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Evaluation of children with neurocutaneous diseases: A five-year clinical experience

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Abstract

Neurocutaneous diseases represent a broad group of disorders that primarily involve the central and peripheral nervous systems and the skin. These conditions are often associated with dysmorphic facial features and possible visceral organ involvement, and they exhibit diverse genetic, clinical, and pathological characteristics. This study aimed to retrospectively evaluate the clinical and laboratory findings of patients diagnosed with neurocutaneous diseases and compare them with the existing literature. A total of 133 patients who presented to the pediatric neurology outpatient clinic of our hospital were included. Of these, 65 (48.9%) were female and 68 (51.1%) were male, with a mean age of 11.12 ± 5.26 years. The most common diagnoses were neurofibromatosis type 1 (NF-1) in 97 patients (72.9%) and tuberous sclerosis complex (TSC) in 32 patients (24.1%). In addition, two patients (1.5%) were diagnosed with incontinentia pigmenti, one (0.8%) with Sturge-Weber syndrome, and one (0.8%) with epidermal nevus syndrome. The most frequent presenting symptom was skin lesions (32.3%), followed by seizures (24%). On physical examination, all patients exhibited dermatological findings. Among NF-1 patients, 49 were male and 48 female, with a mean age of 12.1 ± 4.96 years. In the TSC group, there was an equal gender distribution, with a mean age of 8.68 ± 5.3 years. Our findings highlight the predominance of NF-1 and TSC in pediatric practice and underscore the importance of early dermatological clues in diagnosis. Multidisciplinary management remains crucial due to the progressive nature of these conditions.

Keywords: Neurocutaneous syndromes, neurofibromatosis type 1, tuberous sclerosis complex, incontinentia pigmenti, sturge-weber syndrome, epidermal nevus syndrome

Introduction

Neurocutaneous syndromes, also referred to as phakomatoses, arise from abnormalities in the formation, migration, or differentiation of the neural crest. This impacts the development of the neuroectoderm, consequently affecting tissues derived from it, such as the skin, central and peripheral nervous systems, and the eye [1]. A common characteristic of neurocutaneous syndromes is the predisposition to tumor formation, as their genetic basis often includes mutations in tumor suppressor genes or genes related to cell growth and proliferation [2]. Many of these conditions involve an understood genetic phenomenon, although spontaneous mutations can occur. These conditions also exist on a wide spectrum of phenotypes and often have multi-system involvement [1]. A challenge that occurs with diagnosing these conditions is that certain symptoms present as age progresses, further complicating

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the diagnosis. A significant portion of this group is comprised of tuberous sclerosis complex (TSC), neurofibromatosis (NF), and Sturge-Weber syndrome (SWS).

Early diagnosis during childhood plays a pivotal role in improving long-term outcomes in patients with neurocutaneous diseases. Dermatological and neurological manifestations often appear in infancy or early childhood, but their subtle nature may delay diagnosis until more severe systemic complications—such as epilepsy, intellectual disability, or organ involvement—become apparent [3,4]. Recognizing characteristic skin findings and performing early imaging and genetic evaluations allow timely intervention, multidisciplinary monitoring, and prevention of irreversible neurological or systemic damage [5]. Therefore, raising awareness of early diagnostic clues among pediatricians and neurologists is essential to reduce disease-related morbidity and improve quality of life.

The aim of this study is to document and describe the data that can be obtained regarding the recognition of neurocutaneous diseases in childhood and the potential issues that may arise during follow-up. In this group of diseases, which frequently present to outpatient clinics and are sometimes detected incidentally during examinations, it is possible to recognize and prevent potential systemic issues in advance. While clinical diagnostic criteria are clearly defined, genetic analyses can be challenging in these patients. Therefore, the goal is to review our clinical experiences to enhance awareness of the disease.

Material and Methods

Between January 2010 and December 2015, 133 patients who presented to the pediatric neurology clinic of our hospital and were diagnosed with neurocutaneous syndromes were evaluated retrospectively.

