Nine Syndrome: Case Report and Review of Clinical Signs in Internuclear Ophthalmoplegia

Jennifer Singhdev, Ajay Asranna, Sachin Sureshbabu, Gaurav Kumar Mittal, Sweta Singla, Sudhir Peter[1], Sobhana Chindripu[2]

Department of Neurology, St. Stephen's Hospital, New Delhi, [1]Department of Pathology, Medall Healthcare, Ongole, [2]Department of Pathology, Guntur Medical College, Andhra Pradesh, India

Abstract

The pathologic involvement of brainstem and midbrain nuclei and white matter tracts in various combinations may result in a spectrum of arithmetically derived syndromes. They include 'one and a half syndrome', 'eight and a half syndrome' and 'fifteen and a half syndrome'. We report a case of 'nine syndrome', which has been reported more recently, caused by caused by acute pontine infarcts and characterised clinically by a combination of internuclear ophthalmolplegia, ipsilateral horizontal gaze palsy, lower motor neuron type of facial palsy, contralateral hemiparesis and hemianesthesia. We highlight the genesis of this combination of clinical signs, revisit the different variants of INO and review the literature on 'Nine syndrome'.

Keywords: Brainstem syndromes, internuclear ophthalmoplegia, nine syndrome, pontine vascular syndromes

Introduction

The pons and midbrain contain important nuclei and rich interconnections involved in the gaze circuit including the abducens nucleus, occulomotor nucleus, paramedian pontine reticular formation (PPRF), and medial longitudinal fasciculus (MLF). The pathologic involvement of these structures in various permutations and combinations has been implicated in a spectrum of arithmetically derived syndromes and includes "one and a half syndrome," "eight and a half syndrome," and "fifteen and a half syndrome." Each syndrome denotes a precise localization and a specific pattern of neurologic deficits. We report a case of "nine syndrome" which has been reported more recently and discuss other close mimics.

Case Report

A 65-year-old hypertensive and smoker presented with sudden onset of dizziness, facial deviation, weakness of the left side of the body, and diplopia. He also had one episode of vomiting but had no slurring of speech, loss of consciousness, tinnitus, or urinary incontinence. On examination, he had exotropia of the left eye, partial left eye ptosis, and mild skew deviation with right eye being higher than left. There were right horizontal gaze palsy and internuclear ophthalmoplegia (INO). The pupils were of normal size, reacting to light. In addition, he had right facial palsy, left hemiparesis – left upper limb power 1/5 and left lower limb power 3-/5 – and decreased sensation on the left side of the body. Video 1 demonstrates the eye movements of the patient. The patient essentially had eight and a half syndrome (1½ syndrome + 7th nerve palsy) with hemiparesis and hemianesthesia – the so-called nine syndrome. The magnetic resonance imaging (MRI) showed two acute infarcts in the right paramedian medial pons and dorsal pons, which is shown in Figures 1 and 2.

Discussion

In this report, we describe a case of acute paramedian pontine infarct, resulting in nine syndrome along with exotropia of the left eye (paralytic pontine exotropia) and mild skew

Address for correspondence: Dr. Sachin Sureshbabu, Department of Neurology, St. Stephen's Hospital, New Delhi - 110 054, India.
E-mail: drsachins1@rediffmail.com

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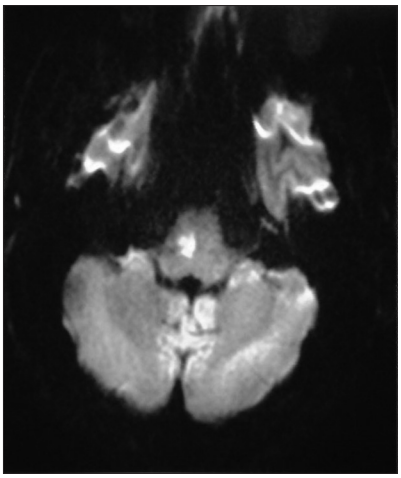

Figure 1: Magnetic resonance imaging brain: Diffusion-weighted images showing restricted diffusion suggesting acute infarct in the right medial pons

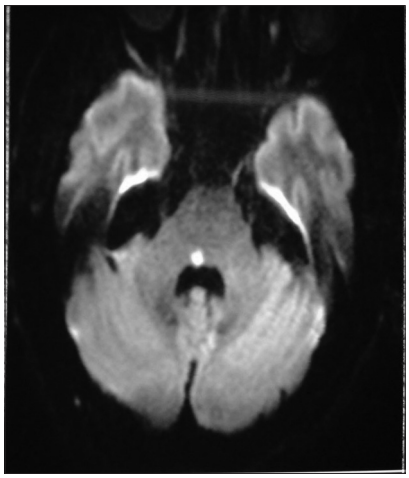

Figure 2: Magnetic resonance imaging brain of the same patient showing a second infarct in right dorsomedial pons

deviation. It is our purpose to highlight the genesis of this combination of clinical signs. We also revisit the different variants of INO and review the literature on "nine syndrome" in this short report.

The functional pathway responsible for horizontal gaze comprises the frontal eye field, PPRF, and MLF. Inputs from the frontal eye fields go to contralateral PPRF (located anterior and lateral to MLF) and then to the contralateral abducens nucleus through which they send fibers to contralateral lateral rectus muscle causing the contralateral eye to abduct. Some fibers from contralateral abducens nucleus also traverse the ipsilateral MLF and reach the ipsilateral oculomotor nucleus, which in turn supply the ipsilateral medial rectus muscle and cause the ipsilateral eye to adduct.

