JPSIM Journal of Pakistan Society of Internal Medicine

Case Report

The 'Ear of Lynx Sign': A Radiodiagnostic Clue in Complicated Hereditary Spastic Paraplegia

Safia Bano, Ahmad Nawaz, Haris Iqbal, Ahsan Numan, Sadaf Iftikhar, M. Abdul Ahad Khawaja, Allina Aslam, Laiba Suhail, Aqsa Umar

Department of Neurology, King Edward Medical University/ Mayo Hospital Lahore

Abstract

Hereditary spastic paraplegia, also known as Strumpell-Lorrain disease, encompasses a group of hereditary neurological disorders characterized by progressive spasticity and lower limb weakness due to corticospinal tract degeneration. This condition can manifest clinically as a pure form with pyramidal signs or a complicated form exhibiting a spectrum of additional neurological and non-neurological manifestations. In this report, we present a compelling familial case of three male siblings, product of first-degree consanguinity, presented with complicated hereditary spastic paraplegia. The radiological evaluation of the case revealed noteworthy findings, including a thinning of the corpus callosum and an abnormal T2/FLAIR cone-shaped hyperintensity at the tip of the frontal horn of the lateral ventricles, resembling the tufts of hair crowning the ears of a lynx, termed the "ear of lynx sign." This unique radiological sign, combined with a thin corpus callosum, is commonly observed in genetic subtypes associated with mutations of the SPG11 and SPG15 genes. Considering the limited access and high cost of genetic studies in our region, the recognition and clinical importance of the 'Ear of Lynx Sign' take on utmost significance. This distinctive radiological clue plays a crucial role in early identification of genetic forms of hereditary spastic paraplegia, leading to better disease management, progression control, and overall enhancement of patients' clinical outcomes and quality of life. Our study underscores the significance of such radiodiagnostic signs, particularly in areas with restricted availability of genetic testing, emphasizing their profound impact on patient care and prognosis.

Keywords: Hereditary spastic paraplegia, 'Ear of Lynx Sign', Radiodiagnostic clue, Spastic paraplegin gene 11, Spastic paraplegin gene 15

How to cite this:

Bano S, Nawaz A, Iqbal H, Numan A, Iftikhar S, Khawaja MAA, Aslam A, Suhail L, Aqsa Umar A. The 'Ear of Lynx Sign': A Radiodiagnostic Clue in Complicated Hereditary Spastic Paraplegia - A Familial Case Report. J Pak Soc Intern Med. 2023;4(4): 324-329

Corresponding Author: Dr. Ahmad Nawaz

Email: ahmad_nawaz3534@yahoo.com

DOI: https://doi.org/10.70302/jpsim.v4i4.2366

Introduction

Hereditary spastic paraplegia (HSP) comprises a group of genetic diseases characterized by a constellation of clinical symptoms, primarily resulting from the progressive degeneration of long tracts, particularly the corticospinal tract and, to a lesser extent, dorsal columns. The clinical presentation can vary, ranging from isolated spastic weakness in the lower limbs to a complex array of neurological signs, including cerebellar ataxia, peripheral neuropathy, sphincteric problems, cognitive decline with memory impairment, visual or hearing disturbances, as well as other manifestations such as adrenal crisis or ichthyosis.[1] The incidence of HSP varies depending on the population studied and the genetic subtypes considered. Overall, it is estimated to be around 2-6 per 100,000 individuals. However, certain regions and populations may have a higher prevalence of specific genetic forms due to founder effects or other factors.[2] HSP can be inherited in various patterns, predominantly in autosomal dominant or autosomal recessive fashion, and rarely as X-linked recessive or sporadic cases. The phenotypic and genetic heterogeneity of HSP poses significant challenges in making an accurate diagnosis. Nevertheless, certain neuroimaging signs have paved the way for identifying distinct genetic subtypes.[3]

In this report, we present a familial case of three brothers, each exhibiting different clinical manifestations but sharing an identical radiological sign, characterized by thinning of the corpus callosum and the presence of the 'ear of lynx sign.' The radiological findings played a pivotal role in their diagnosis and proved valuable in preventing late complications of the disease in younger siblings. From the available literature, genetic studies have shown a specific association between the thinning

of the corpus callosum with the 'ear of lynx sign' and common autosomal recessive genetic subtypes, namely SPG11 and SPG15, of HSP.[4,5] The current case highlights the importance of recognizing and interpreting these neuroimaging signs as invaluable tools in early diagnosis and timely intervention, particularly in regions with limited access to genetic testing facilities. A better understanding of such radiological clues can lead to improved patient outcomes, effective management, and enhanced quality of life for individuals affected by hereditary spastic paraplegia.