The study group was established based on Q85-Q85.0-Q85.1-Q85.8-Q85.9-Q82.3 and D18.0 ICD codes from the hospital medical database, and the relevant data were included. These codes correspond to the following disorders:

Q85 – Phakomatoses, not elsewhere classified (neurocutaneous syndromes); Q85.0 – Neurofibromatosis (nonmalignant); Q85.1 – Tuberous sclerosis; Q85.8 – Other phakomatoses, not elsewhere classified; Q85.9 – Phakomatosis, unspecified; Q82.3 – Incontinentia pigmenti; D18.0 – Hemangioma, any site (used for vascular lesions associated with neurocutaneous disorders).

The patients' ages, age of onset of complaints, sex, presenting complaints, familial relationships, similar family histories, detailed ophthalmological and dermatological examinations, echocardiography, renal ultrasonography, neuroimaging, electroencephalography (EEG), neurological and systemic examination findings, cognitive assessments, types of seizures, anti-seizure medication and follow-up durations were evaluated retrospectively.

The criteria established at the 1987 National Institutes of Health (NIH) Conference (Archives of Neurology 1988) were used for the diagnosis of neurofibromatosis type 1 (NF-1) [6]. For the diagnosis of TSC, the clinically revised Roach diagnostic criteria from 1998 were utilized [7]. The diagnoses were re-evaluated according to the diagnostic criteria from 2012 [4].

Ethics

Ethics Committee Approval: The institutional review board approved the study design and protocols University of Health Sciences, Dr. Sami Ulus Maternity and Children's Health and Disease Training and Research Hospital (No: 73799008, Date: 16 June 2016). The study was conducted in accordance with the principles of the Declaration of Helsinki. Consent was obtained from families for patient photographs.

Statistical Analysis

The data obtained in the study were analyzed using the Statistical Package for Social Sciences (SPSS for Windows 22.0, Chicago, USA). Categorical measurements were presented as frequencies and percentages, while continuous measurements were expressed as means and standard deviations. Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test, and continuous variables were compared using the independent samples t-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. A p-value of <0.05 was considered statistically significant.

Results

Among the patients, 97 (72.9%) were diagnosed with NF-1, 32 (24.1%) with tuberous sclerosis complex (TSC), two (1.5%) with incontinentia pigmenti, one (0.8%) with Sturge-Weber syndrome, and one (0.8%) with epidermal nevus syndrome. The characteristics and clinical features of the 133 patients included in the study are presented in Table 1.

43 (32.3%) of the patients presented with complaints of spots on their bodies, 32 (24%) came with seizure complaints, nine (6.8%) were referred from another center for further evaluation and treatment, eight (6.3%) sought to obtain a committee report, seven (5.3%) came due to developmental delays, two (1.5%) due to the presence of a mass in the heart detected in fetal ultrasound and 32 (23.8%) came for other reasons.

Skin findings were present in all patients (Figure 1). The most common lesions included café-au-lait macules in patients with NF-1 and hypopigmented macules in those with TSC. Other characteristic findings observed across the cohort were adenoma sebaceum, periungual fibromas, and shagreen patches in TSC patients, and axillary freckling or neurofibromas in NF-1 cases. In addition, five patients exhibited uncommon skin manifestations: two had hyperpigmented macules, one had a port-wine stain, one had a congenital giant nevus, and one had a large nevus spilus with vitiligo.