In the anterior nuclear ophthalmoplegia of Cogan, the patient has impaired convergence with failure of adduction in the affected eye. Here, the lesion is located in the anterior midbrain.[1] In INO of abduction described by Lutz, abduction is impaired instead of adduction on the affected side associated with adduction nystagmus of the opposite eye.[2] Wall-eyed bilateral INO is the other member of this group of eye movement disorders wherein bilateral INO is associated with exotropia of both eyes. This clinical presentation requires involvement of bilateral medial rectus, subnuclei of the third nerve nuclear complex, in addition to bilateral MLF pathology.[3] Vertical INO is of two types; in one type, there is bilateral upgaze palsy with additional downgaze impairment on the affected side. Alternatively, in the other type, there is bilateral downgaze palsy with additional upgaze palsy on the affected side. This is caused due to the involvement of the efferent fibers form rostral interstitial MLF which is involved in vertical gaze.

When there is conjugate gaze palsy on the one side and INO leading to impaired adduction on looking on the other side, the resulting condition is called "one and a half syndrome."[4] This is caused by the involvement of ipsilateral PPRF/abducens nucleus and MLF. One and a half syndrome when associated with seventh cranial nerve palsy is called "eight and a half syndrome."[5] Rarely, bilateral facial palsy may be seen with INO which is then called "fifteen and a half syndrome".[6] In the present report, the following clinical signs were noted: (1) conjugate right horizontal gaze palsy, impaired right eye adduction, horizontal left-beating nystagmus on leftward gaze, paralytic pontine exotropia of the left eye, skew deviation with right eye higher than the left, (2) peripheral right facial palsy, and (3) left hemiparesis and hemianesthesia, all of which constitute the so-called nine syndrome.

Nine syndrome is a rare entity which was reported by Rosini *et al*.,[7] and there have been only three cases reported in literature till date.[7-9] This syndrome comprises eight and a half syndrome associated with hemiparesis and hemianesthesia due to additional involvement of the corticospinal tract and medial lemniscus. Mahale *et al*. described a variation to nine syndrome in two patients who had eight and a half syndrome without hemiparesis/hemianesthesia but instead had contralateral hemiataxia due to the involvement of inferior cerebellar peduncle in one patient and red nucleus in another.[8] Our patient had hemiparesis and hemianesthesia similar to the patient first described by Rosini *et al*. The MRI brain showed two areas of diffuse restriction, one in the right paramedial pons and the second more caudal in the dorsal pons.

The structures involved in nine syndrome are as follows:

1. Abducent nucleus/PPRF
2. Adjacent MLF
3. Seventh nerve colliculus/fascicle
4. (a) Hemiparesis/hemianesthesia variant
   - Corticospinal tract and medial lemniscus

   (b) Ataxia variant
   - Inferior cerebellar peduncle/red nucleus in the midbrain

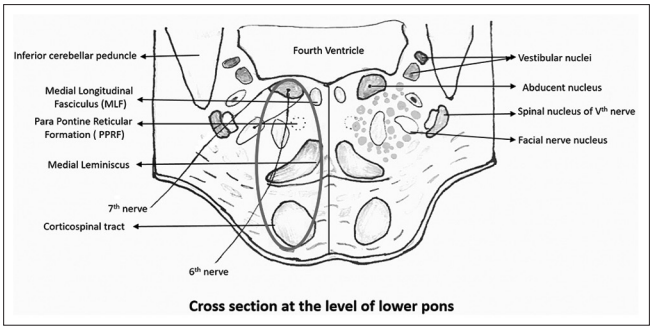

Figure 3: Schematic representation of structures involved in nine syndrome: (1) Abducens nucleus/paramedian pontine reticular formation, (2) median longitudinal fasciculus, (3) seventh nerve colliculus/fascicle, (4) corticospinal tracts, (5) medial lemniscus

A schematic representation of the structures affected in the hemiparesis/hemianesthesia variant of nine syndrome is shown in Figure 3.

The most common causes of INO are ischemic strokes and multiple sclerosis but rarely may be caused by trauma, infection, hemorrhage, and tumors.[10] Paramedian perforating branches of the basilar artery supply the dorsal pons, and occlusion of the perforators results in paramedian pontine syndromes. While an occlusion proximally may cause infarction of the pontine basis and the tegmentum, a distal occlusion causes dorsal pontine tegmental syndrome as clearly seen in the MRI of our patient.[9] Our patient also had ptosis of the left eye which is not reported in previous descriptions of nine syndrome. It is unlikely to be due to oculomotor nuclear/fascicular/nerve involvement and the MRI revealed no midbrain infarcts. The ptosis is probably a manifestation of eyelid malposition which is well known to occur with lower motor neuron (LMN) facial palsy, where contralateral ptosis is also seen quite often.[11]

Conclusion

Nine syndrome is a rare clinical entity with core clinical signs of one and a half syndrome, ipsilateral facial palsy, and contralateral hemiparesis/hemianesthesia and localizing to the dorsal paramedian pontine tegmentum. The awareness of this sign helps in precise localization and consideration of relevant etiologies.

Acknowledgment

We acknowledge the assistance provided by Mr. Tony Verghese in the preparation of illustration of cross section pons used in Figure 3.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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