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INTRACRANIAL CALCIFICATION IN CHILDREN ON COMPUTED TOMOGRAPHY*

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SUMMARY: Erdem E, Ağıldere M, Eryılmaz M, Özdirim E. (Departments of Adult Neurology, Pediatrics and Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey). Intracranial calcification in children on computed tomography. Turk J Pediatr 1994; 36: 111-122.

Pathological intracranial calcifications detected on computed tomography of 83 children during a six-year period were reviewed. The common causes in our series were tuberous sclerosis and intracranial tumors. Other conditions associated with calcification were Sturge-Weber syndrome, neurofibromatosis, Cockayne's syndrome, hypoparathyroidism, arteriovenous malformations, vein of Galen aneurysm, encephalomalacia, cerebral infarcts, subdural hematoma, cerebral infections, birth asphyxia and dihydropteridine reductase deficiency. In two cases (2%), calcifications were idiopathic. The distribution and location of the calcifications in these conditions are discussed. *Key words: Intracranial calcification, computed tomography.*

Computed tomography (CT) detects intracranial calcification more sensitively than do plain X-rays[1]. Intracranial calcification may be of diagnostic importance or may guide etiological study; however, it may also be an incidental finding[1-3].

Studies of the diagnoses of children with intracranial calcifications in the hospital setting are rare[3]. In this investigation, intracranial calcifications on the CTs of 83 patients in the pediatric age-group from the years 1985 to 1990 were studied retrospectively.

Material and Methods

The patients' ages ranged from 2.5 months to 17 years. All CT studies were done with third generation CT scanners. Only the pathological intracranial calcifications on CT were studied. The calcifications were assessed in regard to their appearance as described by Holland et al[4] and their locations.

The calcifications were divided into five categories based on CT appearance:

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linear, punctate, homogeneous fine, homogeneous dense-partial, and homogeneous dense-total. Deposits of calcium large enough to be individually identified but less than 2 mm in diameter were designated as punctate. Homogeneous fine calcification was defined as many minute calcifications resulting in a stippled increase in density with no single deposit large enough to be seen individually. The category of "homogeneous dense, partial" was defined as any calcification larger than 2 mm but forming a component of the lesion; the category "homogeneous dense, total" was defined as any calcification encompassing the entire lesion.

Laboratory tests were selected depending on the clinical features of the patients. Serum calcium, phosphorus and alkaline phosphatase activity were determined in all cases of basal ganglia calcification. In an epileptic patient with depigmented nevi and adenoma sebaceum, a diagnosis of tuberous sclerosis was made, and subependymal calcifications seen on CT were supportive.

Results

In nine patients, there were basal ganglia calcifications; in 64 patients, calcifications, were in other parts of the brain. In eight, calcifications were both on basal ganglia and in other parts. The results are summarized in Table I.

In all cases of intracranial tumors (Case 26-41), histopathological study was performed. In Cases 42-45, a solitary mass was visualized, but neither biopsy nor autopsy could be done because either the patient succumbed before surgery or the family did not permit the operation or the autopsy. CT was the first-performed diagnostic investigation when neurological symptoms developed acutely or subacutely (usually in cases of intracranial tumor or cerebrovascular disease). However, CT findings in tuberous sclerosis were particularly invaluable when cutaneous features were absent; in that case, biochemical studies were performed. In five cases of mental and motor retardation (Cases 72-76), despite extensive investigation no definite cause of the retardation could be demonstrated. Laboratory studies including muscle biopsy were not fruitful in Case 77, a 17-year-old female with cerebellar syndrome. Case 80 presented with secondarily generalized partial seizures, and the CT features suggested a previous hematoma. As no previous history of neurological dysfunction was obtained, the CT abnormality may have been related to an intrauterine hemorrhage. Case 81 was a patient with epilepsy whose developmental and neurological examination were normal, and no cause could be found for the epilepsy. In two cases (Case 82, 83), calcifications were incidental. CT was requested in Case 82 because of convulsions and in Case 83 because of premature thelarche. In both, basal ganglia calcification was found.

