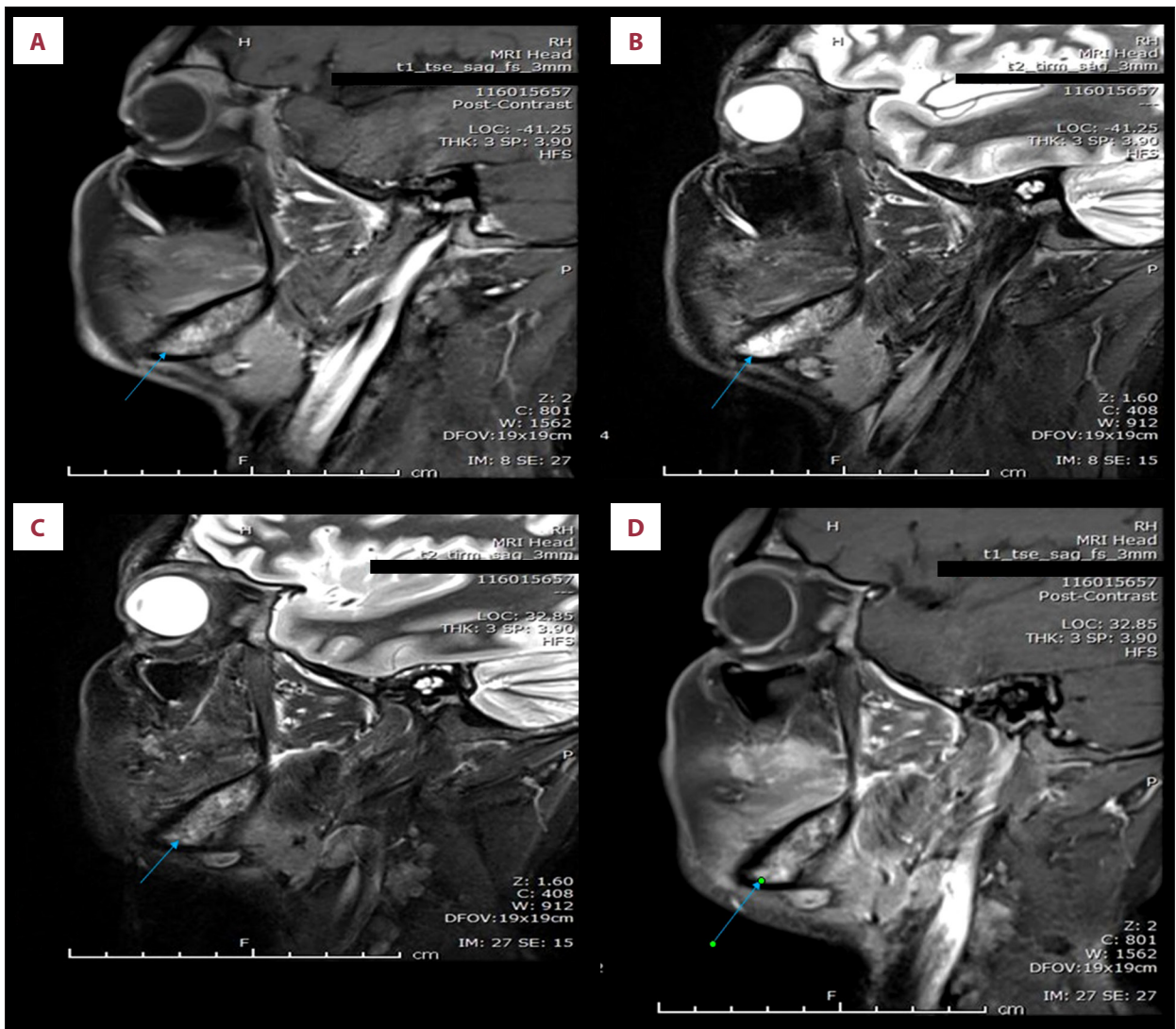


Figure 2. (A, B) Sagittal STIR and post contrast fat saturated images of right mandible. (C, D) Sagittal STIR and post contrast fat saturated images of left mandible show heterogeneous appearance of bone marrow of mandible with high signal intensity in STIR images and heterogeneous enhancement after intravenous contrast administration (blue arrows) suggesting underlying infiltration.

Discussion

Numb chin syndrome is a sensory neuropathy of the mental branch of the inferior alveolar nerve that presents by hypoesthesia, paresthesia, and rarely pain [1].

The non-malignant cause include: trauma, infection (bacterial, viral, Lyme disease, syphilis, HIV, and osteomyelitis), multiple sclerosis, benign sensory trigeminal neuropathy, radiotherapy, chemical exposure, vasculitis, systemic amyloidosis, sickle cell disease, sarcoidosis, diabetes mellitus, and vertebro-basilar insufficiency [23].