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Table 1. Characteristics and clinical manifestations of the patients

Variable	Value
Sex, n (%)	
Male	68 (51.1%)
Female	65 (48.9%)
Age at admission (year)	6.25 ± 4.73
Current age (year)	11.12 ± 5.26
Follow-up period (year)	3.08 ± 2.72
Diagnosis, n (%)	
Neurofibromatosis type 1	97 (72.9%)
Tuberous sclerosis complex	32 (24.1%)
Incontinentia pigmenti	2 (1.5%)
SturgeWeber syndrome	1 (0.8%)
Epidermal nevus syndrome	1 (0.8%)
Family history, n (%)	
Positive	71 (53.4%)
Negative	56 (42.1%)
Unknown	6 (4.5%)
Parental consanguinity, n (%)	
Positive	27 (20.4%)
Negative	76 (57.1%)
Unknown	30 (22.5%)
Ophthalmological findings, n (%)	
Lisch nodules	46 (34.5%)
Retinal hamartomas	6 (4.5%)
Other (e.g., iris mottling, optic disc pallor, total atrophy)	8 (6%)
No finding	73 (55%)
Neurodevelopmental disorders, n (%)	
Intellectual disability	31 (23.3%)
Learning disability	4 (3%)
Autism and intellectual disability	3 (2.2%)
Attention deficit hyperactivity disorder	2 (1.5%)
Autism	1 (0.8%)
No finding	92 (69.2%)
Seizure history, n (%)	
Positive	47 (35.3%)
Infantile spasm	13 (27.6%)
Generalized tonic clonic	11 (23.5%)
Focal seizures	18 (38.3%)
Dialeptic seizures	5 (10.6%)
Negative	86 (64.7%)
Treatment, n (%)	
Positive	45 (33.1%)
Single antiseizure medication	25 (55.5%)
Dual antiseizure medication	14 (31.2%)
≥3 antiseizure medication	5 (11.1%)
Everolimus	1 (2.2%)
Negative	88 (66.9%)

Data are presented as mean ± SD or n (%)

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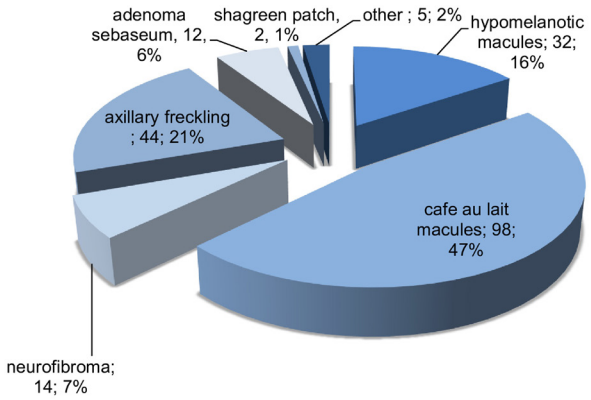

Figure 1. Distribution of skin findings

The imaging findings of the patients are presented in Table 2.

When looking at the systemic findings accompanying neurocutaneous diseases, 13 patients had short stature, four patients had growth hormone deficiency, seven patients had obesity, three patients had hypertension, five patients had microcephaly, two patients had macrocephaly, three patients had familial Mediterranean fever, three patients had hypothyroidism, two patients had prematurity, and two patients had a history of meningitis.

NF-1 Cases

Of the patients diagnosed with NF-1, 40 (41.3%) presented with skin spots, nine (9.3%) with seizures, nine (9.3%) for a disability report, nine (9.3%) were referred from another center for further evaluation and treatment, eight (8.2%) came due to developmental delays and 22 (22.6%) for other reasons. All of our patients with a diagnosis of NF-1 had cafe au lait macules as a skin finding. Axillary freckling was present in 44 (45.3%) patients, and neurofibromas were found in 14 (14.4%) patients (Figure 2). The other clinical characteristics and findings of the NF-1 patients are presented in Table 3. A family history was present in 68% of NF-1 patients, while parental consanguinity was detected in 16.5%. Most patients (83.5%) had no seizure history, consistent with the relatively lower prevalence of epilepsy in NF-1 compared with other neurocutaneous disorders.

