Research Article / Araştırma Makalesi

Neuroradiologic Findings Associated with Tuberous Sclerosis Complex: A Comprehensive Analysis of 24 Cases

Tüberoskleroz Kompleksi ile İlişkili Nöroradyolojik Bulgular: 24 Vakanın Kapsamlı Analizi

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Abstract

Background: This study aims to comprehensively analyze the radiological findings of 24 TSC patients to determine the radiological profile of the disease and potential diagnostic and therapeutic implications.
Materials and Methods: This retrospective study was approved by the Ethics Committee of Harran University. A total of 24 genetically diagnosed TSC patients who underwent brain MRI between 2020-2024 were included. Imaging was performed using a 3 Tesla MRI scanner, employing T2 IDEAL, 3D T1 VIBRANT, and contrast-enhanced T1 sequences. Data were analyzed using IBM SPSS Statistics software, focusing on demographic characteristics and radiological findings.
Results: The study included 24 TSC patients (14 males, 10 females) with a mean age of 8.43±10.24 years (range: 1-46 years). Cortical/subcortical tubers and subependymal hamartomas were identified in all patients (100%). Radial bands were observed in 83.3%, infarctions in 50%, and corpus callosum dysgenesis in 41.6%. Subependymal giant cell astrocytoma (SGCA) was present in 12.5% of cases, while arachnoid cysts were noted in 20.8%.
Conclusions: This study revealed a higher CNS involvement rate in TSC patients compared to the literature, with a higher prevalence among male patients. These findings emphasize the importance of detailed radiological and clinical evaluations in understanding the disease. Changes in radiological findings with age and disease progression can contribute to optimizing treatment protocols.

Keywords: Tuberous Sclerosis Complex, Central Nervous System Involvement, Radiological Findings

Öz

Amaç: Bu çalışmanın amacı, 24 TSC hastasının radyolojik bulgularını detaylı bir şekilde inceleyerek hastalığın radyolojik profilini ve klinik sonuçlarla olan ilişkisini ortaya koymaktır.
Materyal ve Metod: Bu retrospektif çalışma, Harran Üniversitesi Etik Kurulu tarafından onaylanmıştır. Çalışma kapsamında 2020-2024 yılları arasında hastanemizde genetik olarak TSC tanısı konmuş ve beyin MR görüntülemesi yapılmış 24 hasta incelenmiştir. Görüntüleme, 3 Tesla MR cihazı ile gerçekleştirildi. T2 IDEAL, 3D T1 VIBRANT ve kontrastlı T1 sekansları kullanılarak radyolojik bulgular değerlendirildi. Elde edilen veriler, IBM SPSS Statistics yazılımı ile demografik özellikler ve radyolojik bulgular açısından analiz edilmiştir.
Bulgular: Çalışmaya 24 TSC hastası (14 erkek, 10 kadın) dahil edilmiştir. Hastaların yaş ortalaması 8,43±10,24 yıl olup, yaşlar 1 ile 46 arasında değişmektedir. Tüm hastalarda kortikal/subkortikal tüberler ve subependimal hamartomlar saptanmıştır (%100). Radial band %83,3, infarkt %50, korpus kallozum disgenezi %41,6 oranında tespit edilmiştir. Ayrıca, 3 hastada subependimal dev hücreli astrositom (SGCA) (%12,5) ve 5 hastada araknoid kist (%20,8) görülmüştür.
Sonuç: Çalışmamızda TSC'nin CNS tutulum oranının literatürden yüksek olduğu ve özellikle erkek hastalarda daha sık görüldüğü tespit edilmiştir. Bu bulgular, TSC'nin radyolojik ve klinik özelliklerinin daha iyi anlaşılması ve hastalık yönetimi için önem taşımaktadır. Radyolojik bulguların yaş ve hastalık süresi ile değişimi, tedavi protokollerinin optimize edilmesine katkı sağlayabilir.

