Research Article

Numb Chin Syndrome As Sickle Cell Disease Consequence

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Abstract

Numb chin syndrome is a sensory neuropathy in the distribution of the mental or inferior alveolar nerve. It may occur with malignant or benign disease, vascular and hematological conditions, and dental in origin. Our aim is the clearing the relationship between NCS and sickle cell disease SCD as a hematological condition and to propose recommendations for diagnosis and management. The sample size comprised 42 SCD patients. The episodes of NCS occurred in six patients as the context of typical vaso-occlusive crises that involved the mandibular area. Six cases of numb chin syndrome NCS out of 42 sickle cell disease cases (14%), were characterized with varied presentation and management. Male to female ratio was 1:1, mean age 26±6.57 years. Half of NCS 3(50%) undergo unilateral episode 2(33.3%) bilateral and 1(16.7%) bilateral/transient. All patients with numbness chin and sickle cell disease were experienced temporary and transient numbness attacks. Sickle cell disease patients who experienced chin numbness showed a non-significant decreasing in both hemoglobin concentration and white blood cell and platelet counts when compared with Sickle anemic patients without NCS. Hydroxyurea use for sickle cell disease had no positive or negative effect on chin paresthesia. So as an under-recognized sign of malignancy, NCS may result from compression by benign lesions, by localized vascular occlusion as sequence of SCD.

Keywords: numb chin syndrome NCS, sickle cell disease SCD, neuropathy, mandibular nerve Nasseriah.

Introduction

Numb chin syndrome (NCS) is rare sensory neuropathy of the mental nerve manifested by Numbness (hypoesthesia, paresthesia, dysesthesia, and anesthesia) or pain of unilaterally or bilaterally of the chin and lower lip in the area supplied by the mental nerve and its branches [1]. The mental nerve is one of the terminal branches of the inferior alveolar nerve, responsible for the sensory innervation of the half of the chin, lower lip and gingiva of the lower anterior teeth [2]. NCS initially described by Charles Bell in 1830s when he accidentally noticed hypoesthesia to touch on one half of lower lip of female patient with disseminated breast cancer [3]. The causes of NCS can be diverse from most common in odontogenic diseases to less common as infectious or drug toxicity. Even the use of metronidazole has been implicated as a cause of unexplained neuropathy [4]. This syndrome has been reported in various malignant diseases, including lymphoma, acute leukemia, Burkitt lymphoma/leukemia [5], multiple myeloma, Ewing sarcoma, melanoma [6], breast cancer, prostate cancer, small cell lung cancer [7], colon cancer and esophageal cancer [8-10] Non-metastatic causes of NCS are rare including Sjogren's, multiple sclerosis, diabetes mellitus, temporal arteritis, systemic amyloidosis, lupus [11] and even during natural aging.[12]. NCS may be the only neurological manifestation of virus infections (especially HIV), Lyme disease [13], syphilis, post-vaccinal vasculitis [14], and sarcoidosis [15]. The sickle cell disease (SCD), is the most common hemoglobinopathy worldwide, presented as a group of inherited blood cell disorders associated with episodes of acute illness and progressive organ damage [16]. SCD can cause vascular occlusion and ischemia in various tissues due to the sickling of red blood cells [17]. During sickling crises, ischemia can compress or damage nerves. SCD can cause infarcts of jaw bones, lead to mandible bone tissue death due to a lack of blood supply [18]. During an episode of VOC, complication of acute painful crises in the mandibular bone and infarction in the nerve passage within the mandibular canal, has been hypothesized as a reason of NCS which can be triggered by local ischemia due to thrombosis of the vasa vasorum [19-20]. On the other hand, SCD patients are more prone to infections, which accompanied with osteomyelitis of the jaw that could also involve the mental nerve compression. Finally, some patients with SCD may develop secondary hematological malignancies (such as Leukemia or lymphoma), which are classic causes of NCS. In conclusion, despite of NCS is more commonly associated with malignancies, traumatic injuries, and dental interventions, NCS has also been described in patients suffering from SCD [21], therefore the limited published evidence make NCS in SCD, is poorly characterized disease with limited information about the causes, disease course, and treatment.