Table 2. Imaging results of the patients

Variable	Value
Cranial magnetic resonance imaging, n (%)	
Hamartoma/Unidentified Bright Objects (UBOs)	44 (26%)
Cortical tuber	24 (14%)
Astrocytoma/subependymal nodule	21 (12%)
Optic glioma	13 (8%)
Calcification	38 (23%)
Normal	28 (17%)
Renal ultrasonography, n (%)	
Renal angiomyolipoma	9 (6.8%)
Normal	95 (71.4%)
Other (e.g., renal cysts, caliceal ectasia)	29 (21.8%)
Echocardiography, n (%)	
Cardiac rhabdomyoma	20 (15%)
Normal	32 (24.1%)
Other (e.g., mitral insufficiency, aortic insufficiency)	14 (10.5%)
Unknown	67 (50.4%)
Electroencephalography, n (%)	
Focal seizure	47 (35.3%)
Multifocal seizure	8 (6%)
Generalized seizure	4 (3%)
Hypsarrhythmia pattern	8 (6%)
Normal	66 (49.7%)

Data are expressed as n (%)

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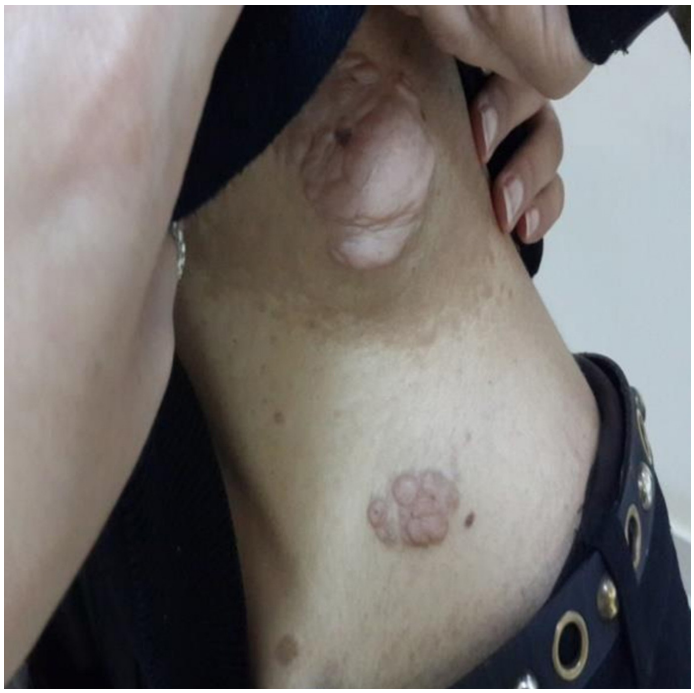

Figure 2. Neurofibroma

The imaging findings of the NF-1 patients are presented in Table 4. Cranial magnetic resonance imaging (MRI) revealed hamartomatous lesions or unidentified bright objects (UBOs) in 63% of patients with NF-1. Optic gliomas were identified in 12% of cases.

TSC Cases

Of the patients diagnosed with TSC, 22 (71%) presented with seizures, two (6.5%) had a mass in the heart detected on fetal ultrasound, and seven (22.5%) came for other reasons. All of our patients with a diagnosis of TSC had hypopigmented macules. Two of these were detected using a Wood's lamp. Adenoma sebaceum was present in 12 (37.5%) patients, periungual fibromas in two (6.2%) patients, and shagreen patches in two (6.2%) patients. The other clinical characteristics and findings of the TSC patients are presented in Table 3. In contrast, only 15.6% of TSC patients had a family history of the disease, and nearly all (93.8%) experienced seizures during follow-up. This clear difference between NF-1 and TSC groups reflects their distinct genetic inheritance patterns and clinical presentations.

The imaging findings of the TSC patients are presented in Table 4. In patients with TSC, cortical tubers and subependymal nodules were the most frequent imaging findings. Renal angiomyolipomas were present in 34.4% of cases.