Anahtar Kelimeler: Tübüloz Skleroz Kompleksi, Merkezi Sinir Sistemi Tutulumu, Radyolojik Bulgular

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Introduction

Tuberous sclerosis (TSC) is a genetic disease caused by mutations in the TSC1 and TSC2 genes and characterized by the formation of benign tumors throughout the body, including the brain, skin, kidneys, heart, lungs, and eyes. TSC is usually diagnosed in early childhood, and affected individuals may present with developmental delay, skin manifestations, or seizures. The diagnosis of the disease may be made earlier or later depending on various clinical findings (1,2). Comprehensive analysis of radiological findings plays a critical role in the early diagnosis of TSC. Cortical tubers are lesions that can cause epileptic seizures, especially in childhood, and can affect neuropsychiatric development. Subependymal giant cell astrocytomas (SGCA), commonly located in the brain ventricles, can lead to hydrocephalus and elevated intracranial pressure due to their progressive growth. Findings such as radial bands and corpus callosum dysgenesis reflect abnormalities in brain development and are often associated with cognitive dysfunction. Therefore, a thorough analysis of radiological findings serves as a cornerstone for disease management and planning targeted intervention strategies (3,4).

In this study, we aim to examine in depth the radiological findings of 24 patients diagnosed with TSC and to reveal the radiological profile of the disease and its relationship with clinical outcomes. The patients we examined were selected from various age groups and different clinical stages. This diversity will help us understand how the radiological findings of TSC may change with age and disease duration. We also aim to the MRI technique was performed with a 3 Tesla MRI scanner (GE, Milwaukee, Wisconsin, USA) for pituitary imaging on tribute to the development of more effective treatment protocols by evaluating the effects of these findings on disease progression and response to treatment (5,6).

This study aims to provide a better understanding and management of the disease by comprehensively analyzing the radiological findings of TSC. The information obtained can be used in early diagnosis, monitoring and optimization of treatment strategies for TSC. When compared with the information available in the literature, the findings of our study can make significant contributions to clinical and radiological practices related to TSC and fill the gaps in this area. In light of this information, necessary steps can be taken to better understand the complex nature of TSC and develop effective interventions (6,7).

Materials and Methods

This retrospective study was approved by the local ethics committee of Harran University (approval number: HRU/24.16.34). The patients consisted of 24 patients who underwent MRI in our hospital's Radiology department between 2020-2024 and were genetically diagnosed.

MRI scans were acquired using a 3 Tesla scanner (GE, Milwaukee, Wisconsin, USA), optimized for cerebral imaging. After acquiring localization and calibration images in three planes, T2 IDEAL (TR: 9300 ms, TE: 102 ms, FOV: 380 x 380 mm, Matrix: 352 x 288, Slice Thickness: 1 mm), 3D T1 VIBRANT (TR: 5.4 ms, TE: 2.6 ms, FOV: 380 x 380 mm, Matrix: 416 x 320, Slice Thickness: 1.4 mm) and fat-suppressed T2 (TR: 7326 ms, TE: 85 ms, FOV: 380 x 380 mm, Matrix: 224 x 224, Slice Thickness: 1 mm) images were obtained. Radiopathological findings on brain MRI images were determined by two radiologists with 5 and 10 years of neuroradiological experience by consensus.

The data analysis process was carried out using IBM SPSS Statistics software. The obtained data set was evaluated in terms of demographic characteristics, radiological findings frequencies and other relevant clinical parameters. Statistical analyses include frequency distributions and table.

Results

The study included 24 TSC patients, of which 14 (58.3%) were male and 10 (41.7%) were female. The mean age of the patients was 8.43±10.24 years. The age range spanned from a minimum of 1 year to a maximum of 46 years. All examined patients demonstrated CNS involvement. The most common findings were cortical tubers and subependymal nodules. In addition, 50% of patients were found to have brain infarct findings, which was higher than the general population. This discrepancy might stem from our patient cohort, which included individuals with more severe clinical presentations.

