ISSN: 2753-7919
British Journal of Healthcare and Medical Research; Vol. 13 No. 06 (2026) (38-43)
https://doi.org/10.14738/bjhr.1306.12638

Pallister-Killian Syndrome: Further MRI and Clinical Findings in a Patient

Elvio Della Giustina[1] & Michele Sintini[2]

1. Gruppo Centro di Medicina, Italy
2. Casa di Cura "Sol et Salus", Rimini, Italy

Abstract: Background: Patients with Pallister-Killian syndrome have received significant attention due to their phenotypic, genetic, and clinical abnormalities, especially their tendency to develop epilepsy. Neuroimaging studies have revealed major brain abnormalities, particularly polymicrogyria in the perisylvian frontotemporal cortex. Nevertheless, each new patient case can contribute to our understanding of the condition. Case presentation: We present a patient with Pallister-Killian syndrome who underwent long-term clinical, neurological, electroencephalographic, and neuroimaging follow-up. This follow-up allowed us to confirm that the type of seizure is variable. Neuroimaging revealed the presence of the known cortical asymmetric polymicrogyria, which extended beyond the typical affected regions. Additionally, we identified previously unreported developmental brain anomalies, including temporal arachnoid cysts, hippocampal dysmorphisms, and brainstem underdevelopment. Conclusions: This study shows that comprehensive follow-up is always recommended for these patients in order to better recognize all developmental brain anomalies. The study also demonstrates that the syndrome can present with a wider range of clinical and brain structural abnormalities than is typically recognized, confirming its heterogeneity. All brain abnormalities are developmental defects except for focal, mostly peri-paraventricular, signal abnormalities that are lesional.

Keywords: Pallister-Killian syndrome, PKS, tetrasomy, polymicrogyria, epilepsy, hippocampal abnormalities

INTRODUCTION

Pallister-Killian syndrome (PKS) (OMIM #601803) is a sporadic disorder caused by mosaic tetrasomy 12p. Depending on whether the chromosome is partially or completely duplicated, patients with PKS exhibit phenotypic heterogeneity. Characteristic features include a prominent forehead with sparse temporal hair, a broad nasal bridge, hypertelorism, a wide mouth with dental anomalies, and pigmentary skin changes. Developmental delay, intellectual disability, hypotonia, and seizures are variably associated with the disorder[1-3]. Previous reports of brain abnormalities have emphasized an abnormal corpus callosum (CC), dilated ventricles, variable parenchymal atrophy, periventricular lesions, and bilateral or unilateral perisylvian polymicrogyria (PMG)[4-8]. Epilepsy is common among affected patients, yet no seizure type has been proven to be specific to the condition[9-10]. This report describes an additional patient with PKS who had some previously unreported neuroimaging findings and interesting electroencephalographic (EEG) recordings during follow-up.