Table 3. Comparative clinical characteristics and findings in NF-1 and TSC patients

Variable	NF-1	TSC	p
Sex, n (%)			
Male	49 (50.5%)		1.000
Female	48 (49.5%)		
Age at admission (years)	7.4 ± 4.42	3.5 ± 4.31	<0.001
Current age (years)	12.1 ± 4.96	8.68 ± 5.3	0.002
Family history, n (%)			
Positive	66 (68%)	5 (15.6%)	<0.001
Negative	26 (26.8%)	27 (84.4%)	<0.001
Unknown	5 (5.2%)	-	-
Parental consanguinity, n (%)			
Positive	16 (16.5%)	8 (25%)	0.30
Negative	55 (56.7%)	20 (62.5%)	0.711
Unknown	26 (26.8%)	4 (12.5%)	-
Ophthalmological findings, n (%)			
Lisch nodules	46 (47.5%)	-	-
Retinal hamartomas	-	6 (18.7%)	0.15
Other (e.g., iris mottling, optic disc pallor, total atrophy)	8 (8.2%)	2 (6.3%)	0.07
No finding	43 (44.3%)	24 (75%)	0.005
Seizure history, n (%)			
Positive	16 (16.5%)	30 (93.8%)	<0.001
Febrile convulsion	-	4 (13.3%)	-
Infantile spasm	3 (18.8%)	8 (26.6%)	<0.001
Generalized tonic clonic	7 (43.7%)	2 (6.7%)	1.000
Focal seizures	4 (25%)	12 (40%)	<0.001
Dialeptic seizures	2 (12.5%)	3 (10%)	0.183
Atonic	-	1 (3.4%)	-
Negative	81 (83.5%)	2 (6.2%)	<0.001

Data are presented as mean ± SD or n (%). Comparisons between groups were performed using the independent samples t-test or Chi-square test, as appropriate. $p<0.05$ was considered statistically significant. NF-1, neurofibromatosis type 1; TSC, tuberous sclerosis complex

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Table 4. Imaging results of the patients of NF-1 and TSC patients

Variable	NF-1	TSC	p
Cranial magnetic resonance imaging, n (%)			
Hamartoma/Unidentified Bright Objects (UBOs)	68 (63%)	4 (6.8%)	<0.001
Cortical tuber	-	24 (40.7%)	-
Astrocytoma/subependymal nodule	3 (2.8%)	21 (35.6%)	<0.001
Optic glioma	13 (12%)	-	-
Calcification	-	8 (13.5%)	-
Normal	24 (22.2%)	2 (3.4%)	<0.05
Renal ultrasonography, n (%)			
Renal angiomyolipoma	-	11 (34.4%)	-
Normal	73 (75.2%)	13 (40.6%)	0.001
Other (e.g., renal cysts, caliceal ectasia)	24 (24.8%)	8 (25%)	1.000
Echocardiography, n (%)			
Cardiac rhabdomyoma	-	20 (62.5%)	-
Normal	22 (22.7%)	9 (28.1%)	0.699
Other (e.g., mitral insufficiency, aortic insufficiency)	10 (10.3%)	3 (9.4%)	1.000
Unknown	65 (67%)	-	-
Electroencephalography, n (%)			
Focal seizure	23 (23.7%)	20 (62.5%)	<0.001
Multifocal seizure	3 (3.1%)	5 (15.6%)	0.033
Generalized seizure	2 (2.1%)	2 (6.3%)	0.550
Hypsarrhythmia pattern	3 (3.1%)	5 (15.6%)	0.033
Normal	66 (68%)	-	-

Data are expressed as n (%). Statistical analysis was performed using the Chi-square test. p<0.05 was considered statistically significant. NF-1, neurofibromatosis type 1; TSC, tuberous sclerosis complex