Case Report

Case description

Three male siblings, born to healthy first-degree cousins, were admitted to the neurology department of a tertiary care hospital. They presented with a common feature of progressive spasticity in their bilateral lower limbs. Patient B-1, 25 years of age at the time of consultation, faced challenges with learning during his primary school years, resulting in discontinuation of his education. At the tender age of 10, he began experiencing frequent falls and gradually became reliant on the assistance of two individuals to walk by the age of 15. Notably, patient B-1's condition worsened, leading to severe difficulties in speaking and marked behavioral changes, including self-aggression and the use of abusive language towards others. Furthermore, he had a history of experiencing generalized tonic-clonic fits, which started at 22 years of age. Patient B-2, the younger sibling aged 23 years, also grappled with learning difficulties, though less severe cognitive impairment compared to B-1, causing impediments to attending secondary school. Gait disturbances surfaced at 9 years of age, culminating in his reliance on support from two individuals to walk. Additionally, patient B-2 presented with dysarthric speech, along with episodes of irrelevant talks and bouts of crying. Patient B-3, the youngest sibling at 22 years of age, first encountered difficulty in walking at 12 years old. Though less severely affected, he required the assistance of one person while walking. Patient B-3 communicated complaints of speech difficulties and tingling sensations in his feet during nighttime. Unlike his brothers, patient B-3 displayed fewer cognitive impairments and did not have a history of behavioral changes or fits. Notably, none of the siblings had a history of blurred vision, difficulty in swallowing, or wasting of hand muscles, nor did they report any sphincteric problems. Additionally, all three brothers demonstrated normal birth histories and achieved expected developmental milestones. Curiously, their elder male sibling (age 28 years), two younger male siblings (age 20 years and 18 years, respectively), and their 17-year-old sister did not exhibit similar complaints [Figure 1].

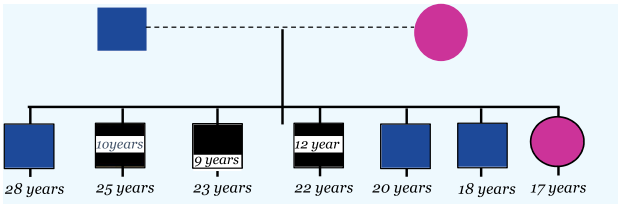

Figure 1: *Pedigree Depicting Consanguinity with Dotted Lines*

"Males represented by blue squares, females by pink circles, and affected males by black squares with age of onset displayed inside the squares. Ages indicated below the symbols."

Physical Examination

On general physical examination, the patients presented with normal vital signs and were afebrile. Ophthalmologic examination revealed 6/6 visual acuity in both eyes, normal color perception, and contrast sensitivity. Pupils were equally reactive to light bilaterally, and dilated fundus examination showed no abnormalities with no afferent pupillary defect. Extraocular movements were normal. Mini Mental State examination scores for Patients B-1, B-2, and B-3 were 14/30, 18/30, and 22/30, respectively. Neurological examination revealed spastic paraparesis, brisk tendon reflexes with sustained ankle clonus, dysarthric speech, and intact spinothalamic tract and dorsal column sensations. All three patients exhibited extensor plantar responses. Patient B-1 had the additional presentation of severe Gastrocnemius soleus contractures in both legs. Patient B-2 showed cerebellar features, including bilateral horizontal nystagmus, dysdiadokinesia, and bilateral intention tremors. Systemic examination in all cases was unremarkable.