Patients and methods

The research is a retrospective study conducted at Nasseriah hematology center. The objective was to determine: how and when sickle cell disease (SCD) may accompanied with numbness chin syndrome (NCS)? During 2024, forty two of (SCD) patients were included to recognize (NCS) having patients. SCD patient's data was classify by: age, sex, the clinical presentation, hemoglobin level (Hb), white blood cell count (WBCs), platelets count (plat), Hydroxyurea taking, and numbness chin attack VOCs /year, the side numbness during crisis and syndrome reversibility. A suitable schedule was designed to collect the above-mentioned patients' data after obtaining their verbal informed consent to use it. The

inclusions criteria were: Confirmed Diagnosis of Sickle Cell Disease, Adults ≥18 years, Hypoesthesia, paresthesia, or anesthesia of NCS, and ability to provide informed consent. While exclusion criteria were: Non-sickle cell causes of NCS, recent dental or maxillofacial procedures and pre-existing peripheral neuropathy or central nervous system disorders.

Statistical analysis

Numerical data were presented as mean and standard deviation for variables with normal distribution. Qualitative data were expressed as frequency and percentage. Comparison between two groups was done using unpaired non-parametric t test by using GraphPad Prism version 8 for windows. Findings presented in tables using excel software version 2013. The differences between taken parameters considered a significant when P value was less than 0.05.

Results

Out of 42 diagnosed cases as sickle cell disease, 6 cases differentiate as benign numb chin syndrome that induced by acute sickle cell crisis. The mean age of patients was 26±6.57 (16-34 years). Patient demographic data (including age, sex), clinical presentation, investigations, and outcomes is summarized in Table (1). Women represented 50% (3/6) of the patients. 6 out of 42 SCD patients (14%) were severing from NCS, three patients reported unilateral numbness or pain of the jaw or lip, two patients reported numbness on both sides, One patient reported the transiently evolution of clarified symptoms in both face sides.

Table (1) Sickle cell disease Patient's demographic and clinical characteristics

SCD+NCS 6(14.3%)			SCD 36 (85.7%)		
Parameters	Mean ± SD	range	Mean ±SD	range	P Values
Age (years)	26±6.57	16-34	28.77±7.7	15-41	0.374051
HB(g/dL)	7.71±0.75	6.9-8.9	8.64±1.32	6.1-10.8	0.102728
WBC **(**109/L)	10.8±4.37	5-16.8	11.3±5	4.9-23	0.819229
Platelet **(**109/L)	248±92	123-376	309.5±103	156-543	0.17444
Attack(VOCs/year)	5.5±2.07	4-9	4.2±1.35	2-8	0.054509
Sex n (%)	M 3(50%), F 3 (50%)		M 15(41.6%), F 21(58.4%)		>0.9999
Hydroxyurea	2/6(33%)		12/36(33%)		-
Side n (%)	3(50%) unilateral,		-		-
	2(33.3%) bilateral				
	1(16.7%) bilateral/transient				
Complications	VOC 6(100%)		VOC 14(38.9%)		
			Anemia 8(22.2%)		
			Avascular necrosis 5(13.9%)		
			Abd pain 4(11.1%)		
			Pneumonia 2(5.6%)		
			Fever 1(2.8%)		
			Hematuria 1(2.8%)		
			Headache 1(2.8%)		

- Indicates not applicable, SCD: sickle cell disease, WBC: white blood cell, NCS: numb chin syndrome, VOCs: vasooclusive crisis

(The figure1) Virtually, there was no significant difference in hemoglobin concentration, white blood cell count, or platelet count between patients with sickle cell disease alone and in those with sickle cell disease who also experienced chin numbness. Only a very significant increase in the rate of vaso-occlusive episodes was observed among patients with SCD who also experienced chin paresthesia compared with those suffering SCD but did not experience NCS (see figure1).