Rare Syndromes

Two patients diagnosed with incontinentia pigmenti included one male and one female. The male patient first presented at the age of 1.1 years, and his current age was 4.1 years. He was admitted to the hospital due to a wound on his body. There was a history of parental consanguinity, but no similar disease history in the family. Skin findings showed hyperpigmented macules, and there were no ophthalmological findings. Echocardiography was normal. Cranial MRI revealed UBOs. There was no history of epilepsy. There were no accompanying neurodevelopmental or systemic diseases. The female patient presented at the age of 1 day, and her current age was 10.1 years. She was admitted to the hospital with a complaint of a wound on her leg. There was a history of parental consanguinity, but no similar disease history in the family. Skin findings showed hyperpigmented macules, and there were no ophthalmological findings. Echocardiography showed patent foramen ovale. Cranial MRI was normal. The patient with a history of epilepsy had focal seizures detected on EEG. Single anti-seizure medication was used for treatment. Hypothyroidism was present as a systemic disease.

The patient diagnosed with Sturge-Weber syndrome was male. His age at presentation was 8 months, and his current age was 2.1 years. He was referred from another center for further evaluation and treatment. There was no family history or parental consanguinity. Skin findings included a port-wine stain. There were no ophthalmological findings, and cranial MRI was normal. The patient had a history of epilepsy, with focal seizures detected on EEG. Treatment involved dual anti-seizure medication. Microcephaly was present as a systemic disease.

The patient diagnosed with epidermal nevus syndrome was male. His age at presentation was 5 days, and his current age was 11 years. The patient presented with a complaint of a lesion on the back, and the skin finding was a congenital giant nevus (Figure 3). Cranial MRI revealed UBOs. The patient had a history of epilepsy, with focal seizures detected on EEG. Treatment involved dual anti-seizure medication. The patient had intellectual disability, obesity, and a history of past meningitis.

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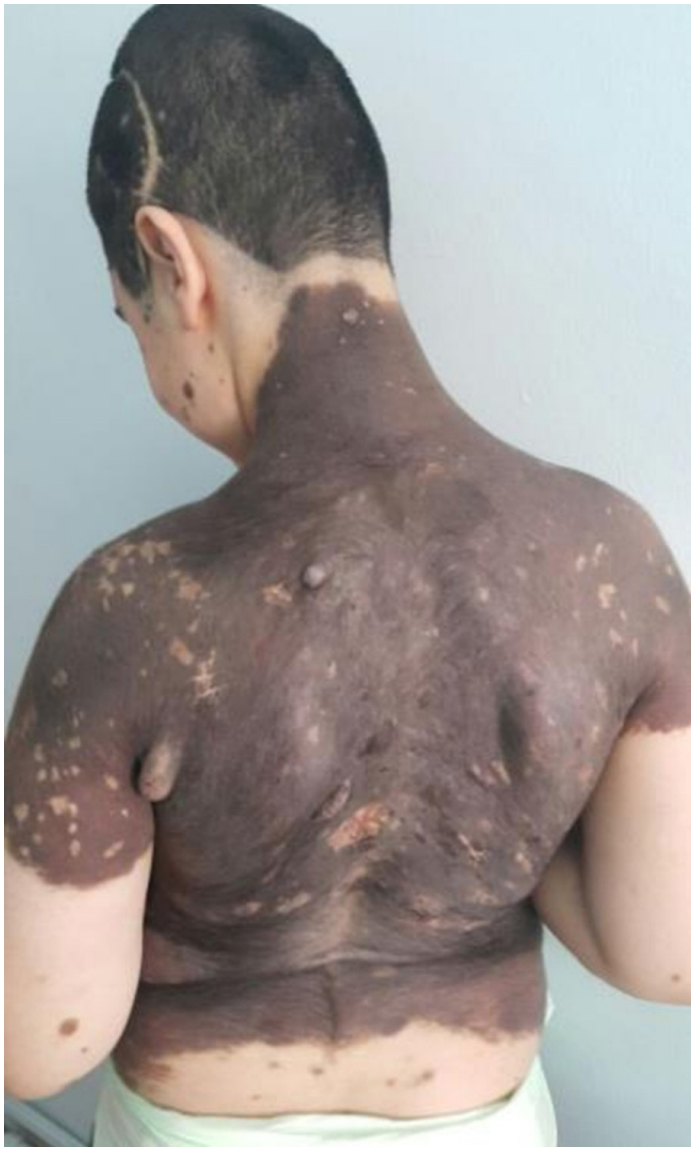