Table I: CT Findings of the Patients

CASE	DIAG	CALCIFICATION		OTHER CT FINDINGS
		basal ganglia	other	
1-22	TS	unilateral dense total in caudate nucleus in 2 cases	subependymal dense total in 6 cases; periventricular dense total in 21 cases; dense total in other sites in 12 cases	hypodensities in various sites in 12 cases
23-24	Sturge-Weber syndrome		left F dense partial; bilateral F dense total; bilateral P dense total; O dense total	left F and P serpiginous enhancement; bilateral O enhancement in the other case
25	neurofibromatosis		right O dense total, left T dense total, right cerebellar dense total	left O, right F homogeneous enhancement, left F and right O craniotomy defects
26-41	brain tumors 3 astrocytomas; 1 astrocytoma associated with tuberous sclerosis; 1 glioma; 1 mixed glioma; 1 glioblastoma, multiforme; 1 meningioma; 1 medulloblastoma; 2 craniopharyngiomas; 1 chordoma; 1 dermoid tumor; 1 malign teratoma; 1 pinealoblastoma; 1 malign primitive ectodermal tumor		focal in 2 and dense partial in 1 of 3 astrocytomas; periventricular dense total and dense partial in 1 astrocytoma associated with tuberous sclerosis; dense total in 1 glioma and 1 mixed glioma; linear in 1 meningioma; dense partial in 1 glioma multiforme, 1 medulloblastoma, 2 craniopharyngiomas, 1 chordoma, 1 dermoid tumor, 1 malign teratoma, 1 pinealoblastoma, 1 malign primitive ectodermal tumor	masses with other features of a brain tumour, usually suggestive of the diagnosis
42-45	solitary masses		dense partial	masses of which 3 enhances after contrast injection and 1 is cystic
46	Cockayne's syndrome	bilateral focal in putamen, globus pallidus and caudate nucleus		cerebral atrophy
47	hypoparathyroidism	bilateral dense total in putamen, globus pallidus and caudate nucleus	multiple dense total in bilateral centrum semiovale	
48-50	AVM		right O dense partial; dense partial in mesencephalon; dense partial intraventricular in both cases posterior midline (linear and dense partial)	O, mesencephalic, thalamic AVMs, in 1 triventricular hydrocephalus exists posteriorly extending enhancement between the lateral ventricles in 1 case
51-52	vein of Galen aneurysm			
53-54	encephalomalacia		right OP dense total; right P dense total, right F dense total, right O dense partial	right O encephalomalacia in both cases, cerebral atrophy in 1 case
55	cerebral infarct		left TP dense partial	left TP old infarct
56	sickle-cell anemia old cerebral infarcts		dense total in right sulcus precentralis	right OP infarct, lacunar infarct in right centrum semiovale, cerebral atrophy

CASE	DIAG	CALCIFICATION basal ganglia	CALCIFICATION other	OTHER CT FINDINGS (continued)
57	subdural hematoma		F-P-O linear	left F-P-O subdural effusion
58	tuberculoma		dense partial	mass with annular enhancement extending from right thalamus to TO region
59-68	TORCH	bilateral dense total in globus pallidus in 2 cases, in putamen in 4 cases, in caudate nucleus in 2 cases, bilateral focal in caudate nucleus in 1 case, unilateral dense total in caudate nucleus in 1 case	dense total P; focal, dense total in capsula interna; focal, dense total periventricular; subcortical dense total; subependymal dense total; O dense total; FP dense total; cerebellar dense total; multiple intracerebral focal, dense total; dense total in bilateral centrum semiovale	cortical atrophy in 3, subcortical atrophy in 1 cases, cavum septum pellucidi et Vergae in 3 cases
69-71	birth asphyxia	bilateral focal in putamen in 1 case	periventricular dense total in 1 case; bilateral partial in thalamus in 1 case	cortical and subcortical atrophy in 1 case
72-76	MMR	bilateral focal in putamen in 2, unilateral dense partial in putamen in 1, in caudate nucleus in 1 case	subependymal, linear around the ventricles in 1; F partial and O partial in 1 case	cortical atrophy in 2; subcortical atrophy in 1 case; megacisterna magna in 1 case
77	cerebellar syndrome	bilateral focal in putamen in 1 case		
78-79	DHPR deficiency	in both cases bilateral dense total in putamen, globus pallidus and caudate nucleus	bilateral P-O dense total in both cases	cortical and subcortical atrophy in both cases
80-81	epilepsy		left F partial obliterating the lateral ventricle in 1 case; focal in bilateral basal ganglia, capsula interna, left P and F white matter in the other	left F hypodense area in 1; prominent left Sylvian fissure in the other case
82-83	idiopathic	bilateral focal in globus pallidus, bilateral dense total and bilateral focal in putamen in the other case		

