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# Nine Syndrome: Two Case Reports

**Haneen A. Siam[1] | Raneen R. Sweity[1] | Yasmeen S. Ashhab[1] | Majd A. AbuAlrob[1] | Mohammad A. Qabaja[2] | Muayad S. Salman[2] | Ismail A. Abudaya[3*] | Mutaz O. Shawar[4]**

***Correspondence:** Ismail A. Abudaya

**Address:** [1]Al-Quds University, Jerusalem, Palestine; [2]Radiology Department, Al-Makassed Islamic Charitable Hospital, Jerusalem, Palestine; [3]Neurology, Princess Alia Governmental Hospital, Hebron, Palestine; [4]Pediatrics, Al-Ahli Hospital, Hebron, Palestine

**e-mail** ✉: ismailabudaya@yahoo.com

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## ABSTRACT

Brainstem lesions have many spectra of presentations like 'one and a half syndrome', 'eight and half and nine syndrome. We report two cases of 'nine syndrome' which is defined as the combination of lower motor facial nerve lesion, one and a half syndrome and hemiparesis or hemiataxia. To our knowledge those are the first two published cases in Palestine. We highlight that one of the cases presented in the pediatric age, which is the first reported case in this age. We focus on the multiple presentations that could present with.

***Keywords:*** *Brainstem, Stroke, Demyelination, Nine Syndrome*

## Introduction

Nine syndrome is defined as the association of one-and-a-half syndrome, ipsilateral facial nerve palsy and hemiataxia or hemiparesis. (7+1.5+0.5) (Mahale *et al*., 2015). One-and-a-half syndrome consists of horizontal conjugate gaze palsy in one eye along with half of gaze palsy in the other eye due to ipsilateral internuclear ophthalmoplegia (Fisher, 1967). This was attributed due to lesions in the pontine paramedian reticular formation (PPRF) and Medial longitudal fasiculus (MLF) (Xue *et al*., 2017). Mostly it is caused by stroke, trauma, demyelinating disorders, astrocytoma and encephalitis (Martyn and Kean, 1988; Bolanos *et al*., 2004).

Here we present two cases of nine syndrome of two different ages and two different causes. A 62 years old patient with stroke and 14 months old patient as a result of demyelinating process.

## Case Presentation

### *Case 1:*

A 62 year old male with a known history of diabetes mellitus type two, hypertension, dyslipidemia and ischemic heart disease presented to the emergency department in Princess Alia

Governmental Hospital with a four days history of gait unsteadiness, blurring of vision, sudden onset right sided headache and ocular pain. He also complained from diplopia that improved when he covers one eye. There was no history of chest pain or fever. He has been on insulin (glargine and glulisine), dual antiplatelet therapy (clopidogrel 75mg and aspirin 100mg), atorvastatin 40mg and amlodopin 5 mg.

On examination, the patient was looking ill and drowsy, his blood pressure was 210/199 mmhg. Neurological assessment revealed limitation of the medial gaze in the right eye and no horizontal movement in the left eye. Vertical movement of the eyes and accommodation were preserved. Also, there was left sided facial palsy and ataxic gait. The rest of neurological exam was unremarkable.

Immediate laboratory studies showed random sugar level 30 mmol/l, serum troponin positive 0.31 mcg/l, Na level 122 mmol/l, Ca level 8.5 mmol/l, K level 4.78 mmol/l, cl level 93.3 mmol/l, complete blood count (WBC: 9.2 * $10^9$/l, PlT: 143 * $10^9$/l, Hb%: 10.4 and MCV 88.1 fl), coagulation panel (PT 12.2 sec, PTT 34 sec, INR 0.9), creatinine 162 µmol/l, BUN 19 mmol/l and HbA1C 10.5. Electrocardiograms revealed T wave inversion in V1-V6 and lateral leads.

The patient managed by continuing his medication (clopidogrel 75mg, aspirin 100mg, atorvastatin 40mg, amlodopin 5 mg and insulin) in addition to heparin 5000unit *4, bisoprolol 5mg and 1000cc normal saline/day. Due to hospital polices MRI was obtained after two days and showed acute mid-brain infarction that involved red nucleus, MLF, PPRF and colliculus of the facial nerve. In addition, echocardiogram, cardiac catheterization and carotid Doppler were planned to be done.

*Imaging:*

Fig. 1 and Fig. 2 showing the lesions observed in the case.