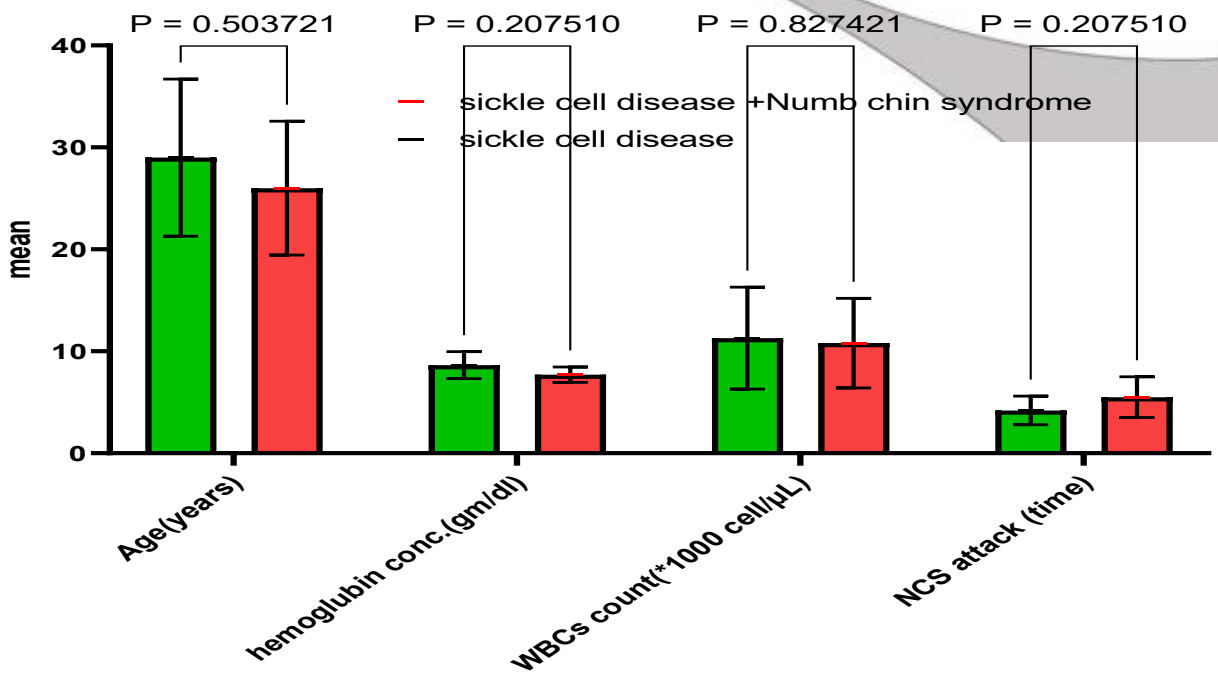

Figure 1: the comparisons between sickle cell disease with numb chin syndrome having patients (SCD+NCS)- red column- and SCD w/o NCS (SCD) –green column- that recorded in Nasseriah hematology center, during year (2024)

The values of P calculated for differences in age, hemoglobin level, and white blood cell (WBCs) count, and times of numb chin syndrome (NCS) Attacking Since NCS may be a clear indicator accompanying the occurrence of malignant tumor metastases, what distinguishes numbness accompanying tumors from that accompanying other non-malignant diseases such as SCD, is the persistence of numbness in the case of tumors and the restoration of chin nerve function in the case of non-tumor causes. Therefore, we observed the reversibility of chin nerve function after a period (varying from one patient to another) in all of our sample of (SCD+NCS) cohort. Beginning from 1984, Hydroxyurea was used for treatment of SCD patients, so here we checked if Hydroxyurea treatment positively or negatively affect NCS accompanied by SCD. Twelve out of 36 of (SCD) and two out of six (SCD+NCS) patient groups (33% of both groups) were take the medicine looks like with positive effects even in (SCD+NCS) patient cohort.