ABBREVIATIONS:

AVM: arteriovenous malformation DIAG: diagnosis
DHPR: dihydropteridine reductase F: frontal
MMR: mental and motor retardation O: occipital
P: parietal T: temporal TS: tuberous sclerosis

Discussion

Intracranial calcification is detected more sensitively by CT than by plain X-rays[1]. There is only one study on the incidence of the pathological calcification in children; the incidence was found to be 1.6 percent in 18,000 patients[3]. Intracranial calcification can be of diagnostic importance and can guide etiological study[1-3]. However, it may be an incidental finding, without any relation to a disease process[1-3]. Pathological intracranial calcifications have been described in a great number of diseases. Harwood-Nash et al[2] classified these in groups of "developmental, inflammatory, neoplastic, vascular, endocrine, and toxic" diseases. After the advent of CT, pathological calcification in some other diseases was described with CT demonstration (Table II).

Table II: Classification of Pathological Intracranial Calcifications in Infants and Children[2,15,16,23-31].

Developmental abnormalities, inherited diseases	
Tuberous sclerosis	Lipoid Proteinosis
Sturge-Weber syndrome	Basal cell nevus syndrome
Neurofibromatosis	Lissencephaly
Cockayne's syndrome	Wilson's disease
Fahr syndrome	Kearns-Sayre syndrome[24]*
MELAS syndrome[25]*	Adrenoleukodystrophy[26,3]*
Krabbe's disease[27]*	Infantile neuroaxonal dystrophy[3]*
Down syndrome[28]*	
Dihydropteridine reductase deficiency[3,23]*	
Osteopetrosis, associated with type-II carbonic anhydrase deficiency[29]*	
Inflammatory	
Systemic lupus erythematosis	
Infectious diseases	
Cytomegalic inclusion disease	
Herpes Simplex	
Congenital rubella	
AIDS[30]*	
Congenital toxoplasmosis	
Bacterial infections	
Pyogenic meningitis	
Tuberculous meningitis	
Tuberculoma	
Other parasitic infections	
Cysticercosis	Trichinosis
Paragonimiasis	Coccidioidomycosis
Echinococcosis	
Neoplastic	
Craniopharyngioma	Medulloblastoma
Teratoma	Corpus Callosum Lipoma
Dermoid tumors	Secondary retinoblastoma
Astrocytoma	Pituitary adenoma
Ependymoma	Chordoma
Oligodendroglioma	Meningeal leukemia
Meningioma	Meningeal neuroblastoma
Choroid plexus neoplasm	Undifferentiated neuroectodermal tumors
Acute lymphocytic leukemia[31]*	
Postradiation calcification	

Table II:

Vascular	
Subdural hematoma	Aneurysm
Extradural hematoma	Vascular hamartoma
Intracranial hematoma	Anoxia
Arteriovenous malformation	Vessel wall
Vein of Galen aneurysm	Therapeutic radiation
Cerebral infarcts[15-16]*	
Endocrine	
Hyperparathyroidism	
Hypoparathyroidism	
Pseudohypoparathyroidism	
Pseudopseudohypoparathyroidism	
Toxic	
Carbon monoxide poisoning	
Lead poisoning	
Vitamin D intoxication	
Hypercalcemia	
Intrathecal methotrexate	

*: described after the advent of CT, with CT demonstration

Tuberous sclerosis was the most common disease in our series. The distribution of calcifications in tuberous sclerosis includes periventricular and subependymal[5]; besides the calcifications, hypodensities representing demyelination or cortical and subcortical tubers may be seen (Fig. 1)[6-7]. The subependymal calcifications are characteristic of tuberous sclerosis and constitute an important diagnostic aid in cases without any positive finding on physical and neurological examination. In Sturge-Weber syndrome (Fig. 2) contrast enhancement resulting from the