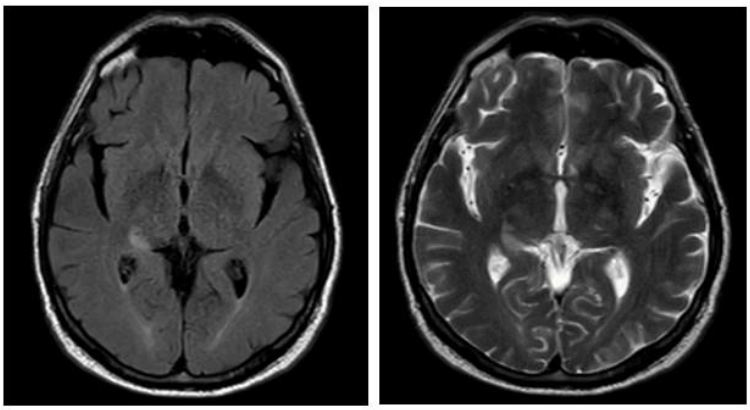


**Figure 1 (a,b):** There is area of high flair and high T2 signal appreciated in the posterior aspect of right thalamus with extension to medial aspect of the temporal lobe and likely involving parts of hippocampus.

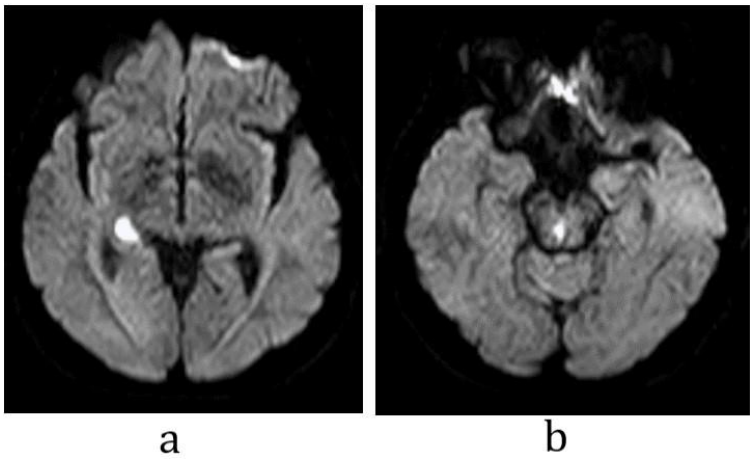


**Figure 2 (a,b):** Diffusion restrection is seen in the involved area as well in the mid-line of lower part of the posterior midbrain.

### *Case 2:*

A previously healthy 14 months old child presented with a five days history of sudden onset of left sided weakness. The patient was unable to stand on his left leg. On the next day, he became unable to walk or use his left hand as he used to use it previously. The family also noticed facial asymmetry and abnormal eye movement that affected his communication with others.

There was a history of fever of 38 degrees axillary that responded to antipyretics and runny nose two days prior to his presentation. There was no history of nausea, vomiting, cough or contact with ill patients.

On examination, the patient was irritable, conscious and not distressed or cyanosed. The temperature was 36.4, respiratory and heart rates were 37 and 128 respectively, blood pressure was 117/72 and O2 sat was 98 off O2.

Neurological examination revealed left sided paralysis manifested as inability to move his left limbs or stand without support. Cranial nerves examination showed right facial palsy presented by patient inability to close his right eye and asymmetrical smile. Eye movement examination revealed right horizontal gaze palsy. The right eye was adducted (right abducent nerve palsy) and there was limitation of left eye horizontal movement medially (Fig. 3). The rest of systemic examination was unremarkable.

**Figure 3:** The patient is looking at the right side of the picture.

Laboratory investigations showed WBCs 16.88* $10^9$/l, CRP 15.3 µg/ml, ESR 30mm/hr, lactic acid 5 mmol/l and ammonia 32µmol/l. Due to suspicion of meningitis lumbar puncture was done and treatment was initiated with IV acyclovir 20mg every 8 hours and IV dexamethasone 15mg every 6 hours. Then CSF analysis showed high protein. So next day MRI was done and demonstrated demyelination process which involved right sided of pons, so acute disseminated encephalomyelitis (ADEM) was suspected. As a result, dexamethasone and acyclovir were discontinued and methylprednisolone pulse therapy was initiated for five days as 300mg once daily over 6 hours infusion with monitoring of blood pressure every 2 hours and glucose in the mid of infusion. Response to steroid therapy was noticed and patient's symptoms started to improve. Control MRI was planned to be done after one month.

*Imaging:*

Fig. 4 and Fig. 5 showing the lesions observed in the MRI.