CASE PRESENTATION

This child was born after a 33-week uneventful gestation to healthy, unrelated parents. At birth, he weighed 2,420 grams. He had dyschromic skin patches on his face and skull, oxycephaly, frontal bossing, and sparse hair implanted retrolaterally in the frontal and parietal regions that converged to form a midline frontal triangle. His eyelids slanted slightly downward, and his eyeballs were prominent with sparse eyebrows. He also had back- and down-set ears, a snub nose with enlarged nostrils, hypertelorism, a long philtrum, a large mouth, microretrognatia, a cleft soft palate, brachydactyly and camptodactyly of the hands and feet, lateral deviation of the fingers and toes, preaxial polydactyly of the right foot, leg asymmetry, cryptorchidism, and an umbilical hernia. (Figure 1) Cardiac ultrasounds revealed double defects in the interventricular and interatrial septa. A funduscopic examination revealed no abnormalities. Leukocyte karyotyping was normal. However, the fibroblast karyotype showed partial tetrasomy, written as 47,XY,+i(12)(p10)(25)/46,XY(25), which confirmed the diagnosis of PKS. The patient was bedridden due to severe hypotonia and limited spontaneous movement. There was no pyramidal involvement, dyskinesia, or dystonia. He also had facial paresis and dysphagia, requiring feeding via percutaneous endoscopic gastrostomy (PEG). Head control was the only motor milestone he achieved, and speech or language skills were never developed. Early in life, he experienced life-threatening episodes of cyanosis, apnea, bradycardia, and hypoxia. Initially, these events were attributed to cardiac septal malformation, pulmonary hypertension, and infections. They required continuous home oxygen administration. The episodes could occur alone or alongside irregular tonic arm jerks, clonic oculomotor movements, staring, oral myoclonic jerks, or generalized tonic-clonic seizures. Thus, he was admitted to the pediatric neurology service. Baseline EEG recordings revealed interhemispheric asymmetry. There was slightly depressed background activity and many slow, high-amplitude centro-temporal delta waves, as well as occasional degraded sharp waves, on the right side. The left side showed higher-voltage, irregular background activity, fewer delta waves, and more frequent sharp waves in the centro-temporal region. The EEG did not change with wakefulness or sleep. Occasionally, the depressed background activity was interrupted by paroxysmal bursts of fast, synchronous, alpha-like rhythms that often corresponded to observed apnea events. These bursts lasted five to ten seconds and were either restricted to the right hemisphere or extended bilaterally. An EEG Holter recording confirmed these abnormalities (Figure 1).