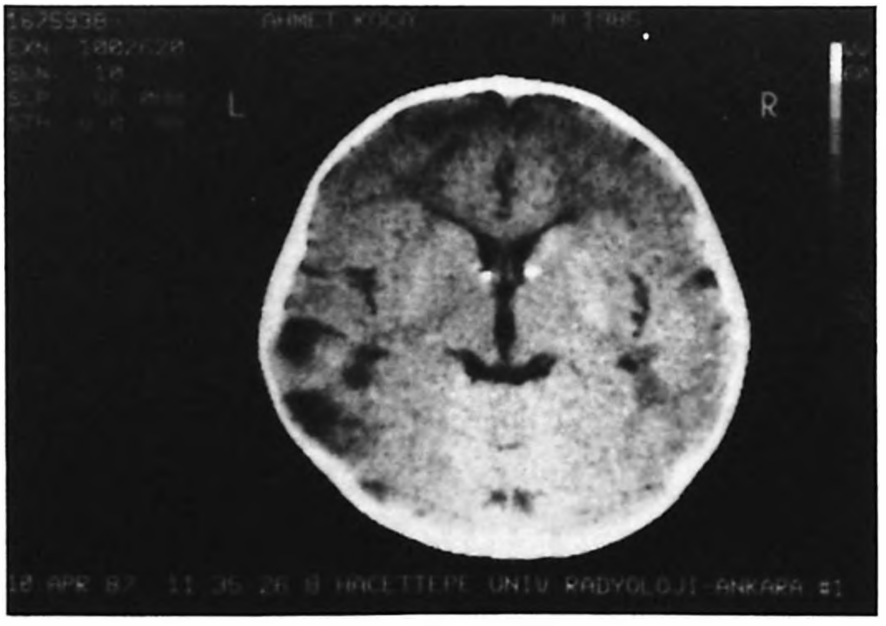

Fig. 1: Tuberous sclerosis, 2-year-old male infant (Case 11). There are subependymal calcifications and left temporal hypodensities representing the tubers.

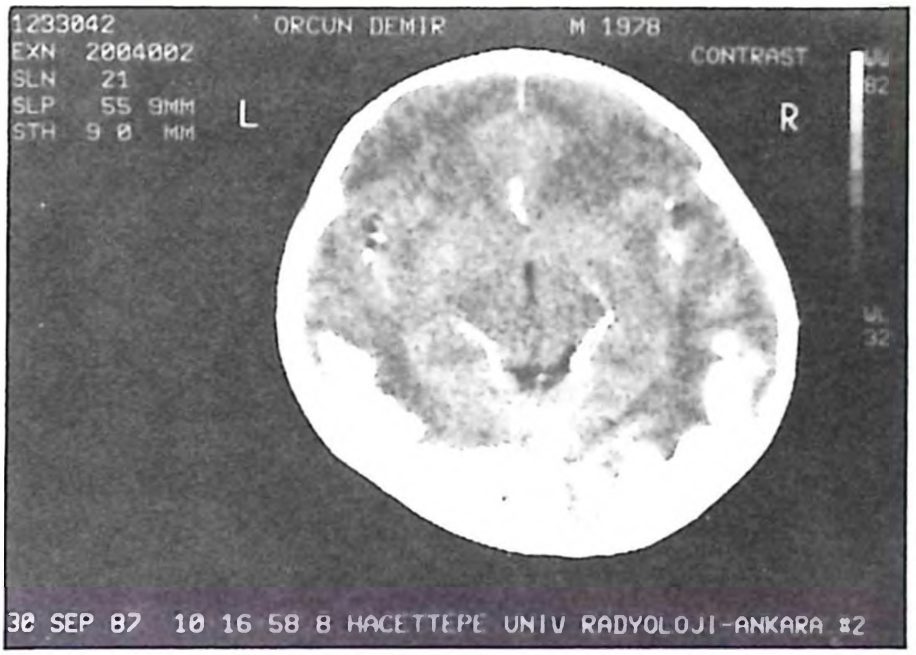

Fig. 2: Sturge-Weber syndrome. 9-year-old boy (Case 24). Bilateral occipitoparietal calcification. Contrast enhancement does not extend beyond the calcified areas.

angiomatosis extends beyond the calcified field[8]. There may be subependymal calcifications thought to be related to glial tissue proliferations in neurofibromatosis besides the acoustic (and less frequently other cranial nerve) neurinomas[9]. Calcification in intracranial tumors is well documented. The appearance of the calcification and the location within the tumor are highly suggestive, being an important feature for differential diagnosis (Fig. 3)[10-11].