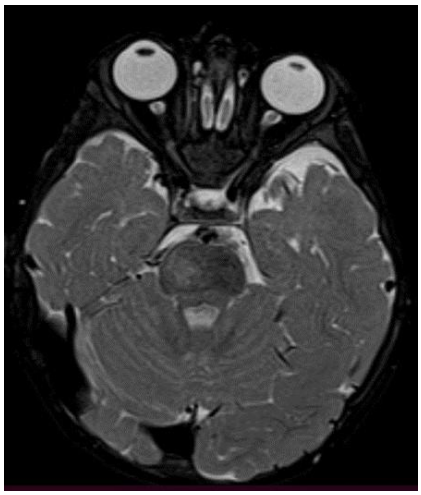

**Figure 4:** There diffuse swelling and high intense T2 signal in the right side of pons.

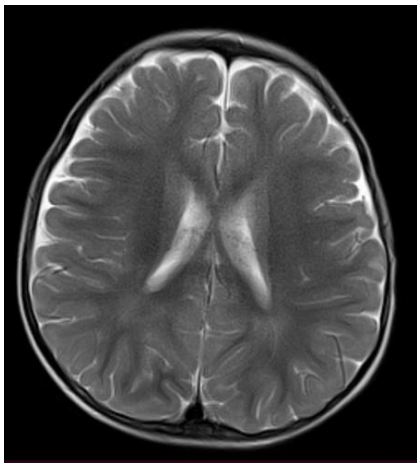

**Figure 5:** Bilateral peritrigonal high flair and T2 intensity with no involvment of carpos calusm, otherwise comma myelination is appropriate.

## Discussion

Nine syndrome is considered as a type of the one and a half spectrum disorders. One and a half syndrome can be due to lesions in paramedian pontine reticular formation (PPRF) or abducent nucleus and medial longitudinal fasciculus (MLF). PPRF or abducent nucleus lesion causes ipsilateral complete horizontal gaze palsy that explains the one while MLF lesion causes ipsilateral internuclear ophthalmoplegia that explains the half (1+0.5 = 1.5) (Ng *et al*., 2017; Mahale *et al*., 2015).

When there is involvement of intra-axial fasciculus or colliculus of the facial nerve (7th) this can result in a facial palsy. Combination of facial nerve palsy and the one and a half syndrome evolve a new entity that called eight and a half syndrome (1.5+7 = 8.5) (Yadegari *et al*., 2018).

Expansion of eight and a half syndrome into a nine syndrome happens due to additional symptoms of hemiparesis and hemianesthesia or hemiataxia (0.5). Lesion in corticospinal tract or medial lemniscus can lead to hemiparesis/hemianesthesia variant. While lesion in inferior cerebellar peduncle or red nucleus in the midbrain constitutes the ataxic variant. (7th nerve palsy+ 1.5 syndrome+ 0.5 hemiparesis/hemianesthesia or hemiataxia = 9 syndrome) (Tiwari *et al*., 2020).

According to the reported cases, nine-syndrome lesions in midbrain and pontine caused most commonly by ischemic or hemorrhagic stroke in six of them (Mahale *et al*., 2015; Xue *et al*., 2017; Martyn and Kean, 1988; Bolanos *et al*., 2004; Rosini *et al*., 2013; Tiwari *et al*., 2020). Other etiologies included demyelinating process in pons and midbrain such as multiple sclerosis in one case (Martyn and Kean, 1988) and HIV associated micro-vasculopathy in one case (Fisher, 1967).

In these two-presented cases, the patients came with the symptoms and signs of nine syndrome with two different ages and two different causes. In case 1, nine syndrome happened in 62 years old patient because of stroke while in case 2, the patient was 14 months old as a result of demyelinating process, which is the first reported case of nine syndrome in pediatric age. Both of them had facial palsy manifested by asymmetrical face appearance.

One and a half component of nine syndrome manifested in case1 by complete loss of horizontal gaze of left eye and right internuclear ophthalmolplegia. It is worth to mention that the patient at his first presentation he was partially closing his left eye so ptosis was suspected, but further examination revealed he could open his eye completely and he intentionally closed it to overcome the diplopia that happened in one and a half syndrome.

While in case 2, one and a half syndrome manifested by right abducent nerve palsy and left right

internuclear ophthalmoplegia (Fig. 2a).

The two variants of the half component of nine syndrome appeared in these two presented cases. In case 1 the patient had unsteadiness that can be explained as hemi-ataxia. In case 2 the patient had the hemiparesis variants which explained his inability to move his left hand and leg.

## Conclusion

Nine syndrome is a variant of eight and a half syndrome resulting from extension of the lesion to involve more structures in the midbrain and medulla. Recognizing the clinical manifestations of nine syndrome from the history and physical examination of the patient can help to expect the anatomical structures that are involved and the etiology. This early recognition assists to immediately start appropriate management for the patient to have better clinical outcome while waiting for radiology and laboratory results.

## Compliance with Ethical Standard

The nature and purpose of case report had been fully explained for the first patient and the second patient family. Privacy and protection of their personal information had been obligated. Verbal consent for publication was taken.

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