In this study, all of our female and male patients diagnosed with TSC had cortical/subcortical tubers and subependymal hamartomas. SGCA was observed in 3 of our patients (12.5%). Infarction was observed in 12 of our patients (50%). Corpus callosum dysgenesis was observed in 10 of our patients (41.6%). Arachnoid cyst was observed in 5 of our patients (20.8%). Cerebellar atrophy, venous anomaly and hydrocephalus were observed in only one patient (4.16%) (Table 1).

Table 1. Distribution of Neuroradiological Findings in TSC Patients (n=24)

Neuroradiological Findings	**n**	**%**
Cortical/Subcortical Tubers and Subependymal Hamartomas	24	100.0
Radial Bands	20	83.3
Infarct	12	50.00
Corpus Callosum Dysgenesis	10	41.6
SGCA	3	12,5
Arachnoid Cyst	5	20,8
Cerebellar Atrophy	1	4,16
Venous Anomaly	1	4,16
Hydrocephalus	1	4,16

SGCA: Subependymal giant cell astrocytoma

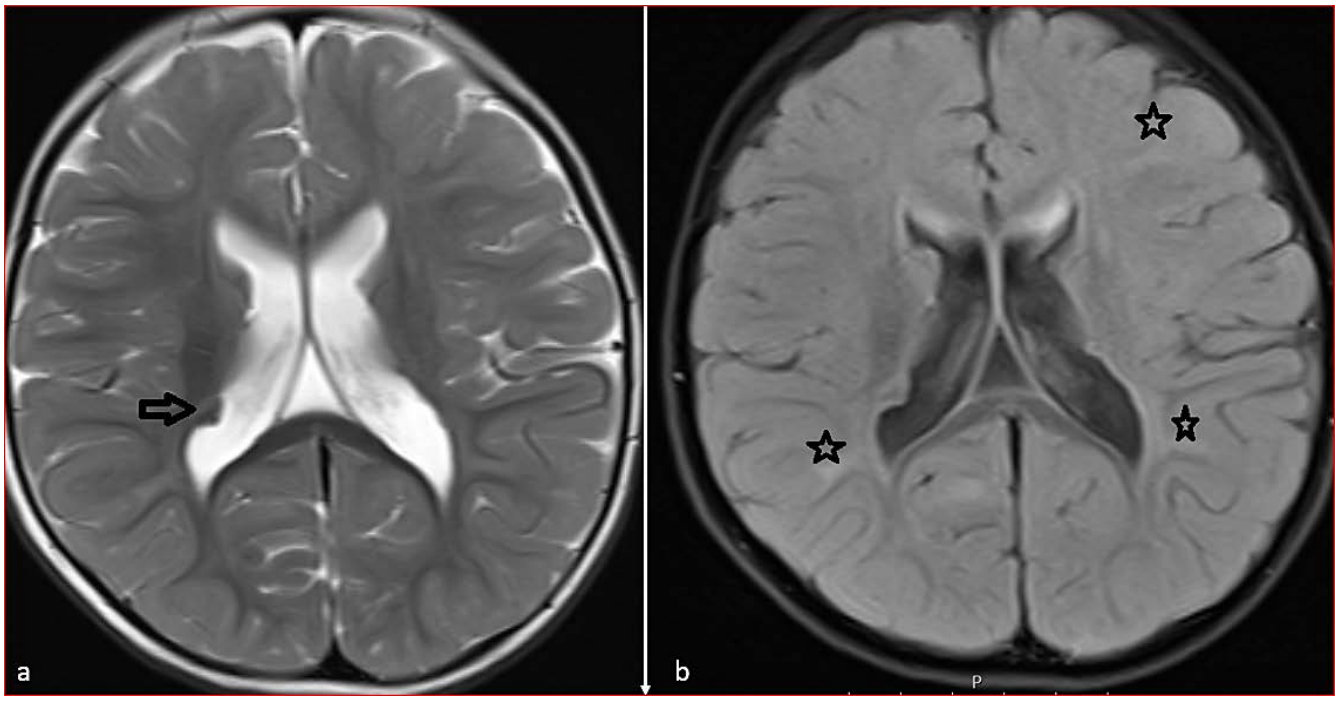

Figure 1. Brain MRI images of a 2-year-old male patient diagnosed with tuberous sclerosis. On T2W axial image, isointense nodular appearance compatible with subependymal nodule on the right lateral ventricular wall is remarkable arrow . On T2 FLAIR W axial image, patchy hyperintense areas consistent with hamartoma in the subcortical areas of bilateral cerebral hemispheres are noted (*).

Discussion

CNS involvement associated with TSC has been reported in the literature at widely varying rates. In general, CNS involvement rates vary widely depending on the genetic and phenotypic diversity of the disease. Studies in the literature show the presence of cortical tubers in 80% to 90% of TSC patients, while subependymal nodules and white matter abnormalities are seen at lower rates (8).

In our study, CNS involvement was observed in all 24 patients, indicating one of the highest rates in the literature (9). This high rate suggests that our study may have focused on a specific subgroup or that particularly severe cases may have been examined. In addition, a gender-based analysis was performed in our study and it was examined whether the findings differed according to gender. Although it is stated in the literature that TSC is seen at similar rates in both genders, it is emphasized that some clinical features may vary according to gender. The findings obtained in our study showed that CNS involvement is more common in male patients. Although this result is consistent with some studies in the literature, more detailed genetic and molecular studies are required to understand the reason for this difference (10). Since studies on the role of gender in TSC are generally conducted on a limited number of patients, it is important to support them with large-scale epidemiological studies.