Investigations

All routine baseline investigations yielded normal results. Electric encephalography (EEG) of Patient B-1 indicated diffuse cerebral dysfunction, while no seizure activity was observed in Patients B-2 and B-3 during recording. Nerve conduction studies revealed axonal motor and sensory polyneuropathy, with more pronounced reduction in action potential in both motor and sensory nerves observed in Patients B-1 and B-2 compared to B-3.MRI brain findings were identical in all affected male siblings, showing marked thinning of the corpus callosum. Axial T2/FLAIR images exhibited high signal intensity extending a short distance from the anterior horns of the lateral ventricles, indicative of the characteristic "Ear of lynx sign" [Figure 2]. Additionally, a prominent ventricular chain was observed due to age-inappropriate cortical atrophy. MRI cervical spine showed mild atrophy in Patients B-1 and B-2, while Patient B-3 exhibited an unremarkable MRI cervical spine [Table:1]. Due to financial constraints and the

highly suggestive neuroimaging findings, further investigations such as hormone profile antibody screening, viral panel, serum vitamin B12 level, and oligoclonal bands were planned but not performed.

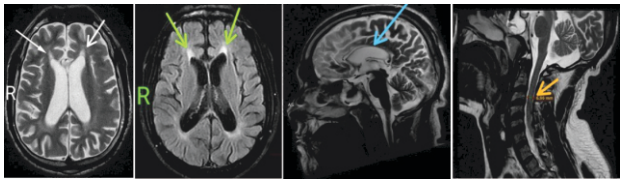

Figure 2: *MRI Brain axial T2-weighted (A) and T2-FLAIR (B) images showing the "Ear of Lynx" sign, Sagittal T2 image (C) highlighting the thinning of the corpus callosum, MRI craniocervical junction (d) demonstrating mild spinal cord atrophy (diameter: 6.9 mm).*

Differential Diagnosis

Initially, considering the patient's clinical history and family background, our differential diagnosis included spinocerebellar ataxia or leukodystrophy. However, these possibilities were ruled out due to the absence of

Table 1: *Comprehensive Summary of Affected Siblings with Hereditary Spastic Paraplegia (HSP) Clinical Features and Investigations.*

Patient ID	Age of Onset of symptoms	Age at presentation	Features suggestive of complicated Hsp	MRI findings	Electrophysiological studies
B-1	10 years	25 years	Severe Cognitive impairment (MMSE: 14) Fits Ataxia Dysarthria Neuropathy	***MRI Brain:*** **1)** Cerebral Atrophy **2)**Prominent ventricular chain due to age inappropriate cortical atrophy **3)** Marked thinning of Corpus callosum **4)Axial T2w/Flair** images showed Hyperintensity at the of frontal horns of lateral ventricles giving appearance of "**EAR OF LYNX** " **MRI cervical Spinal Cord:** Mild atrophy of Spinal cord	***EEG:*** Mild Cerebral Dysfunction ***NCS:*** Sensory and Motor Polyneuropathy with Polyradiculopathy severely affecting lower limbs
B-2	9 years	years	i)Mild Cognitive impairment (MMSE: 20) ii)Dementia iii)Ataxia iv)Dysarthria v)Neuropathy vi)Cerebellar Features (Bilateral Horizontal Nystagmus& Intention tremors & Past Pointing)	**MRI Brain:** **1)** Cerebral Atrophy **2)**Prominent ventricular chain due to age inappropriate cortical atrophy **3)** Marked thinning of Corpus callosum **4)Axial T2w/Flair** images showed Hyperintensity at the of frontal horns of lateral ventricles giving appearance of "**EAR OF LYNX** " **MRI cervical Spinal Cord:** Mild atrophy of Spinal cord	**EEG:** No Seizure activity seen. **NCS:** Sensory and Motor Polyneuropathy
B-3	12 years	22 years	**i)**Borderline Cognitive impairment (MMSE: 22) **ii)**Ataxia **iii)**Dysarthria **iv**)Neuropathy	**MRI Brain:** **1)** Cerebral Atrophy **2)** Marked thinning of Corpus callosum **3)Axial T2w/Flair** images showed Hyperintensity at the of frontal horns of lateral ventricles giving appearance of "**EAR OF LYNX** " **MRI cervical Spinal Cord:** unremarkable	**EEG:** No Seizure activity seen. **NCS:** Sensory and Motor Polyneuropathy

Abbreviations: *Hsp - Hereditary Spastic Paraplegia, MMSE - Mini Mental State Examination, MRI - Magnetic Resonance Imaging, T2W/FLAIR - T2-weighted/Fluid-attenuated inversion recovery, EEG - Electroencephalography, NCS - Nerve Conduction Studies, SPG - Spastic Paraplegin Gene.*

radiological evidence, such as cerebellar atrophy in spinocerebellar ataxia or white matter aggression in leukodystrophy. Instead, the presence of "ear of lynx sign" along with thinning of the corpus callosum in the MRI brain led to the final diagnosis of familial spastic paraplegia.