Figure 3. Giant epidermal nevus

Discussion

Neurocutaneous syndromes are a hereditary group of disorders characterized by developmental lesions in the skin, central nervous system, and peripheral nervous system, exhibiting various genetic, clinical, and pathological features. In this study, the largest group of our patients consisted of those with NF-1 (72.9%), followed by patients with TSC (24.1%).

In our cohort, the most common reason for initial presentation was characteristic skin lesions, followed by seizures and developmental delay. This aligns with literature indicating that cutaneous manifestations may precede neurological symptoms in many neurocutaneous disorders [8,5]. However, a subset of patients presented with nonspecific or incidental findings, underscoring the importance of clinical vigilance among pediatricians and dermatologists for early detection and timely referral.

In NF-1, which follows an autosomal dominant inheritance pattern, approximately 50% of patients have a family history of the disease, while the remaining 50% develop the condition due to new mutations in the gene [9]. In our study, we found that 68% of children with NF-1 had a family history of the disease. In another study, a family history of 63% was reported, close to our findings [10]. The literature indicates that NF-1 is more common in males [11]. In our findings, the male-to-female ratio among NF-1 patients was 50.5%, showing no significant numerical predominance of males. In another study, a male sex ratio of 50.5% was reported, similar to our findings [12].

In a study by McGaughran and his team involving a cohort of 523 patients, it was reported that cafe au lait macules were observed in 86.7% of the cases [13]. In healthy individuals, the frequency of macules can vary between 0.3% and 36%, depending on age, but the number never exceeds six [14]. In our cases, all patients had more than six cafe au lait macules, and there were no NF-1 patients who did not meet this criterion. One of the diagnostic criteria for NF-1, axillary freckling, usually appears in late childhood, around school age [15]. In our study, axillary freckling was present in 45.3% of patients with NF-1. In another study, axillary freckling was reported in 42.8% of cases, similar to our findings [10]. Cutaneous and subcutaneous neurofibromas are benign tumors, and their prevalence in NF-1 cases increases with age [3]. In a different study, the rate of neurofibromas in patients with NF-1 was reported to be 20.4% [16]. In another study, this rate was reported to be 23.8% [17]. In our study, we found a lower prevalence of neurofibromas (14.4%) in patients with NF-1 compared to the literature. We hypothesized that this could be related to the average age of our patients.

One of the diagnostic criteria for NF-1, the Lisch nodule, is usually not present at birth; however, its frequency increases with age [18]. In this study, we found a prevalence of 47.5% for Lisch nodules in children with NF-1, which is consistent with the literature. Another study reported a prevalence of 43% for Lisch nodules [10]. In another study, this prevalence was found to be 52.3% [17].

The literature reports a prevalence of 15-20% for optic gliomas in NF-1 [19]. We identified optic gliomas in 12% of our patients with NF-1. In another study, a similar prevalence of 13% for optic gliomas was reported [10]. Another study reported a higher prevalence of 22.9% [12].

Convulsions can occur during the course of NF-1. Unlike neurocutaneous disorders such as TSC and SWS, convulsions are less commonly observed in NF-1. A study reported an epilepsy rate of 9.5% [17]. Another study found this rate to be 4.8% [12]. In our study, we found convulsions in 16.5% of our patients with NF-1. Although this rate is somewhat high compared to the literature, it suggests that conducting electroencephalographic examinations even during asymptomatic periods could be important for increasing awareness of seizures.