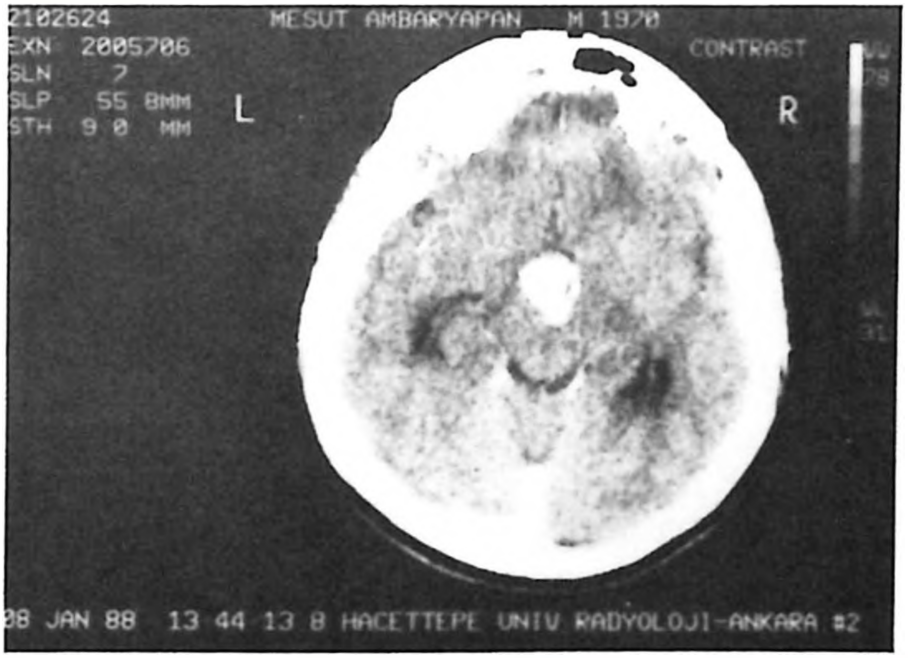

Fig. 3: Craniopharyngioma. 17-year-old boy (Case 35). Calcified mass with posterior enhancement in the location of the supracellar cistern.

In hypoparathyroidism, there may be extensive calcifications involving the cerebral gray and white matter and the dentate nucleus (Fig. 4)[12].

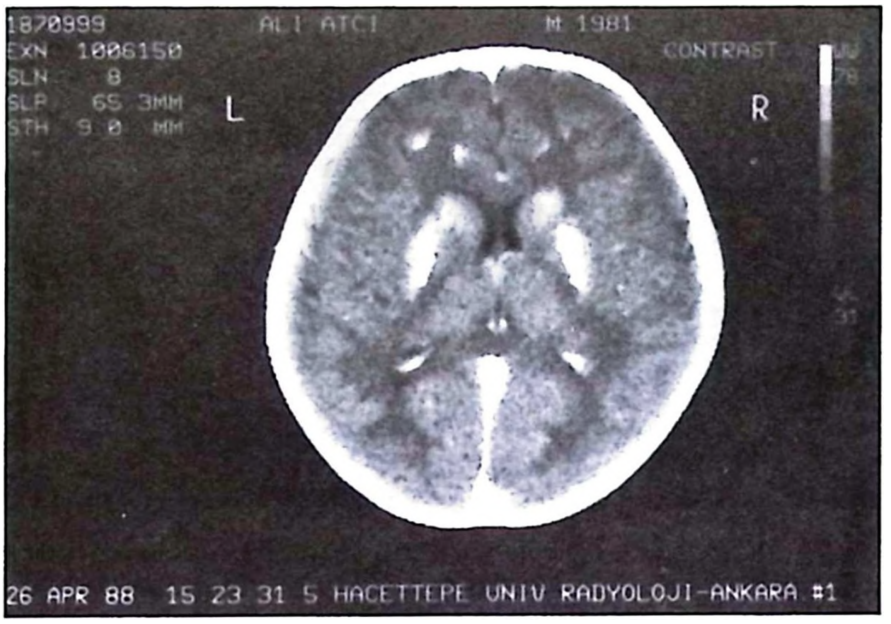

Fig. 4: Hypoparathyroidism. 7-year-old boy (Case 47). Calcifications are seen in the basal ganglia and left frontal white matter.

Calcifications may be seen within the globus pallidus, putamen and cerebellum in Cockayne's syndrome. In the only case in our series, bilateral calcification occurred at these sites[13].

Calcifications scattered in the cerebral white and gray matter may be found in vein of Galen aneurysms and are attributed to the secondary hypoxic effect of the aneurysm[14].