Discussion

NCS is a rare syndrome, involves the mental or inferior alveolar nerves, which is a branch of the mandibular division of the trigeminal nerve [22]. It is follows a long course in the mandibular canal, under the teeth roots, and this narrow canal is prone to compression and ischemia reperfusion the occupied nerve when infiltrated. Broad spectrum of situations are associated with NCS caused by nerve compression: dental procedures and local trauma are the most common cause [23], then the systemic neoplasms should be considered. The three most common malignancies associated with NCS were: breast cancer (40.4%), lymphomas (20.5%), and prostate cancer (6.6%) [24]. the infectious, autoimmune [25], inflammatory conditions, and toxic etiologies comes next in order. The particular importance of NCS is its association with systemic conditions including amyloidosis, sickle cell anemia, vasculitis, aneurysms, diabetes mellitus, drugs and age related mandibular atrophy. In spite of NCS is not a common complication of SCD, vascular occlusion, or bone infarction which related to SCD, can easily lead to NCS. NCS seems to affect patients of all ages and sex. So we found SCD affected around 50% of each sex that distributed into range of age between (16-41 years). The age range of our patient's, still near the lower limit of life expectancy for people living with SCD in developing countries (50yrs) [26]. Typically, NCS symptoms are unilateral, but in approximately 15 % of cases can have bilateral numbness [27]. We found a little bit higher percentage of bilateral (33%) in comparison with previous study, may be due to our small sample of NCS patients. There are several factors that may contribute to SCD being accompanied by NCS. Vaso-occlusion and the resulting tissue ischemia are unique features of SCD resulting from the presence of the pathological crystallizable polymer hemoglobin (S) which distorted red blood cell shape into sickle shape that also impaired RBCs passage through narrow blood vessels leading to ischemia and hemolysis [28]. Sickle red blood cells could block the small inferior alveolar artery and prevent blood perfusion into the inferior alveolar and mental nerves [29]. Additionally, edema due to bone infarction and osteomyelitis could compress these structures would thus typically occur in the area of the chin and lower lip, where the mental nerve, provides sensory innervation [30]. The vasa nervorum is another potential locus of vascular injury in the case of NCS which associated with SCD. SCD leads to a generalized inflammatory state and widespread vascular changes that can, in turn, result in vasculitis. In these small blood vessels, the vascular supply is compromise and causing

neuropathy involving single nerves [31]. In addition, SCD make patients significantly more prone to may be serious bacterial infections that postulated leading to early and progressed fibrosis and atrophy of the spleen [32]. The spleen atrophy may have compressed the distribution of the left inferior alveolar and mental nerves resulting in mandibular neuropathy. Thus, vulnerability to infection may predispose SCD patients to NCS. SCD patients are also at risk of electrolyte disorders, such as hypocalcaemia, due to repetitive blood transfusions that can present with circumorally numbness or paresthesia which typically resolve with the correction of the hypocalcaemia. NCS from malignant metastases characterized by persistent or progressively worsening numbness usually unilaterally often does not resolve spontaneously. Otherwise NCS from non-malignant causes is characterized by transient or self-limiting attacks Therefore, we noticed that all SCD+NCS patients in our sample experienced reversibly numbness, which indicates that the cause of their paresthesia was SCD and not tumor metastasis. We also found that NCS does not cause significant changes in hemoglobin levels or white blood cell and platelet counts in sickle cell disease patients. Finally we found there is no direct correlation between Hydroxyurea use and the development of NCS in patients with SCD as based on current medical literature [33]. The Hydroxyurea medicine is given to makes red blood cells bigger, helps them to stay rounder and more flexible, and makes them less likely to turn into an unhealthy sickle shape [34]. Also Hydroxyurea could increasing fetal hemoglobin (HbF) which has a higher affinity for oxygen than adult hemoglobin (HbA) [35], reducing the polymerization of sickle hemoglobin and improving oxygen delivery. For these positive effects of medicine it is used to treat SCD. Therefore twelve out of 36 of (SCD) and two out of six (SCD+NCS) patient groups (33% of both groups) were take Hydroxyurea. This indicates its subtle overlap with NCS presentation. Our result could be attempt to shed a light on a rare consequence of SCD which precisely rule out alternative differential causes of NCS, including local infection, primary neoplasm, or metastatic causes. Benign systemic causes are rare but important to recognize because they are amenable to specific treatments. On the other hand, NCS is not in itself a very serious condition but it is usually a very advanced symptom of metastatic disease so, in the absence of a benign cause, this sign is always indicative of disease progression. [36]

Conclusion

This study attempted to correlate the clinical manifestations, investigations, and treatment approaches of Numb chin syndrome (NCS) in sickle cell disease (SCD) patients. The data obtained support the hypothesis that occlusion of the microvascular vessels passing through the mandible may be a pathological mechanism of NCS. A thorough evaluation necessitates ruling out alternative differential causes of NCS, including local infections, primary tumors, or metastatic diseases. This study highlights a rare and under-recognized complication of sickle cell disease (SCD), which warrants further investigation to improve diagnosis and management.

Authors' contributions: Amer Shareef: Study concept design, Data acquisition and Study supervision, Talib Hassan achieved analysis and interpretation Write-up of the manuscript for intellectual content.

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