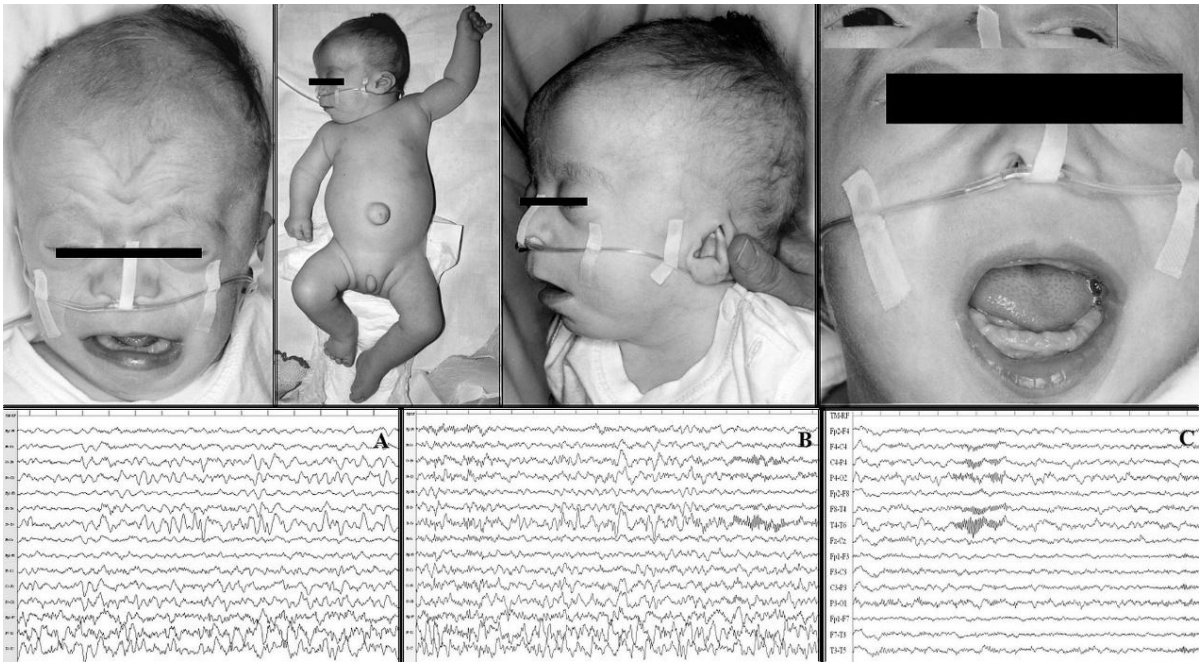


Figure 1: Phenotype and EEG Features

Legend: The patient's phenotype exhibits all the characteristics of PKS. In Panel **A**, the EEG recording shows asymmetric background activity, including anterior fast rhythms and slow, bilateral centro-temporal and parieto-temporal high-voltage delta activity, particularly on the right. Isolated low-voltage spikes or sharp waves mix with the background activity. Panel **B** confirms these features. Additionally, the EEG shows brief, paroxysmal, pure electrical events of fast, alpha-like anachronistic activity that predominantly or exclusively occur in the right centro-temporo-parietal region. Panel **C** confirms this anomaly and shows diffuse depressed activity.

Initial treatment with valproic acid was only partially effective. Adding levetiracetam at 40 -50 mg/kg twice daily resulted in better control of ictal events. Cranial computed tomography (CT) revealed severe cerebellar vermis hypoplasia, enlarged lateral ventricles, and reduced density of the periventricular hemispheric white matter (WM). A 1.5 Tesla magnetic resonance imaging (MRI) scanner was used to obtain T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) images of the brain. Extensive fronto-insulo-temporo-parietal polymicrogyria was present on the right, accompanied by short tracts of apparent pachygyria. Focal polymicrogyria was present at the insulo-parietal junction on the left. The hemispheric WM was hypoplastic and poorly myelinated. Both thalami were severely hypoplastic. Overall, the basal ganglia showed moderate-to-severe hypoplasia, though there was no clear evidence of abnormal signals. The lateral ventricles were dilated, as were the third and fourth ventricles, and the frontal horns were square. The CC was hypoplastic and extremely thin. Additionally, voluminous arachnoid cysts were present on both temporal poles. The hippocampi were severely hypoplastic and retained abnormal fetal morphology, particularly on the left side. Notably, the right parahippocampus and subiculum exhibited an abnormal increase in small cortical folds. The entire brainstem was diffusely hypoplastic, and the prepontine spaces were significantly dilated. The cerebellar hemispheres appeared normal, though the vermis was moderately

hypoplastic (Figure 2). The infant died at home at 15 months of age. The parents did not consent to an autopsy.