Treatment

Our primary goal, regardless of the specific diagnosis, was to enhance the patients' quality of life and mitigate disease-related complications. The mainstay of treatment for our patients involved physiotherapy focused on improving lower limb function. To manage spasticity, we prescribed clonazepam (0.5mg *bd), baclofen (initially 10 mg *PO* TDS, then 10mg*po*TDS), and Tizanidine (4mg*PO*BD). Addressing mood liabilities and depressive symptoms, an antidepressant (Tab. sertraline *50mg *BD) was incorporated into the treatment regimen. For Patient B-1, who experienced generalized tonic-clonic fits, we administered antiepileptic medication (Tab.epival 500mg*PO*BD). Furthermore, to alleviate Gastrocnemius-soleus contractures, we planned a contracture release surgery along with serial casting and orthostatic footwear. Patient B-3, who presented with neuropathic features, was managed with Pregabalin (100mg *po*BD) to address the neuropathic symptoms effectively.

Outcome and Follow-up

Notable improvement in spasticity was evident after two to three weeks of hospitalization following the prescribed treatment. Patients B-2 and B-3 demonstrated significant progress owing to their less advanced disease and timely interventions. For Patient B-1, the fits were effectively controlled. Moreover, the recommended antidepressant led to the resolution of mood disturbances and behavioral issues. Additionally, all patients experienced a considerable enhancement in voice quality as early as the first week of their hospital stay.

Discussion

Diagnosing familial spastic paraplegia has posed significant challenges for physicians. However, by correlating clinical history, physical examination, and specific neuroimaging characteristics, the differentiation of genetic subtypes has become more feasible. Spinal cord imaging aids in ruling out common differentials like inflammatory, compressive, traumatic, or vascular causes of spastic paraparesis. Similarly, brain imaging provides characteristic findings that can guide towards specific genetic subtypes of hereditary spastic paraplegia, as summarized in Figure 3.6

The thinning of the corpus callosum has been associated with various genetic subtypes. Specifically, the thinned corpus callosum, along with cone-shaped hyperintensities on T2W/FLAIR in the frontal horn of lateral ventricles, represents the most classic and useful radiological finding of Hereditary Spastic Paraplegia. Literature review demonstrates that the combination of thinning of the corpus callosum and the ear of lynx sign is highly diagnostic for HSP genetic subtypes SPG11 & SPG15.[7,8]

Moreover, reports by B. Pascal highlight the high specificity of the ear of lynx sign for SPG11 or SPG15, even in the absence of a family history. Additionally, C. Passian's studies indicate that the presence of thinning of the corpus callosum with the ear of lynx sign is associated with Spastic paraparesis 11 and 15, both in familial and sporadic cases.[9] Furthermore, Somesh Singh's sporadic case report of a 23-year-old female with spastic paraparesis, displaying thinning of the corpus callosum and ear lynx sign in genetically classified subtype SPG15, contributes valuable information to the literature.[4]

In contrast, we acknowledge case reports of Marchavia Bignami disease, where an ear of lynx sign was reported on Magnetic Resonance Brain imaging. However, the diagnosis differed due to a history of alcohol abuse and rapid deterioration of gait in elderly individuals without previous neurological complaints or family history, making it difficult to definitively rule out the disease. Although gliosis at the calloso-caudate angle of the frontal horn may mimic the ear of lynx sign, it differs in shape, resembling a rounded cap rather than a cone, and is usually smaller than the true ear of lynx.[10]

Our reported case involves a complicated form of hereditary spastic paraplegia with various clinical manifestations, including epileptic fits in Patient B-1 and cerebellar features in B-2. Additionally, all affected siblings exhibited clinically evident neuropathic features and cognitive decline, along with common radiological findings. Notably, this case is the first familial report of epileptic fits in hereditary spastic paraplegia, contributing to the existing knowledge of this condition.