It is known that CNS involvement associated with TSC can directly affect the course of the disease and treatment responses. In this context, a better understanding of CNS involvement rates and gender differences may provide important strategic information in the management of the disease. This information is crucial for early diagnosis and intervention, facilitating the development of personalized treatment approaches. We can compare the findings of CNS infarction in the literature with the results of our own study. In the literature, the prevalence of silent brain infarction (SBI) was determined as 20.2% in Asian countries, 12.4% in Europe and 15.6% in the USA. These studies revealed that age is the main determinant in the prevalence of SBI (11,12).

Signs of infarction were observed in 15 patients, reflecting a higher prevalence compared to general population rates reported in the literature. This difference may be due to differences in the selection of our study population. For example, the selection of patients with more severe symptoms or certain demographic characteristics may affect these rates. The literature also indicates that risk factors for ischemic stroke (IS) in young patients are similar to those in older populations; modifiable risk factors such as hypertension, smoking, low physical activity and hyperlipidemia are associated with an increased incidence of stroke among young people (13,14). When the distribution of patients with infarction in our study was examined according to gender, it was observed that gender does not have a significant effect on risk in the literature; however, the role of gender may become apparent in combination with certain risk factors (e.g. smoking and hypertension) (15).

This study has some limitations. First of all, the limited number of cases limits the generalizability of the findings. In addition, the lack of detailed clinical data such as seizure history

in the patients made it difficult to fully evaluate the relationship between central nervous system involvement and neurological symptoms. The lack of data on other organ involvement in the study prevented a more comprehensive analysis of the multisystemic nature of the disease. These limitations indicate that the results obtained should be supported in larger patient groups and with multidisciplinary approaches.

In conclusion, the effects of TSC on the central nervous system are an important source of morbidity in terms of neurological and neurodevelopmental disorders. Our study emphasizes the importance of clinical and radiological evaluations in TSC patients with prominent CNS involvement.

Ethical Approval: *This retrospective study was approved by the local ethics committee of Harran University (approval number: HRU/24.16.34).*

Author Contributions:
Concept: M.D.
Literature Review: M.D., M.S.B
Design : M.D.
Data acquisition: M.S.B
Analysis and interpretation: M.D., Ö.Ö.
Writing manuscript: M.D., MS.B.
Critical revision of manuscript: Ö.Ö.

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