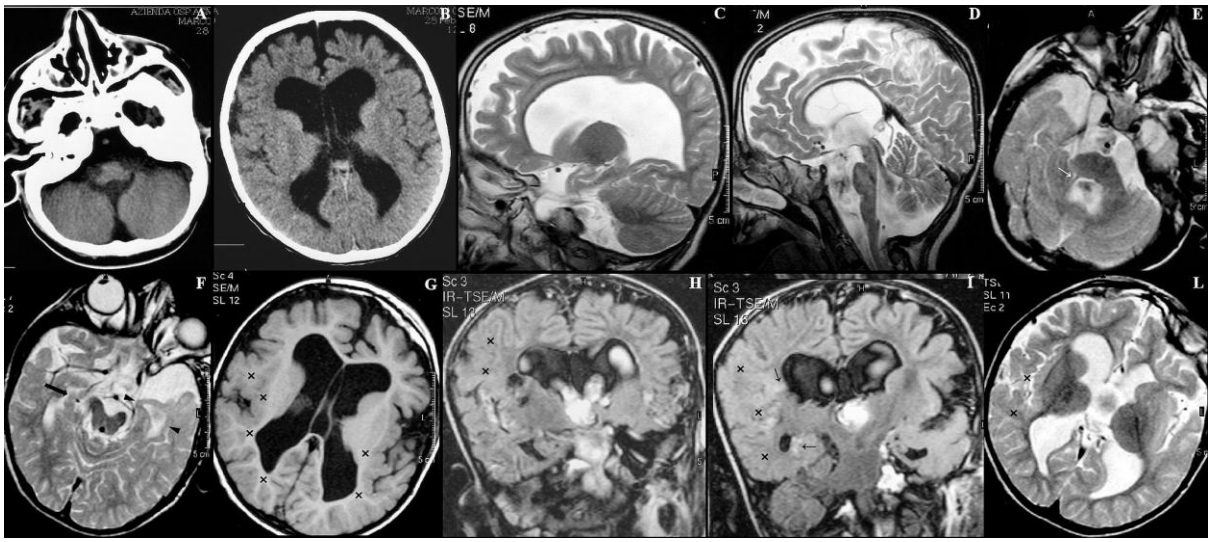


Figure 2: Neuroimaging Findings

Legend: A brain CT scan showed dilatation of the ventricular system, particularly the frontal horns; moderate hypoplasia of the basal ganglia; and thinning of the CC. (Panels **A** and **B**). The brain MRI revealed the following: diffuse and severe brain underdevelopment; abnormal and widespread ventricular dilation; whole CC hypoplasia; marked brainstem hypoplasia; a normal cerebellum with mild vermis hypoplasia (Panels **C** and **D**; sagittal T2); hypoplasia of the pons and pontocerebellar peduncle (*small white arrow),* with abnormally dilated prepontine spaces (Panel **E**)**;** bilateral polar temporal cysts (Panels **E** and **F**, axial T2); persistence of fetal developmental morphology of both hippocampi (*small dark arrowhead on the left*), with apparent microgyric transformation of the subiculum and Ammon's horn (*dark arrow on the right*) (Panel **F**, axial T2; extensive cortical fronto-temporo-parietal PMG on the right side, with more limited left temporo-parietal PMG (*small dark cross symbols*) (Panel **G**, axial FLAIR T1; Panel **H** and **I**, coronal FLAIR SE; Panel **L**, axial T2); small, abnormal periventricular signals likely representing ischemic injury (*small, thin white arrows*) (Panel **I**, coronal FLAIR SE).

DISCUSSION

Most patients with PKS experience severe neurological complications, including epilepsy. Generalized, partial, and myoclonic seizures have been reported[8-10], yet a few patients do not have epilepsy[1-3]. Accordingly, EEG findings are heterogeneous. Neuroimaging is essential for detecting brain anomalies. The first MRI-based descriptions documented delayed myelination, lateral ventricular dilation, asymmetric bilateral fronto-parietal atrophy, and abnormal cortical gyration. Recent neuroimaging studies have described these abnormalities in detail[6-8]. In particular, Poulton et al.[6] studied two patients, and Fetta et al.[8] recruited a cohort of thirty-one patients. The extended study by Fetta et al.[8] identified the following abnormalities: brain atrophy with enlarged sulci, ventricular dilatation (particularly in the

temporal horns), and malformations of cortical development (MCD). Specifically, fourteen patients showed bilateral perisylvian PMG. Two-thirds of the patients had CC hypoplasia, and a few showed periventricular leukomalacia. The brainstem and cerebellum appeared normal. Interestingly, neuroimaging studies of older individuals revealed widespread lesion signals without cortical dysplasia[5]. Rodríguez conducted the only comprehensive neuropathological study of PKS, clearly describing dilated cerebral ventricles, bilateral PMG, heterotopic WM in the meninges, and abnormal olivary and dentate nuclei morphology[4]. The patient described here had a classic form of PKS, including the rarely described cardiac malformations. The patient also experienced sudden episodes of respiratory arrest or episodic hyperventilation, which were occasionally accompanied by uncommon, fast EEG degraded rhythms. Interestingly, Blyth et al.[2] also reported this autonomic involvement, observing the phenomenon in a cohort of 22 British patients. The patient's extensive cortical malformation of PMG in the right fronto-temporo-parietal and insular cortex, along with a smaller PMG in the left fronto-parietal region, confirms the previously reported asymmetry of the malformation[6-8]. This patient also presented with severe and previously unreported thalamic hypoplasia, bilateral temporal arachnoid cysts, and severe brainstem hypoplasia. This included hypoplasia of the brachium pontis and the middle pontocerebellar peduncle, particularly on the left. There was also mild-to-moderate hypoplasia of the cerebellar vermis. Abnormalities of the pons and middle cerebellar peduncles have only been reported by Barkovich et al.[7] in one other child, albeit with slight differences. Notably, both hippocampi exhibited abnormal persistence of fetal morphology, particularly on the left side. Additionally, the excessively small cortical folding in the right parahippocampal and subicular cortices was clearly abnormal. These findings suggest abnormal development rather than injury. The same applies to global brainstem hypoplasia. Furthermore, widespread brain atrophy appears to primarily result from underdevelopment rather than from long-term cerebral hypoperfusion caused by cardiac insufficiency. Neuroimages of peri – paraventricular signal abnormalities have usually been described as periventricular leukomalacia (PVL). PVL is the most common type of brain damage in hypoxic-ischemic preterm neonates. Our case was a term newborn, as were most of the patients with PKS previously reported. In contrast, focal ischemic lesions are often found in the brains of newborns with severe cardiac malformations and are generally located far from the ventricular wall. Therefore, those observed in our case are likely ischemic lesions secondary to cardiac insufficiency rather than true PVL. The same may be true for other previously reported PKS cases.