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Although TSC is inherited in an autosomal dominant pattern, it is important to note that approximately 70% of cases arise from new mutations in the germline, rather than being inherited from the parents [20]. In the study we presented, we found a family history of TSC in 15.6% of cases. In a previous study, a family history of TSC was reported in 31% of cases [21]. In the study conducted by Rebelo et al. [12] a family history was found in 31.4% of cases.

Regarding clinical manifestations, hypomelanocytic macules were observed in all our patients. This manifestation occurs in about 90% of TSC patients and is present at birth or during early infancy [4]. Adenoma sebaceum, formerly known as facial angiofibroma, manifests as small hyperpigmented macules in a butterfly pattern on bilateral cheeks [22]. A study reported that adenoma sebaceum was observed in 40% of patients [23]. In our study, similarly, adenoma sebaceum was observed in 37.5% of patients.

In TSC, ophthalmologic findings include both retinal and non-retinal lesions. These lesions usually do not impair vision and do not require treatment. In a study examining the ophthalmologic findings of 100 patients with TSC, aged between 2 and 76 years, retinal hamartomas were detected in 44 patients [24]. In our study, retinal hamartomas were detected in 18.7% of our cases. We believe that the lower incidence of these lesions compared to the literature is likely related to their later onset.

TSC is characterized by cardiac findings, with rhabdomyomas being the typical heart lesions. These tumors are generally benign and appear as multiple lesions [25]. In this study, we found cardiac rhabdomyomas in 62.5% of patients diagnosed with TSC. In the study conducted by Rebelo et al. [12] reported that 48.6% of the patients had cardiac rhabdomyomas.

Renal complications arise from renal angiomyolipomas, which are benign tumors forming in the kidneys [5]. We detected renal angiomyolipomas in 34.4% of our patients. Rebelo et al. [12] reported in their study that renal angiomyolipomas were found in 51.4% of their patients. The smaller number of patients with renal angiomyolipomas, are probably related to a later age of appearance.

Study Limitations

The primary limitation of the present study is its retrospective design, which restricted the ability to obtain comprehensive data and perform uniform follow-up evaluations. In addition, standardized diagnostic and neurodevelopmental assessment tools, such as the Bayley Scales of Infant Development and the Wechsler Intelligence Scale for Children – Revised (WISC-R), were not applied to objectively evaluate developmental delay or intellectual disability. Furthermore, neuroimaging and genetic analyses could not be performed for all patients, resulting in incomplete characterization of certain cases. These factors may have led to an underestimation of the frequency or severity of some findings. Future prospective, multicenter studies with standardized diagnostic approaches are needed to validate and expand upon our results.

Conclusion

Neurocutaneous diseases comprise a varied and intricate collection of disorders whose clinical manifestations can differ widely and evolve throughout life, leading to significant morbidity. Early recognition of dermatological findings plays a critical role in the diagnosis of these disorders, as cutaneous clues often precede neurological or systemic involvement. In particular, careful dermatological examination by pediatricians and neurologists can facilitate timely diagnosis and appropriate referral.

Moreover, the relatively high frequency of seizures observed in patients with NF-1 highlights the potential benefit of performing EEG evaluations even in asymptomatic cases. Routine EEG screening may contribute to earlier identification of subclinical epileptiform activity, allowing for prompt treatment and improved neurological outcomes.

Taken together, our findings emphasize the need for a multidisciplinary approach involving pediatric neurology, dermatology, radiology, and genetics to ensure early detection, accurate diagnosis, and optimal management of children with neurocutaneous diseases.

Ethical Approval
Approved by the University of Health Sciences, Dr. Sami Ulus Maternity and Children's Health and Disease Training and Research Hospital (No: 73799008, Date: 16 June 2016).

Patient Consent
Written informed consent was obtained from the patients' parents or legal guardians for the use of clinical data and images.

Conflict of Interest
The authors declare no conflict of interest.

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