Early diagnosis of HSP is crucial to prevent long-term complications, such as muscle contracture, back and knee pain, stress, and depression, which significantly impact patients' quality of life. We successfully managed the complications of HSP through early diagnosis based on radiological specific signs, family history, and clinical examination, effectively preventing contracture formation in Patients B-2 and B-3.

Certain limitations should be acknowledged, as neuroimaging of normal siblings was not performed due to limited accessibility to facilities. Additionally, genetic testing, requiring better laboratory facilities and being expensive, was not carried out in this familial case of spastic paraplegia. Nonetheless, the educational value of our case for practicing physicians remains paramount. Early radiological investigations, including brain ima-

ging in individuals with a significant family history of spastic paraplegia, hold great importance. Familiarity with specific signs for SPG11 & SPG15 can aid in timely diagnosis and prevention of disease-related complications, even in countries with limited access to genetic testing facilities.

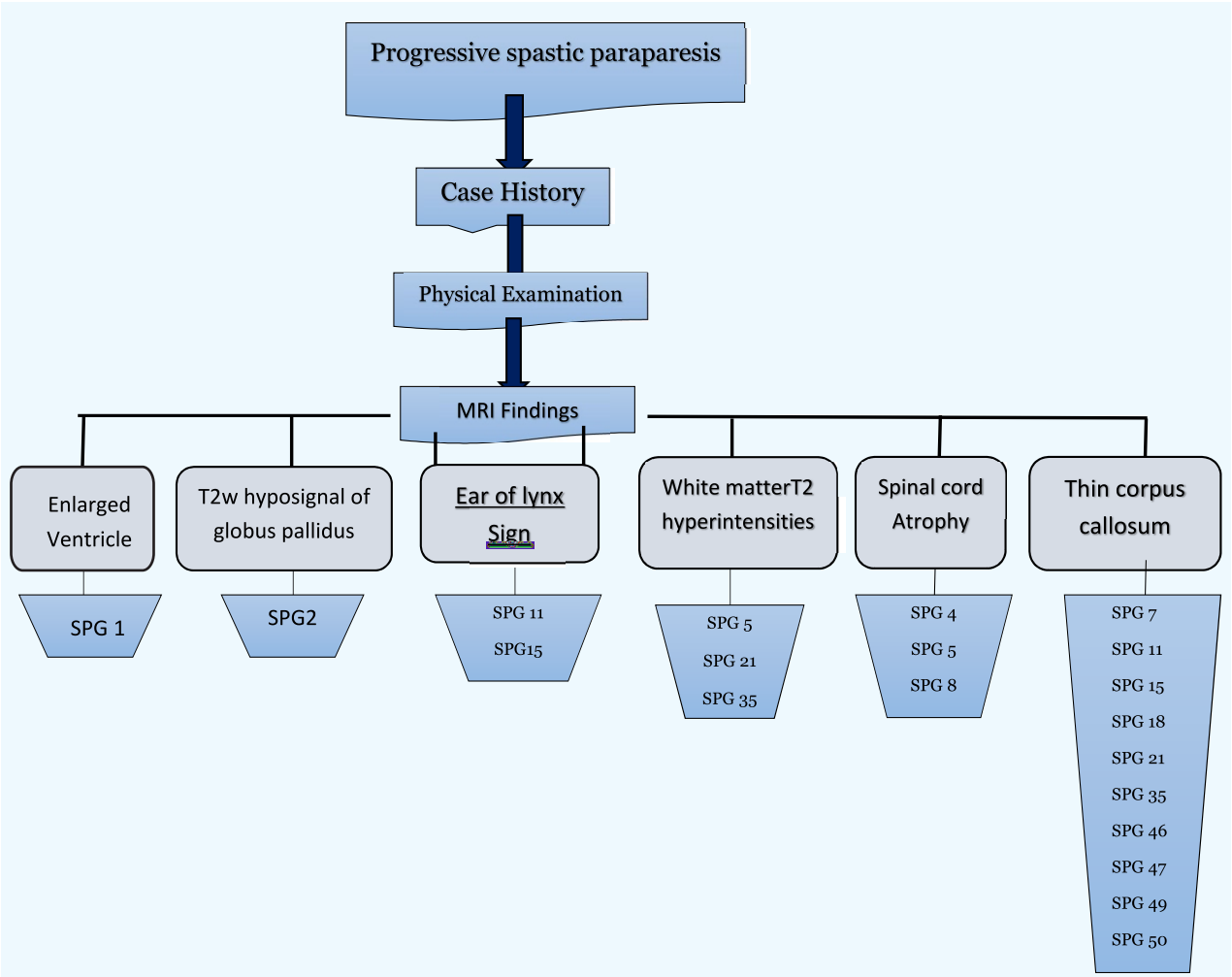

Figure 2: *Flowchart illustrating the correlation between different neuroimaging findings and HSP genetic subtypes.*

Conclusion

We reported a familial case of Complicated Hereditary spastic paraplegia with common radiological findings of thinning of corpus callosum and Ear of lynx sign in all affected family members. It is essential to know these radiological signs as they act as ladder for the diagnosis of this rare genetic disorder in those countries where genetic testing facilities are expensive to approach or not readily available. By this we can prevent further disease related complications and can improve the clinical outcome of subsequent affected family members.

Acknowledgments

The authors extend theirs heartfelt appreciation to the Radiology Department, Mayo Hospital, King Edward Medical University for their invaluable assistance in reporting and interpreting the MRI images. Their expertise and dedication significantly contributed to the accurate diagnosis and management of our patients with hereditary spastic paraplegia.