Calcifications may develop several months after cerebral infarcts[15-16]. Small infarcts may develop during the neonatal or infancy period; when they are clouded by other clinical symptoms or are in the clinically silent areas of the brain, they may remain undetected for years. When radiologic verification is absent at the time of the infarct development, the detected hypodensities may be related to previous hematomas or infections besides the infarction. Encephalomalacia is the appropriate term for cases with hypodensities on CT in which there is significant loss of brain tissue[17]. The cases with encephalomalacia in our series were not investigated with CT at the onset of symptoms, and the large tissue loss which appeared on CT in two cases (Case 53 and 54) may be ascribed to previous infarctions, considering the clinical and CT features of the cases.

Subdural hematomas may calcify months later. The calcification is usually peripheral[18].

Calcification of the meninges at the base of the brain was demonstrated in 48 percent of the patients, 18 months to three years after tuberculous meningitis[19].

In tuberculomas, calcifications may be seen as a target sign of central calcified nidus surrounded by a ring of enhancement. The calcification of the case in our series was an example of tuberculomas.

In TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes) infections, calcifications are usually periventricular, but they may be scattered in the basal ganglia and in other parts of the brain (Fig. 5)[20-22]. Other CT findings, hydrocephalus, cortical and subcortical atrophy are usually present, and clinical findings aid in making the diagnosis. As cytomegalovirus and herpes infections are rather prevalent in the population, serological tests are only helpful if used in the acute stages of the infections. Calcifications are seen not only in the congenital form, but also after the infections in later years.

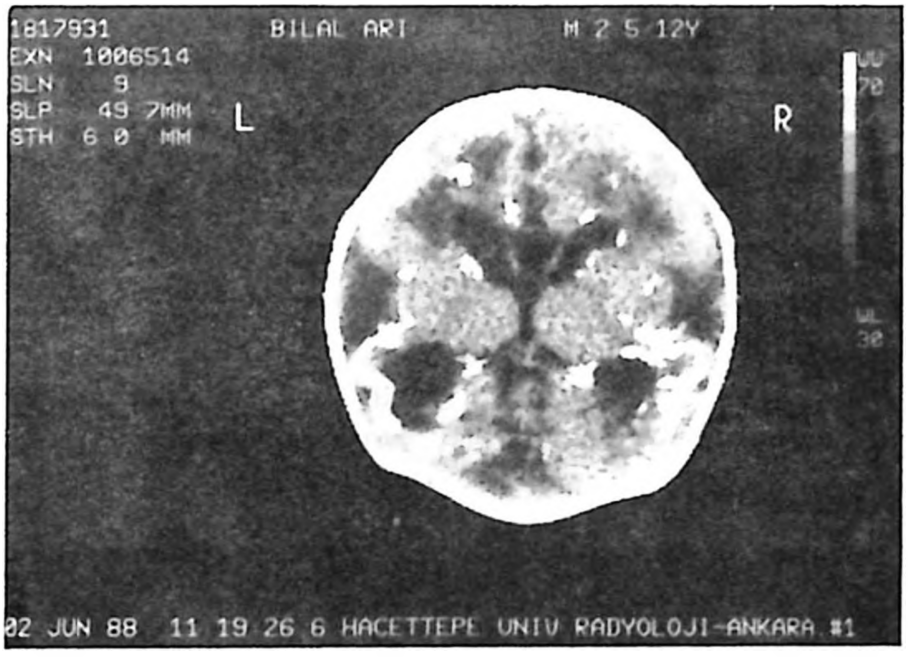

Fig. 5: Congenital toxoplasmosis. 2.5-month-old male infant (Case 68). Calcifications are scattered throughout the brain.

Calcifications associated with birth asphyxia are usually seen in the basal ganglia or in the thalamus[3].

In dihydropteridine reductase (DHPR) deficiency, calcifications have been demonstrated in the basal ganglia and deep hemispheric white matter. Kendall et al[3] emphasized the linkage between the metabolisms of pterins and folate as well as the development of intracranial calcifications following the use of methotrexate, a folic acid antagonist. We observed calcifications in the basal ganglia and in the corticomedullary junction in two cases with DHPR deficiency (Fig. 6). These two cases were previously reported by Coşkun et al[23].