Any lesion along the course of the trigeminal nerve from its nucleolus in the Pons down to the mandibular endings can result in numb chin syndrome. The proposed mechanisms for malignancy-associated NCS are: direct infiltration of the bone or nerve, leptomeningeal seeding, or inflammation or compression of the nerve [23].

The malignant causes are very important to know and to be noticed by physicians, as NCS can be the first sign of both solid and hematological malignancies, and it can be the sign of recurrence as well. It is reported with metastatic malignancies of the liver, lung, kidney, breast, and prostate, among others. We suggest as an approach the taking detailed history including previous history of malignancies and risk factors, physical

Table 1. Summary of acute myeloid leukemia (AML) with numb chin syndrome case reports and some of the acute lymphocytic leukemia (ALL) with numb chin syndrome cases.

Author	Year	Age	Gender	Primary diagnosis	Chromosome analysis	NCS timing
Barrett [17]	1985	28	M	ALL	NA	Progression
Nagano [15]	1991	21	F	AML	NA	Presentation
Ohno [16]	1994	32	F	AML-M5	NA	Presentation
Kuklok [18]	1997	35	M	ALL	NA	Presentation
Kraigher-Krainer [2]	2008	11	M	ALL (B-cell)	NA	Presentation
Mantadakis [19]	2008	17	M	ALL (B-cell)	46,XY,del(9)(p22.1),add(16)(q22) and 46,XY,add(9)(p22.1),del(9)(p11.2)add(16)(q22)]	Presentation
Liapis [20]	2010	52	M	AMKL	(+Y, +1, +3q, -3p, -4, -5q, +6, -7q, +8, -9q, -15)	Presentation
Lata [13]	2010	45	M	NHL	NA	Presentation
Sasaki [11]	2011	48	F	Burkitt's cell acute lymphocytic leukemia	NA	Presentation
Fan [12]	2011	51	F	NHL	NA	Presentation
Jenkins [1]	2012	33	F	AML	t(8;21) translocation	Presentation
Romo [21]	2014	22	M	ALL	NA	Relapse
Algahtani [10]	2016	57	M	Burkitt's lymphoma/leukemia	Translocation (8;14)	Presentation
Algahtani [10]	2016	39	M	Burkitt's lymphoma/leukemia	t(8;14)(q24;q32)	Presentation
Quintela [22]	2017	27	M	AML	47, XX, ?8[4]/46, XY[16]	Presentation
Present case	2017	30	M	AML	45, X,-Y with t(8;21)(q22;q22);RUNX1-RUNX1T1	Presentation

AML – acute myeloid leukemia; AML-M5 – acute monoblastic leukemia; ALL – acute lymphoblastic leukemia; AMKL – acute megakaryoblastic leukemia; NA – not available; NHL – Non-Hodgkin's lymphoma.

examination of the aforementioned solid organs followed by appropriate imaging.

For hematological malignancies, in particular, there are very few cases reported in the literature of this sign to be the presenting sign. It has been reported mostly with non-Hodgkin lymphoma and acute lymphoblastic leukemia. For acute myeloid leukemia, 5 cases were reported to our knowledge and literature review. Our case is the sixth case. One of the most interesting findings in our case, the chromosomal abnormalities, which were t(8,21), which carries favorable prognosis, same like Jenkins et al. reported case who is a 33-year-old female presented with chills, malaise, nausea and vomiting, and

numbness of the lower lip and chin. Her computed tomography scan of the brain was normal and she had leukocytosis with circulating blast forms, morphologically it was consistent with FAB M2 subtype, numbness improved completely on day 12 of induction chemotherapy with cytarabine and daunorubicin (7+3) in contrast to our case in which pain resolved but paresthesia persisted [1].

Another observation that all the cases reported were *de novo* acute myeloid leukemia. See Table 1 for a summary of the cases.

It is difficult to tell whether the presentation was due to infiltration of the mental nerve itself by leukemic cells or due to

entrapment caused by marrow infiltration at the mandible area. Biopsy of the mandible was not obtained as the risk of bleeding (given the severe thrombocytopenia at presentation) and further damage to the nerve outweigh the small benefit of identifying the exact pathophysiology of numb chin in this patient.

Conclusions

Acute myeloid leukemia is one of the most sinister diagnoses which should not be missed in a patient presenting with numb chin syndrome. Our case report highlights this association to encourage physicians to look deliberately for a malignant cause in patients who present with such sign without preceding trauma or infection. Further research is needed to study the link between NCS and specific cytogenetic abnormalities and its prognostic value.

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Conflict of interest

None.