Conflict of Interest: *None*

Funding Source: *None*

References

1 Da Graca FF, De Rezende TJR, Vasconcellos LFR, Pedroso JL, Barsottini OGP, França Jr MC. Neuroimaging in hereditary spastic paraplegias: current use and future perspectives. Front Neurol. 2019; https:// doi.org/10.3389/fneur.2018.01117.

2 Fink JK. Hereditary spastic paraplegia. Curr Neurol Neurosci Rep. 2006;6(1):65-76.

3 Kara E, Tucci A, Manzoni C, Lynch DS, Elpidorou M, Bettencourt C, et al. Genetic and phenotypic characterization of complex hereditary spastic paraplegia. Brain. 2016;139(7):1904-18.

4 Singh S, Israrahmed A, Mall RV, Singh V. 'Ears of the Lynx' sign: an important and useful MRI clue for the diagnosis of hereditary spastic paraplegia (HSP) caused by mutation in SPG15 gene. BMJ Case Rep. 2021; 14(10): e242275.

5 Hourani R, El-Hajj T, Barada W, Hourani M, Yamout B. MR imaging findings in autosomal recessive hereditary spastic paraplegia. AJNR Am J Neuroradiol. 2009; 30(5):936-40.

6 Faber I, Servelhere KR, Martinez AR, D'Abreu A, Lopes-Cendes I, França Jr MC. Clinical features and management of hereditary spastic paraplegia. Nat Rev Neurol. 2014;72:219-26.

7 França Jr MC, D'Abreu A, Maurer-Morelli CV, Seccolin R, Appenzeller S, Alessio A, et al. Prospective neuroimaging study in hereditary spastic paraplegia with thin corpus callosum. Neurology. 2007;22(11):1556-62.

8 Romagnoli ER, Akly MP, Miquelini LA, Funes JA, Besada CH. Hereditary spastic paraplegia: an "ears of the lynx" magnetic resonance imaging sign in a patient with recessive genetic type 11. Tremor Other Hyperkinet Mov (N Y). 2021;34(1):42-4.

9 Paisan-Ruiz C, Dogu O, Yilmaz A, Houlden H, Singleton A. SPG11 mutations are common in familial cases of complicated hereditary spastic paraplegia. Neurology. 2008;70(16 Part 2):1384-9.

10 Pacheco FT, Rego MM, do Rego JIM, da Rocha AJ. "Ears of the Lynx" Sign in a Marchiafava–Bignami patient: Structural Basis and Fiber-Tracking DTI Contribution to the Understanding of this Imaging Abnormality. J Neuroimaging. 2014;24(2):205-7.