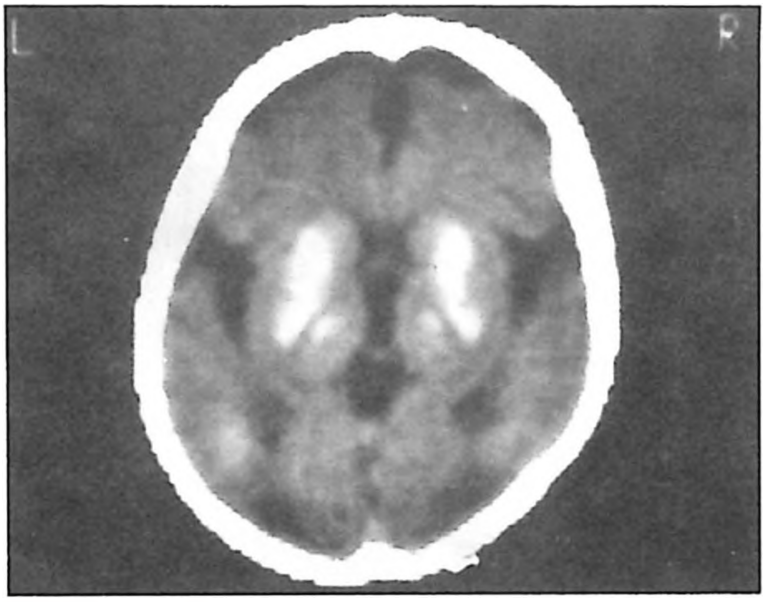

Fig. 6: Dihydropteridine reductase deficiency. 5-year-old girl (Case 79). Bilateral basal ganglia calcification and left occipital calcification in the corticomedullary junction.

In five cases with mental and motor retardation, no cause could be found despite extensive etiological investigation (Fig. 7). In Case 77, clinical (cerebellar syndrome) and CT features were suggestive of mitochondrial myopathy, but biochemical studies and muscle biopsy were not positive.

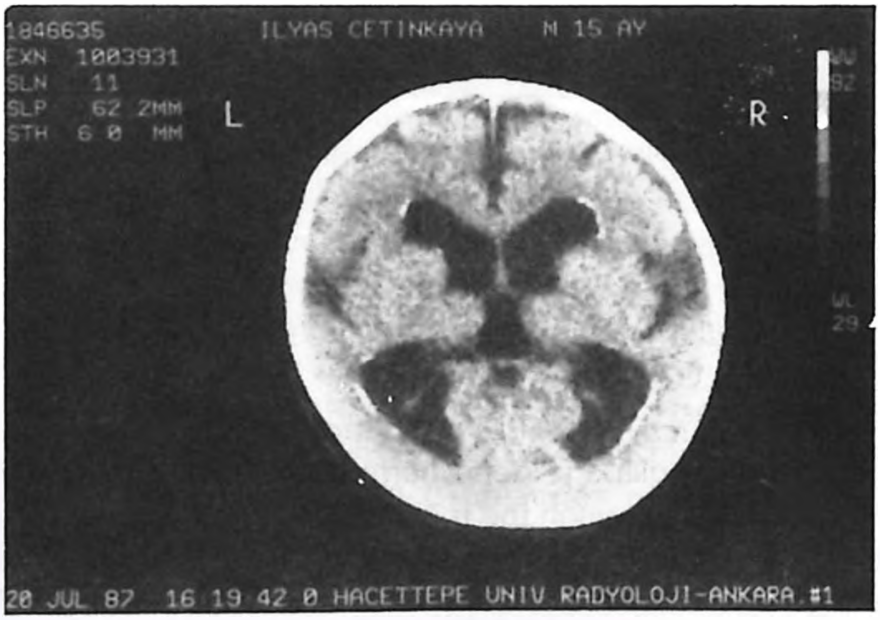

Fig. 7: Case of mental and motor retardation. No definite cause could be identified. 15-month-old male infant (Case 75). Frontal and occipital periventricular linear calcifications.

In two Cases (Cases 82, 83), CT scans were done because the first had a seizure and the second had premature thelarche. In both cases, basal ganglia calcifications were found. The basal ganglia calcifications in these cases did not have any relation with the clinical symptomatology, and we believe that they were idiopathic.

Intracranial calcification on CT offers an important aid in differential diagnosis. However, the calcification may also be an incidental finding without any relation to a disease process.

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