Conflict of interest disclosure. The authors declare that there is no conflict of interest to disclose

Funding statement. The authors declare that the study received no funding.

Authorship contribution. The authors contributed equally to this work.

Patient consent. Consent was obtained verbally from the parents during the observation period. This case is historical material from our archives, and we can no longer contact the family. Patient anonymity is maintained.

REFERENCES

1. Schaefer GB, Jochar A, Muneer R, Sanger WG. Clinical variability of tetrasomy 12p. Clin Genet 1997; 51: 102-108
2. Blyth M, Maloney V, Beal S, et al. Pallyster-Killian syndrome: a study of 22 British patients. J Med Genet 2015; 52: 454-464. https://doi.org/10.1136/jmedgenet-2014-102877
3. Karaman B, Kayserili H, Ghanbari A, et al. Pallister-Killian syndrome: clinical, cytogenetic and molecular findings in 15 cases. Molecular Cytogenetics 2018; 11: 45. https://doi.org/10.1186/s13039-018-0395-z
4. Rodriguez JI, Garcia I, Alvarez J, Delicado A, Palacios J. Lethal Pallister-Killian Syndrome: Phenotypic Similarity With Fryns Syndrome. Am J Med Genet 1994: 53: 176-181. https://doi.org/10.1002/ajmg.1320530211
5. Saito Y, Masuko K, Kaneko K, et al. Brain MRI findings of older patients with Pallister-Killian syndrome. Brain Dev 2006; 28: 34-38. https://doi.org/10.1016/j.braindev.2005.04.004
6. Poulton C, Baynam G, Yates C, et al. A review of structural brain abnormalities in Pallister-Killian syndrome. Mol Genet Genomic Med 2018; 6: 92-98. https://doi.org/10.1002/mgg3.351
7. Barkovich EJ, Lateef TM, Whitehead MT. Neuroimaging findings in Pallister-Killian syndrome. Neuroradiol J 2018; 31: 403-411. https://doi.org/10.1177/1971400917744798
8. Fetta A, Toni F, Pettenuzzo I, et al. Structural brain abnormalities in Pallister-Killian syndrome: a neuroimaging study of 31 children. Orphanet Journal of Rare Diseases 2024; 19: 107. https://doi.org/10.1186/s13023-024-03065-5
9. Filloux FM, Carey JC, Krantz ID, Ekstrand JJ, Candee MS. Occurrence and clinical features of epileptic and non-epileptic paraxysmal events in five children with Pallister-Killian syndrome. Eur J Med Genet 2012; 55: 367-373. https://doi.org/10.1016/j.ejmg.2012.01.006
10. Giordano L, Viri M, Borgatti R, et al. Seizures and EEG patterns in Pallister-Killian syndrome: 13 new Italian patients. Eur J Paediatr Neurol 2012; 16: 636-641. https://doi.org/10.1016/j.ejpn.2012.03.003